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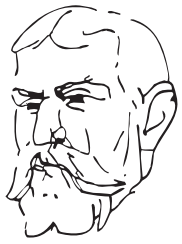

Memory of
dr Władysław
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ANALYSIS OF THE LEGISLATIVE ACTIVITY OF THE MINISTRY OF HEALTH OF UKRAINE IN THE CONDITIONS OF THE RUSSIAN-UKRAINIAN WAR IN 2022

DOI: 10.36740/WLek202206101

Viacheslav M. Zhdan, Iryna A. Holovanova, Maksym V. Khorosh, Inna V. Bielikova, Natalia A. Lyakhova
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To analize the legislative activity of MOH of Ukraine in wartime.

Materials and methods: Were conducted a study of the orders for the first 30 days of the Russian military invasion by the method of content analysis. Using the method of deduction, the all orders was divided into areas of their influence.

Conclusions: Twenty-nine orders were found during the first month of the war, which regulated the issues of medical care, circulation of drugs, blood transfusions, drugs, medical records, etc. Particular attention is paid to the organization of affordable medical care for all segments of the population, including the involvement of interns, senior students of medical institutions of higher education, as well as foreign professionals.

The analysis of the legislative activity of the Ministry of Health of Ukraine to optimize the functioning of the medical care system for both military and civilian population in the context of Russian military aggression showed the Ministry's prompt response to time and high activity in the first two weeks of the war.

KEY WORDS: war, Ukraine, medical care, legislation, organization and management

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INTRODUCTION

The Russian invasion of Ukraine is an open military attack by Russia with the support of Belarus, which began at 3:40 on February 24, 2022 [1]. The armed conflict involved the emergence of conditions such as injuries and violent killings with weapons. Already the first day of the war confirmed these expectations, and on February 24, more than 40 Ukrainian soldiers and 18 civilians were killed. According to the Ministry of Health of Ukraine, a total of 57 people were killed and 169 wounded in the first days of the war [2].

Wartime conditions create tensions for all processes in the country, and this is especially true for the organization of medical care for both servicemen directly involved in hostilities and civilians affected by the actions of the aggressor country. Along with this, it is extremely important to ensure the proper functioning of the health care system, for the planned needs of medical care, rehabilitation, medical and social examination, preparation of medical and accounting documents, etc.

To ensure this goal, it is extremely important to create a new and optimize the existing regulatory framework for the functioning of the medical sector, and in this regard the most important role belongs to the Ministry of Health, on the actions of which the successful resolution of these issues is depends.

THE AIM

The aim of the study was to establish the character of the response of the health care system on the invasion of the Russian Federation and to examine the completeness of the regulatory framework of the main health care processes in Ukraine in terms of wartime.

MATERIALS AND METHODS

In order to achieve our aim, we conducted a study of the orders of the Ministry of Health of Ukraine for the first 30 days of the Russian military invasion of Ukraine by the method of content analysis: of all orders, only those that related to the organization of health care in wartime were selected. To analyze the background processes in the country (dynamics of the number of wounded and dead, the issue of internally displaced persons), which took place during the issuance of orders the official information resources were analyzed - the media, the website of the Government Contact Center, the website of the International Organization for Migration. Using the method of deduction, the conglomerate of relevant orders was divided into areas of their influence: the organization of medical care; outpatient medical care; regulation of demographic phenomena; regulation of blood products, narcotic and psychotropic drugs; issues related to mobilization; regulation of drug

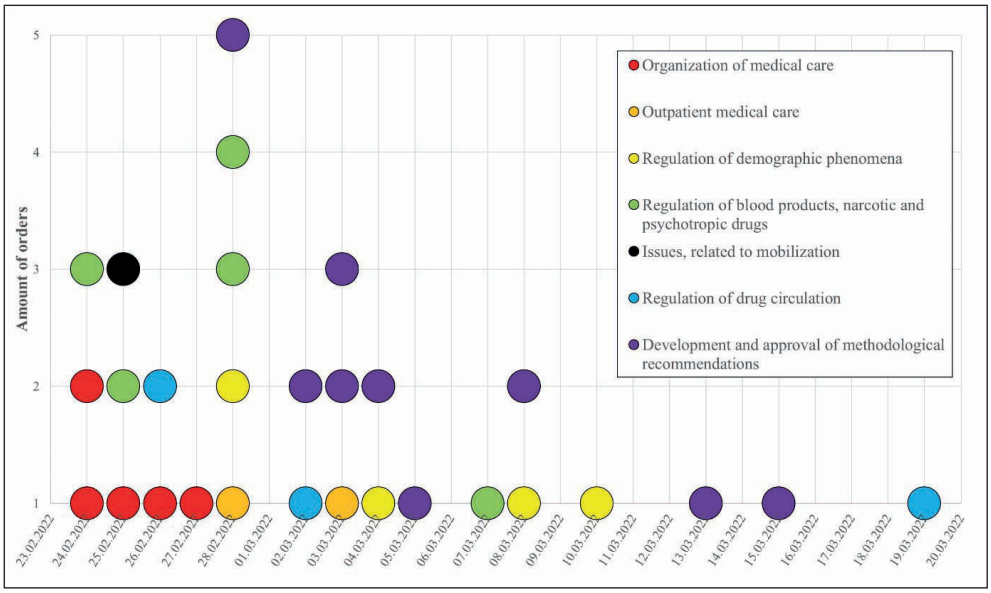

Fig.1. Frequency analysis of issuing of orders by the Ministry of Health of Ukraine during the first month of Russian-Ukrainian war, 2022

circulation; development and approval of methodological recommendations. The last step of the study was to conduct a frequency analysis of the issued orders.

REVIEW

Selected orders that met the purpose of the article were distributed according to the field of health care they regulate (Table I).

ORGANIZATION OF MEDICAL CARE

Challenges to the organization of health care are changing - prerogatives are shifting from routine, planned care to the standards of disaster medicine, when a large number of victims is expected and at the same time there is a shortage of resources and medical forces. Therefore, the Ministry of Health on the first day of the war generates an order that allows to establish the priority of medical care. This standard of emergency medical care "Medical sorting for mass admission of victims in the early hospital stage" allows you to create an effective algorithm for medical sorting of victims who come to the emergency department, which will quickly determine the severity of their condition and division into related sorting groups.

The algorithm includes the main clinical elements: the state of consciousness, respiratory and cardiovascular systems, the presence and frequency of respiration, the state of perfusion - consistent and comprehensive analysis of which would quickly and accurately determine the severity of the victims and their distribution into sorting groups, which ensures the adoption of the most accurate clinical decisions on the scope of medical care (to the extent possible in the conditions of available forces and means) and further correct determination of the patient's route to health care facilities [3].

Shifting the emphasis on the benefits of providing medical care to the wounded and injured as a result of hostilities has led to legislative optimization and the Order of the Ministry of Health of Ukraine №374 of 24.02.2022 made a number of adjustments, resulting in temporary measures: temporary suspension of planned hospitalizations of patients; conducting medical and social examination in a simplified procedure and in absentia; prepare additional surgical teams to help victims; take measures to increase the provision of medical care with the use of telemedicine. At the same time, this order emphasized that urgent hospitalizations and hospitalizations, that cannot be transferred and related to: provision of medical care due to the complicated course of pregnancy and childbirth are not subject to termination; providing medical care to pregnant women, parturient, newborns; providing medical care to patients with cancer; providing palliative care in an inpatient setting; other urgent hospitalization and planned operations, when their transfer poses a serious risk to life and health stay without changes [4].

Regulatory changes were implemented to ensure the work organization of all health care facilities under management to ensure the uninterrupted provision of medical care to all victims and wounded around the clock; ensuring the hospitalization of the injured and wounded in the nearest health care facilities that are able to provide care in accordance with the profile of the lesion; suspension of planned secondary and tertiary assistance to the Armed Forces till the situation in the country became stabilize [5].

For the same purpose doctors-interns, junior specialists with medical education, as well as doctors-specialists without requirements for certification for assignment or confirmation of qualification category are involved for the period of martial law in Ukraine. However, it is noted that these categories are involved in the presence of the need that has arisen in the relevant administrative-territorial units in connection with hostilities, and also emphasizes that it is recommended to involve interns who are currently undergoing practical training in internships. In addition, on a voluntary basis, applicants for 4-6 years of study in

Table I. Orders issued by the Ministry of Health during the first month of the war

Scope of the order	Order	Date
Organization of medical care	№368. «About the statement of the Standard of emergency medical care «Medical sorting at mass receipt of victims at an early hospital stage.»	24.02.2022
	№374. «About approval of Temporary measures in health care institutions for the purpose of ensuring their readiness for rendering of medical aid to victims of military aggression of the Russian Federation against Ukraine.»	24.02.2022
	№ 379. «On the provision of medical care in martial law to servicemen participating in a joint force operation.»	25.02.2022
	№ 383. «On the involvement of foreign medical workers to provide assistance to victims of martial law.»	26.02.2022
	№ 385. «On the involvement of interns and some other persons in the implementation of measures related to the provision of medical care to persons affected by the emergency situation that arose during the martial law in Ukraine.»	27.02.2022
Outpatient medical care	№ 388. «To ensure the functioning of the health care sector.»	28.02.2022
	№ 404. «About providing patients with medicines in inpatient health care facilities.»	03.03.2022
Regulation of demographic phenomena	№ 390. «Some questions of establishing the fact of death.»	28.02.2022
	№ 407. «About ensuring registration of the newborn child in the conditions of martial law.»	04.03.2022
	№ 428. «On approval of the Procedure for equipping special groups during the collection of bodies with materials and equipment.»	08.03.2022
	№ 458. «About approval of the Minimum requirements for ensuring sanitary and epidemic well-being of the population during emergency arrangement of places of temporary stay of the persons who are compelled to leave places of permanent residence in connection with military aggression of the Russian Federation.»	10.03.2022
Regulation of blood products, narcotic and psychotropic drugs	№ 377. «On meeting of the needs of donated blood and blood components in martial law.»	24.02.2022
	№ 382. «On the establishment of a special regime in the field of production and sale of drugs containing narcotic drugs, psychotropic substances and precursors, other potent substances.»	25.02.2022
	№ 386. « On the establishment of the operational headquarters of the Ministry of Health to coordinate activities in the field of blood donation and blood components, the functioning of the blood system in martial law»	28.02.2022
	№ 387. «On amendments to the order of the Ministry of Health of Ukraine of February 24, 2022 № 377.»	28.02.2022
	№ 425. «About storage of drugs, psychotropic substances and precursors in martial law.»	07.03.2022
Issues, related to mobilization	№ 381. «About bringing the functional subsystem of medical protection in readiness for performance of tasks on purpose in the special period.»	25.02.2022
Regulation of drug circulation	№ 384. «Some issues of emergency state registration of medicines during martial law.»	26.02.2022
	№ 394. «About a ban on use in the territory of Ukraine of separate medicines.»	02.03.2022
	№ 503. «About a ban on use in the territory of Ukraine of medicines, originating from the Republic of Belarus.»	19.03.2022
Development and approval of methodological recommendation	№ 389. «On approval of Methodical recommendations concerning primary surgical treatment of gunshot wounds.»	28.02.2022
	№ 391. « On approval of Methodological recommendations on the phased provision of medical care to the wounded and injured.»	02.03.2022
	№ 402. «On approval of Methodical recommendations concerning medical care to victims with burns at stages of evacuation «	03.03.2022
	№ 405. «On approval of Methodical recommendations for the provision of first aid and prevention of post-traumatic stress disorder.»	03.03.2022
	№ 412. «On approval of Methodical recommendations concerning conversion of a turnstile at the injured in zones of tactical emergency medical care.»	04.03.2022
	№ 418. «On approval of Methodical recommendations concerning application of the protocol of mass transfusion of components of blood to victims at evacuation stages.»	05.03.2022
	№ 431. «On approval of Methodical recommendations concerning tactics of surgery of control of damages and stabilization of a condition of victims at evacuation stages.»	08.03.2022
	№ 478. «On approval of Methodical recommendations concerning the organization of rendering of emergency medical care to victims as a result of action of chemical agents at stages of evacuation.»	13.03.2022
	№ 488. «On approval of Methodical recommendations concerning rendering of emergency medical care to victims at a pre-hospital stage in the conditions of military operations / martial law.»	15.03.2022

the field of knowledge 22 "Health care" can be involved in providing assistance to victims entering health care facilities [6].

The requirements of wartime in the context of full-scale aggression of the Russian Federation in Ukraine require maximum efficiency in providing medical care, so the order of the Ministry of Health was adopted, which allows voluntary admission to victims by foreigners and stateless persons who staying in Ukraine legally, provided that they have documents confirming the relevant education and professional qualifications [7].

OUTPATIENT MEDICAL CARE

The reduction in planned hospitalization has affected the outpatient medical service, which is to take over the lion's share of medical care. Given the fact that some cities in Ukraine are occupied and some accept large numbers of migrants, there is an urgent need to provide medicines to patients who are discharged from hospitals. An order was introduced, according to which the heads of structural units for health care of regional military administrations to form stocks of medicines for the organization of outpatient treatment of patients discharged from the hospital - should be free of charge.

It is also necessary to ensure the possibility of free distribution of medicines to patients who have sought outpatient care in primary or secondary health care facilities (subject to the availability of appropriate medicines) [8].

Prior to the war, some drugs, registered in Ukraine, were subject to reimbursement according the medical guarantee program. The dispensing of such medicinal products was carried out on the basis of prescriptions issued in accordance with the rules for prescribing medicinal products and medical devices [9] through the electronic health care system [10]. In the absence of the possibility of issuing electronic prescriptions for drugs to be reimbursed, primary care physicians obtain the right to prescribe paper prescriptions for such drugs. Electronic referrals for examination or treatment, medical records in the electronic health care system are also allowed to be made on paper forms of primary accounting records, and health professionals enter these medical records in the Register after obtaining of technical capacity [11].

REGULATION OF DEMOGRAPHIC PHENOMENA

There is 36,425 children have been born in Ukraine since the beginning of the full-scale war. The largest number of them was born in Lviv region - 3640 children [12]. This number can be explained by the fact that this region has the largest number of migrants, reaching almost 290 thousand people. At the same time, on March 9, in Mariupol, the occupiers shelled a maternity hospital and a children's hospital: three people were killed, including a one child, and 17 people were injured.

Anticipating such consequences of the war, the Ministry of Health of Ukraine adopts Order № 388 of 28.02.2022 "On ensuring the functioning of the health care sector" which simplifies the registration of births: in the absence of technical feasibility of forming of medical certificates about birth, in accordance with the Procedure for maintaining the register of medical opinions in the electronic health care system, the record is not made, and filling in and issuing a paper medical birth certificate (form № 103/o). If it is not possible to fill in a medical birth certificate, the medical worker is obliged to issue a certificate of any form for each case of birth of a living child [11, 13].

During the period since the beginning of hostilities in Ukraine, 2,665 civilians were killed [14]. The death registration procedure required temporary changes in these circumstances, which were introduced in the issue of registration of deaths. According to these changes, health care facilities are allowed in case of inability to comply with the joint order of the Ministry of Health of Ukraine, the Ministry of Internal Affairs of Ukraine and the Prosecutor General's Office of Ukraine of September 29, 2017 № 807/1193/279 "On approval of the Procedure for interaction bodies and subdivisions of the National Police, health care institutions and prosecutor's offices of Ukraine in establishing the fact of death" [15], to issue a permit for burial of bodies, subject to mandatory examination of the corpse at the place of his discovery and drawing up an appropriate protocol and conducting photo-recording of injuries in case of presence (in case of signs of violent death). Copies of the completed documents together with the completed certificate of the cause of death should be kept in a health care facility until a separate order [16].

After the start of a full-scale war with Russia, more than 7.7 million Ukrainians became internally displaced persons [17]. The World Health Organization and the World Migration Organization in many reports emphasize the urgency of regulating of migration issues and health care organization in view of the challenges of the worldwide spread of many diseases [18]. A study of the needs of internally displaced persons found that 34% had problems with medicines and medical services [19].

Therefore, taking into account the problems arising in the process of migration, the Ministry of Health of Ukraine adopted Order № 458 "On Approval of the Minimum Requirements for Ensuring Sanitary and Epidemic Welfare of the Population during Emergency Arrangements Of the Russian Federation "according to which places of temporary stay of migrants are arranged at a sufficient distance from conflict zones and other potentially dangerous areas, issues of sanitary and epidemiological well-being of persons in temporary places are regulated, infrastructural requirements are determined (available transport, medical, trade, sports and health facilities) hygienic norms are determined: lighting, water supply; moments of comfort are recommended - access to the Internet, etc. [20].

Timely collection of bodies of victims of hostilities is important during the war, so the Ministry of Health of Ukraine issues an order approving the Procedure for equipping special groups during the collection of bodies with materials and equipment, which approves equipping

special groups during the collection of bodies (remains): protective equipment, equipment for collecting, transporting and storing the bodies (remains) of the dead and equipment for recording of information [21].

REGULATION OF BLOOD PRODUCTS, NARCOTIC AND PSYCHOTROPIC DRUG

Given the imposition of martial law and active hostilities, to cover existing needs and to form a strategic stock of blood components by order of the Ministry of Health of Ukraine provides for the involvement of regular donors of blood and blood components, and also organized the reception of donors in accordance with the curfew and the establishment of a special regime of light masking. In addition, fast and free (based on expense invoices) donation of blood and blood components is provided at the request of the Ministry of Internal Affairs of Ukraine, the Ministry of Defense of Ukraine, the State Emergency Service, the Security Service of Ukraine and the State Border Service of Ukraine [22, 23].

An operational headquarters of the Ministry of Health of Ukraine has been set up to coordinate the activities of blood system entities in martial law to ensure uninterrupted supply of needs. This headquarters coordinates and takes measures to manage, monitor and control the activities of the blood system, as well as cooperation with central and local executive authorities, health care institutions, specialists in various fields [24].

Due to the severe consequences of the war on human health, manifested in numerous injuries and contusions, accompanied by severe pain, special attention is paid to an important aspect of drugs that contain narcotic agents.

The Order of the Ministry of Health of Ukraine № 382 establishes a special regime in the field of production and sale of drugs containing narcotic agents, psychotropic substances and precursors, other potent substances, which consists in restricting access to the apartments where medicines are stored; strengthening the protection of facilities and apartments intended for the production and sale of medicines, as well as changes in the order of transportation which provides for transportation only accompanied by police or security [25].

A separate order allows the storage of narcotic drugs, psychotropic substances and precursors in health care facilities in quantities not exceeding the three-month needs of the institution in them [26].

ISSUES, RELATED TO MOBILIZATION

The urgent step was to prepare the medical service for wartime requirements, so the order of the Ministry of Health of Ukraine № 381 decided to bring the functional subsystem of medical protection ready to perform the assigned tasks in a special period. This envisages the implementation of the civil protection plan of the functional subsystem of medical protection for a special period, establishing the degree of readiness "FULLY READY" and ensure the management of the functional subsystem at the state level by organizing cooperation with the State Emergency Service of Ukraine. The content of this order, all subjects of the functional subsystem must ensure the implementation of civil protection measures in accordance with the plans of civil protection for a special period [27].

REGULATION OF DRUG CIRCULATION

Along with legislative activity to improve and optimize the work of the health care system in wartime, some orders were adopted on the circulation of medicines in Ukraine. First of all, the procedure of emergency state registration of medicines, medical immunobiological drugs, blood products supplied to Ukraine was approved and in accordance with this procedure the Ministry of Health introduces a simplified algorithm for filing an application for registration and accelerated mechanism for reviewing this application [28].

In connection with the imposition of martial law in the country issued an order, which prohibits by terminating the registration certificates the use in Ukraine of medicinal products, manufacturers of which according to the State Register of Medicinal Products of Ukraine have a legal address and/or address of the place of business in the Russian Federation [29]. A similar situation was adopted in relation to medicinal products from the Republic of Belarus [30].

DEVELOPMENT AND APPROVAL OF METHODOLOGICAL RECOMMENDATIONS

A separate important function of the Ministry of Health is the implementation of modern medical guidelines for the prevention and treatment of various conditions and diseases. Within this function and in accordance with the requirements of wartime The Ministry of Health of Ukraine implements in practice methodical recommendations on primary surgical treatment of gunshot wounds [31], on the phasing of medical care for the wounded and injured [32], on medical care for victims of burns during evacuation [33], on first aid and prevention of post-traumatic stress disorder [34], on the conversion of the turnstile in the injured in the areas of tactical emergency care [35], on the application of the protocol of mass transfusion of blood components to victims of evacuation [36], on tactics of surgery to control injuries and stabilize the victims of evacuation [37], on the organization of emergency medical care for victims of chemical agents during the evacuation stages [38], on the provision of emergency medical care to victims in the pre-hospital stage in combat / martial law [28].

FREQUENCY ANALYSIS OF ISSUING OF ORDERS BY THE MINISTRY OF HEALTH OF UKRAINE

The frequency analysis of the publication of normative documents of the Ministry of Health of Ukraine showed that among the 29 orders aimed at regulating health care during the war showed that the vast majority of orders were

developed and issued in the first two weeks of the war - 25 orders, against 4 orders issued in the next 2 weeks. At the same time, 16 orders were issued during the first week, and 9 orders in the second week (Fig. 1).

Qualitative analysis of the content of the adopted orders shows that first of all orders were issued on the organization of medical care, mobilization and regulation of blood products, narcotic and psychotropic drugs and regulation of drug circulation, and only after that the focus was on regulating outpatient care and demographic processes. The implementation of methodological recommendations was considered gradually throughout.

DISCUSSION

The largest number of orders was adopted in the first days of the war and the first of them concerned the organization of medical care – 5 orders. One of the first was an order about sorting of wounded soldiers. Ukrainian doctors have previously had experience in providing of medical care to the wounded since the beginning of the war in Donbass (2014), so the organization of this service was of paramount importance. The importance of sorting the wounded was proved by M. Pirogov in the Crimean War as an important guarantee of successful military field surgery: "Well-organized sorting of the wounded," he wrote, "is the main way to provide proper care and prevent helplessness and harmful disorder."

Given the consequences of the war (bombing, shelling, etc.) on the health of military and civilians (wounds, fractures, bleeding), a number of orders were adopted to regulate the circulation of blood products, narcotic and psychotropic drugs – 5 orders.

Recognizing the importance of the issue of registration of births and deaths (natural population movements) and the issue of providing assistance to displaced persons (mechanical population movements), the Ministry of Health of Ukraine issues 4 orders that regulate these circumstances.

The Ministry of Health did not ignore the provision of assistance to civilians, the most common diseases of which - non-communicable diseases forced the government to focus on outpatient care - 2 orders.

One orders were devoted to the regulation of the circulation of medicines - this concerned the simplification of the procedure for state registration of drugs acquired during the war. Two orders were approved specifically to ban the use of medicines in the territory of Ukraine by the Russian Federation and the Republic of Belarus in response to aggression by these states against Ukraine.

Methodological work was devoted to 9 orders and they were dedicated to urgent medical needs or were a response to threats from the aggressor to use prohibited weapons. Thus, the guidelines covered the algorithm of medical care for all possible injuries from the war.

CONCLUSIONS

The analysis of the legislative activity of the Ministry of Health of Ukraine to optimize the functioning of the medical care system for both military and civilian population in the context of Russian military aggression showed the Ministry's prompt response to time and high activity in the first two weeks of the war. At the same time, the orders qualitatively covered all important aspects of health care - the provision of medical care, the turnover of medical products, medical records, and so on.

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ORCID and contributionship:
Viacheslav M. Zhdan: 0000-0002-4633-5477 [E,F]
Iryna A. Holovanova: 0000-0002-8114-8319 [E,F]
Maksym V. Khorosh: 0000-0002-2083-1333 [A,B,D]
Inna V. Bielikova: 0000-0002-0104-3083 [A,B,D]
Natalia A. Lyakhova: 0000-0003-0503-9935 [A,B,D]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Natalia A. Lyakhova
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
tel: +380506147638
e-mail: natanew2017@ukr.net

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ORIGINAL ARTICLE

FEATURES OF THE CONNECTIVE TISSUE COMPONENT OF THE PALATINE TONSILS IN PATIENTS WITH RECURRENT TONSILLITIS

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Ruslana M. Orlovska[1], Vasyl I. Popovych[1], Ivanna V. Koshel[1], Olexandr O. Bondarenko[2]
[1]IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE
[2]DNIPRO STATE MEDICAL UNIVERSITY, DNIPRO, UKRAINE

ABSTRACT

The aim: To explore the morphological changes of palatine tonsil at the levels of the epithelial layer and connective tissue; to determine the relative area of the connective tissue component in the tonsillar tissue (fibrosis) in patients with recurrent tonsillitis compared to the control.

Materials and methods: This study presents a morphological assessment of the palatine tonsils of 10 people. Tonsils' material with surrounding tissue was fixed in 10% formalin solution. The samples were dehydrated in increasing ethanol concentrations, cleared in xylol, impregnated with paraffin. Microscopy was then performed with samples stained beforehand.

Results: In the samples of patients with recurrent tonsillitis pericapsular sclerosis was noted, along with thickening of interlobular septa and pronounced subepithelial fibrosis. A ratio of the dense connective tissue surface area to the total surface area of tonsil tissue was determined. The control group showed a statistically significant decrease in the degree of sclerosis of the tonsil stroma.

Conclusions: Multiple changes were found in the tonsils of patients with recurrent tonsillitis at the level of the epithelial layer that manifested in structural alterations. Significant and irreversible changes were also observed in the connective stroma of the tonsil - pericapsular sclerosis, thickening of interlobular septa, and pronounced subepithelial fibrosis. A statistically significant increase in the relative surface area of the connective tissue component of the tonsil (fibrosis) by a factor of 1,26 was noted in patients with recurrent tonsillitis compared to the results of the control group of patients.

KEY WORDS: respiratory tract, tonsillitis, tonsils, morphology

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INTRODUCTION

Palatine tonsils belong to peripheral hematopoietic and defensive immunological organs and represent a parenchymal organ. Their parenchyma is made of myeloid and lymphoid tissues, while stroma is divided into dense and soft. Dense stroma is represented by connective tissue, while soft stroma - by reticular tissue. The connective tissue of the tonsils is dominated by loose connective tissue which is a combination of various cells, a small number of multidirectional fibres (mostly collagen), and a relatively large volume of intercellular substance [1]. Reticular tissue is no less significant, being a specialized connective tissue. It ensures a stromal foundation for lymphoid elements. Being a part of the loose connective tissue, collagen fibres form a connective capsule around the tonsil where the connective tissue strands branch along the crypts. Hypothetically the following sections of the collagen stroma can be defined: peritonsillar, subepithelial, and septal.

Palatine tonsils have a large surface contact area with the external environment, they come in contact with a large number of antigen materials originating in the air and food, and take an active part in reactions of the cell and antibody-mediated immunity. They perform their functions on the verge of normal and pathological, ensuring a high level of regional and systemic immunity. Palatine tonsils induce both antibody-mediated and cell-mediated immune responses. This can be explained by the fact that the contact with antigens in the lymphoid tissue leads to an immune reaction, and therefore - to inflammation, where lymphocytes, macrophages, and granulocytes are involved. It is considered that palatine tonsils exist in the state of so-called "physiological" inflammation at rest [2]. Thus the term "tonsillitis" is relevant only when some clinical symptoms are present, such as sore throat, patches on the tonsils, absence of cough, or increased body temperature. There is data that at the histological level a lymphocytic inflammatory reaction is observed in cases of viral inflammation, and granulocytic - in bacterial inflammation [2-4].

Presently the term "chronic tonsillitis" is not going to be used in line with new evidence-based definitions [2,5,6]. It is mentioned that the term "chronic tonsillitis" is as deceptive as the fact that the tonsils are not in a physiological inflammatory reaction. In recurrent inflammatory reactions on top of physiological one in the tonsils the process of fibrosis takes place along with the spread of inflammatory process to the surrounding tissues, particularly the peritonsillar tissue which clinically manifests as fixation of the tonsil in its bed or so-called "discoursity" of the tonsil [2,7,8].

The study of the morphological changes in the tonsil and peritonsillar space in patients with recurrent tonsillitis, particularly their connective component, could explain the development of irreversible fibrous alterations in their structure.

THE AIM

The aim of our study was to explore the morphological changes of the palatine tonsil at the level of the epithelial layer and connective tissue, to determine the relative surface area of the connective component of the tonsil tissue (fibrosis) in patients with recurrent tonsillitis compared to the control group.

MATERIALS AND METHODS

The study group included 10 people, their ages ranging from 21 to 40 years old, average age 30 years old. Seven of them were the experimental group of patients who had recurrent tonsillitis and had tonsillectomy performed, while the rest three were the control group that included intact palatine tonsils of tragically deceased patients.

Material of the tonsils along with the surrounding tissue was fixed in 10% formalin solution (pH 7,4) for no less than 24 hours at room temperature [9]. The samples were then dehydrated in the increasing concentrations of ethanol, cleared in xylol, and impregnated with paraffin. Afterward, the paraffin impregnated tissue was poured into paraffin blocks. Serial sections with a thickness of no more than 4 μm were made of the blocks using Thermo HM 355S microtome (Thermo Scientific, Germany). Sections of each tissue sample were used for general histological tissue staining using Goldner's Masson trichrome. Prior to staining the sections were deparaffinized in xylol, rehydrated in decreasing (100, 95, 70%) ethanol concentrations, and were placed in Bouin's solution (10% formalin in saturated picric acid solution) for 1 hour for additional fixation to improve nuclear staining. Following the rinsing in distilled water the samples had been stained in Weigert's iron hematoxylin (components: hematoxylin and ferrous chloride - both produced by Sigma, Germany) for 10 minutes and were then rinsed in the running water for 20 minutes. The samples were stained in acid fuchsin solution (Sigma, Germany) and Xylidine ponceau (Sigma, Germany) for 10 minutes, and processed in 2% phosphomolybdic acid solution (Sigma, Germany) for 10 minutes. Afterward, the samples were immersed in the solution of Light green SF yellowish (Sigma, Germany) for 10 minutes. They were then dehydrated in increasing ethanol concentrations, differentiated in xylol, and mounted under cover slips.

Microscopic examination of the histological sections was performed using an Axio Imager 2 (Zeiss, Germany) microscope at × 200 and × 400 magnifications.

Taking into account a small number of studied samples (n = 14 for the study group and n = 6 for the comparison group) the nonparametric Mann–Whitney U test (U) was utilized using Microsoft Excel 2010. The statistical result was considered significant when $p \leq 0,05$.

RESULTS

Histological examination of the tissues in the control group showed that the mucous membrane of the palatine tonsil was covered with mature non keratinized stratified squamous epithelium, however, over its transition to the crypt it gradually lost its maturity and became thinner. Multiple microvessels were found directly underneath the epithelium of the crypts (fig. 1). Postcapillary venules with high endothelium also known as "high endothelial venules" are specific microcirculatory structures, present only in the peripheral lymphoid organs, including palatine tonsils. They were easily identified among the other vessels of the microcirculation in the researched material due to the presence of a cuboid endothelium with a noticeable nucleus. These blood vessels reached up to 50 μm in diameter, here and there their nuclei significantly bulged in the vessel lumen. Such postcapillary veins in particular serve as a recirculation pathway for T and B cells.

Both areas of non keratinized and keratinized epithelium were noted in the superficial epithelium of the tonsil samples in the experimental group (fig. 2). Microscopically erosions of the superficial epithelium were discovered as well, especially at the level of the crypts, although such alterations were not common. In addition, moderate and in some places pronounced leukocytic infiltration of the epithelium and adjacent connective tissue was found. The cytoplasm of epitheliocytes was vacuolized, the nuclei were hyperchromic, apoptotic phenomena were occasionally observed. The basal membrane had a convoluted form across significant areas of the epithelium. In some areas of the epithelium lesions of desquamation of the epithelial layer were identified. Intense leukocytic infiltration was found in the epithelial tissue of the crypts and superficial epithelium, expressed in the epithelium of the crypts the most. Among the leukocytes lymphocytes were prevalent, but plasmocytes, individual macrophages, and tissue basophils were observed as well. Microcirculatory vessels were dilated, and in some cases, stasis of blood cells was noted. Here and there minor bleeding in subepithelial and subcapsular areas was observed which could be explained by additional injury in the course of tonsillectomy.

It should be mentioned that connective tissue of the tonsils in the control group was represented by soft reticular fibres that served as a stromal foundation for lymphoid elements, and by well-developed collagen strands that spread circularly around the tissue of the tonsil, forming a connective capsule, and descended deep within lymphoid elements making up their trabecular structures. Trabecular strands in turn followed the direction of descending

Table I. Morphometric analysis results

Groups	Specific surface area of the connective tissue ±SD (%)
Recurrent tonsillitis (n=14)	29,72±9,73*
Control (n=6)	23,6±4,1

* – $p<0,05$.

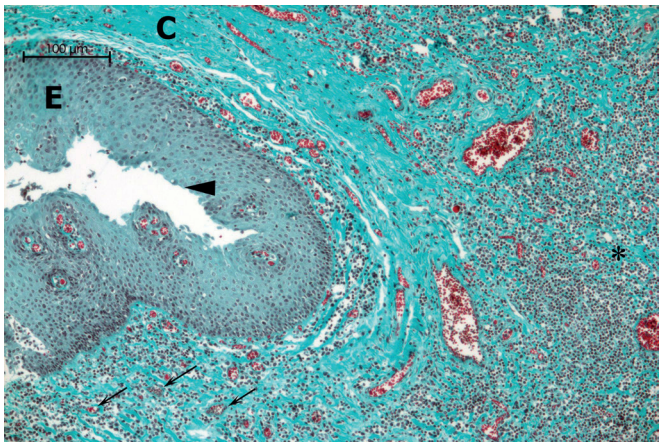

Fig. 1. Tissue of an intact tonsil with a fragment of a crypt (arrowhead) covered with stratified squamous epithelium (E) and surrounded by connective tissue stroma (C). Parafollicular lymphoid tissue with multiple microvessels - on the left (*). In the subepithelial area postcapillary venules with high epithelium are noted (arrows). ×100. Masson-Goldner trichrome staining

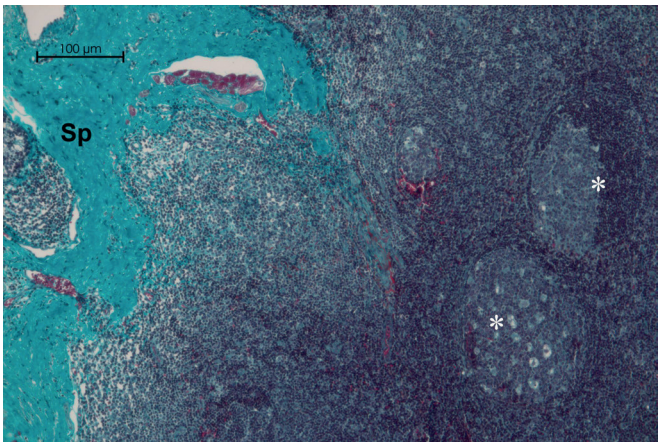

Fig. 2. Female, 33 years old, recurrent tonsillitis. Parafollicular fibrosis (F). Hyperplasia of lymphoid follicles (*), in the lacune - leukocytic infiltration of epithelium, hyperkeratosis (arrowhead). ×100. Masson-Goldner trichrome staining

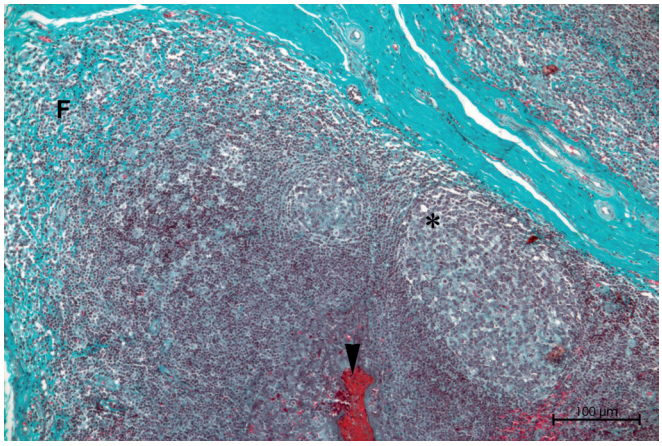

Fig. 3. Female, 30 years old, recurrent tonsillitis. Significant thickening of the connective tissue septa (Sp), follicular hyperplasia(*). ×100. Masson-Goldner trichrome staining

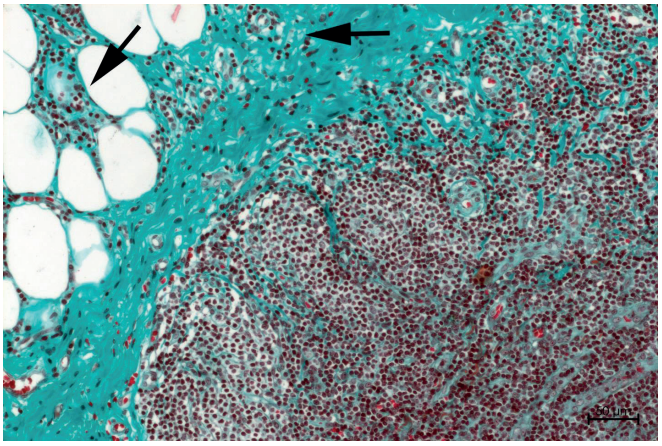

Fig. 4. Female, 33 years old, recurrent tonsillitis. Inflammatory lymphohistiocytic infiltrates are immersed in fibrous and adipose tissue (arrows). ×200. Masson-Goldner trichrome staining

crypts. The connective capsule extended into connective elements of the neck and was surrounded by striated muscles and salivary glands. Thus the following sections of tonsillar collagen stroma could be defined: peritonsillar, subepithelial, and septal (trabecular). Respectively, when some parts of the stroma were thickened, pericapsular sclerosis, thickening of interlobular septa, and marked subepithelial fibrosis were observed. Naturally, all three of these patterns were present in the samples of patients in the experimental group, compared to the control group (fig. 2, 3). Examination of the peritonsillar connective tissue of tonsils in the experimental group allows for a description of the connective stroma as collagen fibres that were often assembled in thick bundles (fig. 2) These patients were also found to have inflammatory infiltrates located separately from lymphoid tissue and immersed in fibrous tissue (fig. 4). Diffuse infiltration of adjacent muscle and adipose tissue with the chronic inflammatory infiltrate mentioned above was observed as well.

Having performed the aforementioned research the following histomorphometric parameter was measured: ratio of the surface area of the dense tissue to the total surface area of the tonsillar tissue as a percentage. The proportion of tonsillar tissue and its capsule that corresponded to the existing dense connective tissue, and which was stained using the trichromatic staining method, to the total tonsillar tissue volume that consisted of lymphoid tissue, stratified squamous epithelium, and connective tissue capsule was measured.

The extent of the collagen stroma varied significantly among the patients of the experimental group. The maximum value of the connective tissue-specific surface area was 47% of the total surface area of the section. It should also be mentioned separately that in the control group the minimum average value of connective tissue component was 19,8% of the total surface area of the section. When comparing the rates of fibrosis between the experimental group and the control (29,72±9,73% and 23,6±4,1%, re-

spectively), the latter demonstrated a significantly lower degree of sclerosis of the tonsillar stroma ($p < 0.05$).

Morphometric analysis results are presented in Table I.

DISCUSSION

Analysis of the histological examination of the palatine tonsils tissue revealed that the mucous membrane of palatine tonsils in the control group was covered with mature non keratinized stratified squamous epithelium while the tonsil samples of the patients in the experimental group showed areas of both non keratinized and keratinized epithelium. Moreover, erosions of the superficial epithelium were noted, especially at the level of the crypts, and moderate, in some places pronounced leukocytic infiltration of the epithelium and underlying connective tissue. In some parts of epithelium the lesions of desquamation of the epithelial layer were identified which were not observed in the control group. Microcirculatory vessels were dilated, and stasis of blood cells was noted in the capillaries, while these alterations were not seen in the tonsils of the control group.

Comparing the structure of connective tissue of the two studied groups, a connective tissue in the control group was represented by soft reticular fibres that combined into trabecular structures thus forming the tonsil stroma of normal thickness. The following sections of tonsillar collagen stroma were defined: peritonsillar, subepithelial, and septal (trabecular). Instead, three important features were found in the experimental group. Particularly, these include pericapsular sclerosis, thickening of interlobular septa, and pronounced subepithelial fibrosis. These samples were also found to have inflammatory infiltrates that were located separately from the lymphoid tissue and immersed in fibrous tissue. Diffuse infiltration of the adjacent muscle and adipose tissue with chronic inflammatory infiltrate was observed.

Having measured such a histomorphometric parameter as the ratio of the surface area of dense connective tissue to the total surface area of tonsil tissue, we were able to attain the results that demonstrated a significant difference in the surface area of connective tissue between the patients of the experimental group and the control, which was about 29.7% and 23.6% respectively (statistically significant difference $p < 0.05$). These results match the contemporary research that observed the tendency of an increasing fraction of connective tissue in recurrent tonsillitis [10]. Thickening of the parenchyma and scarring of the connective tissue due to chronic inflammation is one of the major changes in patients with recurrent tonsillitis [11]. Moreover, fibrosis of tonsillar tissue as a morphological manifestation of recurrent tonsillitis can lead to damage to the barrier function of this organ. As a result, dysfunction of local immunity may develop that might later lead to the perpetuation of infections [12]. At the same time, immunologic dysfunction is explained by the presence of chronic inflammation that promotes migration and proliferation of fibroblasts that as a result of their activity lead to an increase in the amount of stromal collagen, and thus occurs substitution of immunologically active elements with fibrous tissue [10,13].

CONCLUSIONS

1. In patients with recurrent tonsillitis, multiple changes were found at the level of epithelial level in the tonsils, which reflects in the structural change of the latter (emergence of keratinized epithelium, erosions, leukocytic infiltration, local desquamation).
2. Significant and irreversible changes were noted in the connective tissue stroma of the tonsil - pericapsular sclerosis thickened interlobular septa and pronounced subepithelial fibrosis.
3. Statistically significant increase by a factor of 1.26 in the surface area of connective tissue component of the tonsil tissue (fibrosis) in patients with recurrent tonsillitis compared to the results of the control group of patients ($p<0.05$), which is explained by a persistent inflammatory process that could be caused by repeated antigen stimulation.

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ORCID and contributionship:
Vasyl I. Popovych: 0000-0002-2898-8474 [A, F]
Ivanna V. Koshel: 0000-0002-5466-4537 [B, E, D]
Ruslana M. Orlovska: 0000-0002-8669-7026 [B-E]
Oleksandr O. Bondarenko: 0000-0002-9739-9219 [B-E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Vasyl I. Popovych
Ivano-Frankivsk National Medical University
2 Halytska Str., 76018 Ivano-Frankivsk, Ukraine
tel: +38 (050) 373-4839
e-mail: popovychvasyl@gmail.com

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ORIGINAL ARTICLE

SURGICAL ISCHEMIC ASPECTS OF COVID-19: MANAGEMENT OF PATIENTS WITH COVID TOES AND FINGERS

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Oleksandr Yu. Ioffe[1], Stepan L. Kindzer[1], Mykola S. Kryvopustov[1], Yuri A. Dibrova[1], Yuri P. Tsiura[1], Mykhailo O. Havrylchenko[2], Oleg V. Lobanov[2]

[1] BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

[2] KYIV CITY CLINICAL HOSPITAL №3, KYIV, UKRAINE

ABSTRACT

The aim: Study of clinical manifestations and management of patients with COVID toes and fingers.

Materials and methods: 1,841 patients with laboratory-confirmed SARS-CoV-2 infection were hospitalized. All patients were divided into two groups: without surgical pathology – 1,693 (91.96%) and with surgical pathology (patients with COVID toes and fingers and abdominal syndrome) - 148 (8.04%). The diagnosis of COVID-19 was made on the basis of clinical data, laboratory test results (PCR test for SARS-CoV-2) and computed tomography of the chest. On admission, in addition to the general laboratory tests, mandatory special methods of examination included determination of D-dimer, procalcitonin (PCT), C-reactive protein, and interleukin-6 (IL-6).

Results: Surgical ischemic manifestations were observed in 8.04% of all patients with COVID-19, of which 86.48% presented with ischemic abdominal syndrome and 13.52% with COVID toes and fingers. C-reactive protein and procalcitonin are the markers that may indicate the development of ischemic surgical problems. A direct statistically significant linear correlation was found between the severity of the underlying disease and the mean D-dimer ($r = 0.815$; $p = 0.01$).

Conclusions: The confirmed phenomenon of COVID toes and fingers does not require active surgical tactics. It is necessary to conduct pathogenetic treatment of COVID-19 and dynamic monitoring of its clinical course.

KEY WORDS: COVID-19, phenomenon of COVID toes and fingers

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious condition first diagnosed in humans in December, 2019 in Wuhan (Central China) [1]. The disease began to spread rapidly in China and beyond and very quickly became a pandemic. As of February 14, 2022, 412,213,783 cases of COVID-19 were registered worldwide, including 5,818,108 deaths (COVID-19 Dashboard by the Center for Systems Science and Engineering at Johns Hopkins University) [2].

The actual number of cases undoubtedly far exceeds official statistics. In particular, it can be explained by the asymptomatic course of the disease, inconsistent health-care-seeking behaviour in clinically mild cases, specific characteristics of diagnostic testing in different countries, false-negative virological test results, and incomplete data on COVID-19 cases [3-6].

Signs and symptoms of COVID-19 are quite diverse, but during the course of the disease many people with COVID-19 report fever or chills, cough, shortness of breath, difficulty breathing, fatigue, muscle pain throughout the body, headache, loss of taste and smell, sore throat, nasal congestion or runny nose, nausea or vomiting, and diarrhoea [4].

Dermatological manifestations may also be associated with COVID-19. Their frequency ranges from 0.2% to 20.4%. The clinical picture is diverse, although in a study of 171 patients with laboratory-confirmed COVID-19 (mild to severe), the most common skin manifestations reported were maculopapular rash (22%), discoloration of the fingers and toes (18%), and urticaria (16%). About 60% of all patients with COVID-19 and with any skin manifestations reported fever and / or cough. Assessment of skin manifestations in COVID-19 patients remains difficult because the symptoms may be linked to a variety of other diseases [4].

Some comorbid conditions can cause severe COVID-19. Hypertension and disorders of lipid metabolism are the most common, while obesity, complicated diabetes mellitus and anxiety disorders are the major risk factors for severe COVID-19 [7].

THE AIM

The aim of the work is the study of clinical manifestations and management of patients with COVID toes and fingers.

MATERIALS AND METHODS

On September 1, 2020, a medical center for the treatment of patients with SARS-CoV-2 was opened at the Kyiv

Table I. Distribution of patients with surgical pathology by gender, age and concomitant pathology

	Abdominal syndrome (n=128)	COVID toes and fingers (without concomitant pathology) (n=17)	COVID toes and fingers (with concomitant pathology) (n=3)	Total
Age (min-max)	55,4 ± 6,43 (45 - 67)	31,47 ± 7,21 (22 - 45)	59 ± 7,21 (53 - 67)	52,72 ± 10,07 (22 - 67)
Gender (male/female), abs, %	63 (49,22%) / 65 (50,78%)	8 (47,06%) / 9 (52,94%)	2 (66,67%) / 1 (33,33%)	73 (49,32%) / 75 (50,68%)
Ischemic heart disease, abs, %	111 (86,72%)	0 (0%)	3 (2,34%)	114 (89,06%)
Type 2 diabetes mellitus, abs, %	87 (67,97%)	0 (0%)	3 (2,34%)	90 (70,31%)
Hypertension, abs, %	100 (78,13%)	0 (0%)	1 (0,78%)	101 (78,91%)
Respiratory diseases, abs, %	8 (6,25%)	0 (0%)	0 (0%)	8 (6,25%)
Overweight, abs, %	79 (61,72%)	10 (7,81%)	2 (1,56%)	91 (71,09%)

Table II. Comparison of mean values of specific markers in groups with and without surgical pathology

	Mean value in the group with surgical pathology (excluding severity) (n=148)	Mean value in the group without surgical pathology (excluding severity) (n=1693)	P
Lymphocytes, %	7,02 ± 2,35 (0 - 10)	7,17 ± 2,24 (0 - 11)	0,528
Thrombocytes, x10^9	155,5 ± 16,28 (90 - 170)	156,54 ± 14,72 (92 - 171)	0,637
C-reactive protein, mg / l	48,32 ± 30,93 (6 - 187)	36,72 ± 19,37 (5 - 90)	< 0,001
D-dimer, µg / ml	3,24 ± 2,25 (1 - 8)	3,18 ± 2,22 (1 - 8)	0,787
Procalcitonin, ng / mg	1,15 ± 0,42 (0,5 - 2,1)	0,9 ± 0,49 (0,11 - 1,7)	< 0,001
Interleukin-6, pg / ml	75,99 ± 56,71 (7 - 200)	75,24 ± 61,46 (7 - 203)	0,641

City Clinical Hospital #3. Between September, 2020 and February, 2021, 1,841 patients with laboratory-confirmed SARS-CoV-2 infection were hospitalized. All patients were divided into two groups: without surgical pathology – 1,693 (91.96%) and with surgical pathology (patients with COVID toes and fingers and abdominal syndrome) - 148 (8.04%). Subsequently, these patients were divided into 3 groups: Group I - patients with ischemic syndrome of the upper and lower extremities (COVID toes and fingers) without concomitant pathology - 17 (11.49%), Group II - patients with COVID toes and fingers and with concomitant pathology - 3 (2.03%) and group III - patients with abdominal syndrome - 128 (86.48%), which was clinically manifested by nausea and loose stools, aching pain in the abdomen that was sometimes described as cramping and without clear localization.

Among patients with COVID toes and fingers, 12 patients developed chilblain-like lesions on their toes, whereas 8 patients on their fingers. In our observations, there were no patients with simultaneous affection of their toes and fingers.

For the study of changes in the capillary bed, patients underwent digital computer capillaroscopy using a digital optical capillaroscope "MICROPOTOK" manufactured by CJSC "Engineering Enterprise" POTOK" (Ukraine). Arterial and venous blood flow was investigated by dopplerography of the vessels of the upper and lower extremities using an ultrasound machine MyLab ™ X6 manufactured by Esaote (Italy).

The diagnosis of COVID-19 was made on the basis of clinical data, laboratory test results (PCR test for SARS-CoV-2) and computed tomography of the chest.

On admission, patients complained of severe weakness, difficulty breathing, shortness of breath, fever, loss of taste and smell, muscle aches, severe headache, unexplained anxiety, chest pain, nausea, and abdominal discomfort. In addition to the general laboratory tests, mandatory special methods of examination included determination of D-dimer, procalcitonin (PCT), C-reactive protein, and interleukin-6 (IL-6).

RESULTS

The data in Table I show that patients with surgical pathology could suffer from a very severe concomitant pathology, in particular chronic coronary heart disease, hypertension, type 2 diabetes mellitus, and respiratory diseases. These conditions could be frequently diagnosed simultaneously in one patient. In this case, the frequency of comorbidities did not depend on gender characteristics. The largest group with ischemic syndrome of the upper and lower extremities (COVID fingers and toes) consisted of patients of young age and without concomitant pathology. Patients with abdominal syndrome were not divided into groups depending

Table III. Changes in laboratory findings in COVID-19 patients with surgical pathology depending on the severity of the underlying condition

	Mean value in the group with surgical pathology (moderate condition) (n=74)	Mean value in the group with surgical pathology (severe condition) (n=74)	P
Lymphocytes, %	7,7 ± 1,75 (5 - 10)	6,34 ± 2,67 (0 - 10)	0,021
Thrombocytes, x10^9	160,27 ± 5,79 (150 - 170)	150,73 ± 21,31 (90 - 170)	0,070
C-reactive protein, mg / l	41,09 ± 22,85 (6 - 79)	55,55 ± 36,03 (7 - 187)	0,250
D-dimer, µg / ml	1,53 ± 0,5 (1 - 2)	4,96 ± 2 (2 - 8)	< 0,001
Procalcitonin, ng / mg	0,98 ± 0,4 (0,5 - 1,7)	1,32 ± 0,37 (0,58 - 2,1)	< 0,001
Interleukin-6, pg / ml	27,8 ± 11,9 (7 - 49)	124,18 ± 40,32 (50 - 200)	< 0,001

Table IV. Stages of the development of COVID toes and fingers and their duration

Stages	Onset time (a day)	Average duration (days)
I	1-3	2 ± 0,86
II	4-5	4,5 ± 0,51
III	6 - 17	12,1 ± 3,91
IV	18 - 23	20,9 ± 1,92

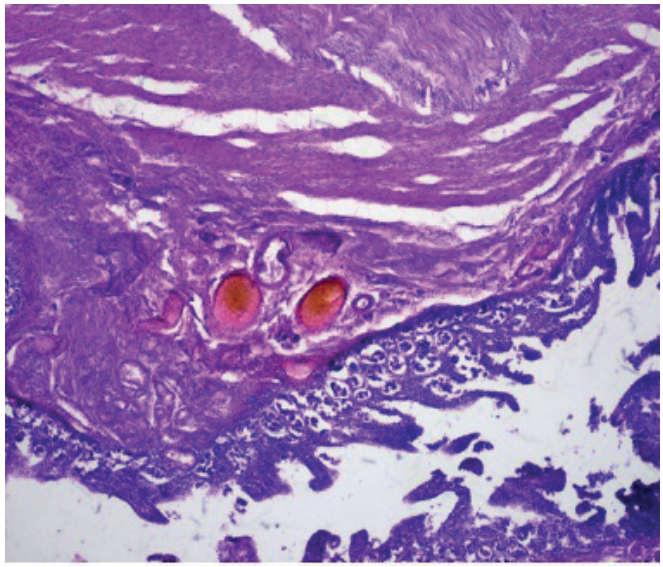

Fig. 1. Patient B., age 67, small intestinal micropreparation, hematoxylin staining with eosin, Leica DM LS2 microscope

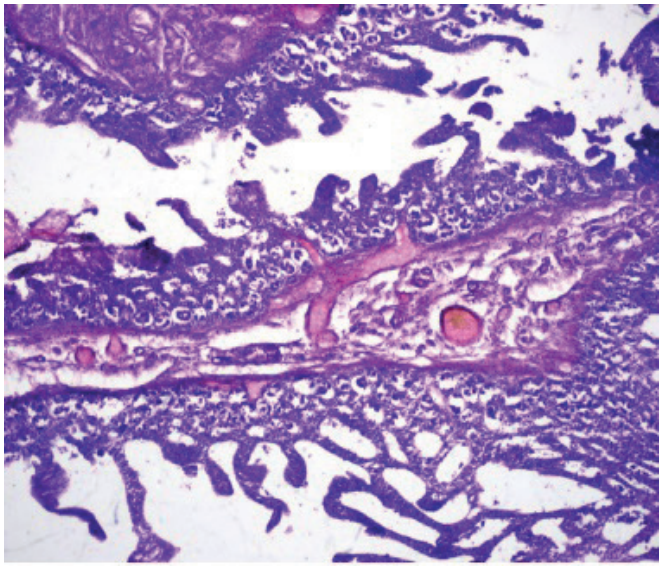

Fig. 2. Patient B., age 67, small intestinal micropreparation, hematoxylin staining with eosin, Leica DM LS2 microscope

on the presence or absence of concomitant pathology, as the latter occurred with the same frequency in all patients with COVID-19 regardless of their age and gender.

For the study of specific markers of surgical pathology in COVID-19 patients, the following quantitative indicators were analyzed: lymphocytes, platelets, C-reactive protein, D-dimer, procalcitonin, and interleukin-6. The mean values of these indicators were compared in groups with and without surgical pathology, without taking into account the severity of the underlying disease (Table II).

For the study of changes in the count of lymphocytes, platelets, C-reactive protein, D-dimer, procalcitonin, and IL-6 in COVID-19 patients with surgical pathology, depending on the severity of the underlying condition, patients were divided into two groups: moderate (n = 74) and severe disease (n = 74). The data are shown in Table III.

The severity of COVID-19 was determined in accordance with the protocol "Provision of medical care for the treatment of coronavirus disease (COVID-19)", approved by the order of the Ministry of Health of Ukraine as of April 2, 2020, №762 (as amended by the Ministry of Health of Ukraine as of September 20, 2021, №1979) [18].

The study of laboratory findings in a group of COVID-19 patients with surgical pathology allowed establishing correlations using Spearman's rank correlation coefficient, given that the distribution of data differed from normal. A direct statistically significant linear correlation between age and severity of the underlying disease (r = 0.495; p = 0.01) was observed. Therefore, age was an important factor

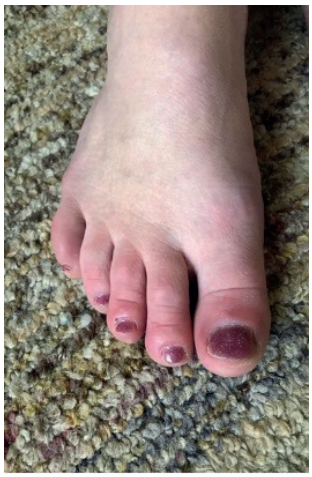

Fig. 3. Patient V., age 47, COVID toes, stage II - "hyperaemia".

Fig. 4. Patient T., age 34, COVID toes of the right foot, stage III - "ischemia".

Fig. 5. Patient T., age 41, COVID fingers of the right hand, stage III - "ischemia".

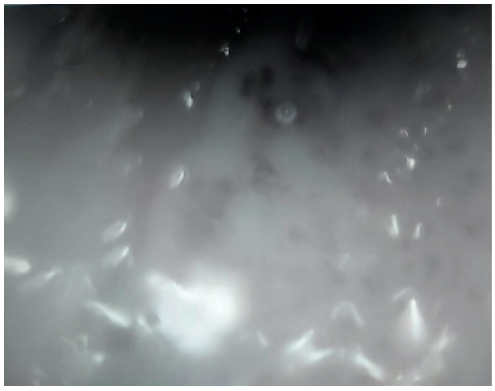

Fig. 6. Patient T., age 34, COVID toes of the right foot, stage IV - reversible changes

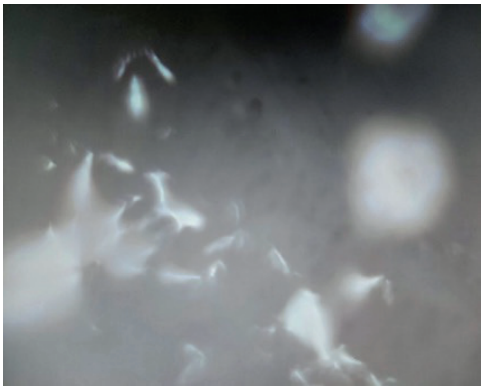

Fig. 7. Patient S., age 38, COVID fingers of the right hand, stage II – "ischemia". Capillaroscopy of the fingers of the hand.

Fig. 8. Patient O., age 31, COVID toes of both feet, stage III - "ischemia". Capillaroscopy of the toes.

contributing to the severity of COVID-19 in this group. A direct statistically significant linear correlation between age and mean D-dimer ($r = 0.475$; $p = 0.01$) was also noted. This correlation appears probably due to the predisposition of elderly patients to increased thrombosis.

The investigation of the relationship between the number of comorbidities and other factors revealed direct statistically significant linear correlations with the severity of the disease ($r = 0.491$; $p = 0.01$), the level of D-dimer ($r = 0.471$; $p = 0.01$), and interleukin-6 ($r = 0.423$; $p = 0.01$). Thus, the more comorbidities were seen the higher those indicators were, as each of them had its negative impact on the course of COVID-19.

The study of the factors associated with the course of COVID-19 in the group of patients with surgical pathology revealed a direct statistically significant linear correlation of the strong relationship between the severity of the underlying disease and the mean value of D-dimer ($r = 0.815$; $p = 0.01$), which could be due to the severity of the inflammatory process, vascular endothelium, including intestinal vessels and the development of thrombosis in them.

Severe inflammatory infiltration of the mucous layer and the presence of focal erosive defects were revealed on histological slides of the small intestinal wall (samples taken during autopsy, the cause of death - respiratory failure) (Fig. 1 and Fig. 2). Swelling and focal growth of connective tissue were also noted along the submucosal layer of the small intestinal wall. Endothelial thickening and vascular thrombosis were observed in a number of fields of view.

In addition, a direct statistically significant linear correlation was found between the severity of the underlying disease and the increase in the mean value of procalcitonin ($r = 0.395$; $p = 0.01$). The latter was due to the development of secondary bacterial infection, which in turn aggravated the course of COVID-19. There was also a statistically significant linear correlation between the severity of the underlying disease and the increased mean value of IL-6 ($r = 0.866$; $p = 0.01$), due to the body's protective response to SARS-CoV-2 and the onset of secondary bacterial infection.

An inverse statistically significant linear correlation was found between the average count of lymphocytes and C-reactive protein ($r = -0.315$; $p = 0.01$). The latter can be explained by the fact that the level of lymphocytes under viral load is reduced, the body's immune response

to inflammation is enhanced and thus increases the rate of C-reactive protein.

The group of COVID-19 patients with COVID toes and fingers included 20 patients (13.5%) without visible hemodynamic disorders of the main blood flow, without concomitant pathology - 17 patients, and with concomitant pathology - 3 patients. According to Doppler data, the main type of blood flow was preserved in all patients.

In our observations of the development of COVID toes and fingers, we identified four stages: I - stage of initial manifestations, II - stage of hyperaemia, III - stage of ischemia, IV - stage of reversible changes (Table IV).

At onset, chilblain-like lesions on the fingers and toes were detected on the 3rd - 5th day after the initial clinical manifestations of COVID-19.

At the first stage, patients noted the appearance of itchy skin on the toes or fingers, burning and tingling sensations in the fingertips. However, there were no visible skin manifestations.

In stage II, burning sensations disappeared, whereas noticeable redness of the skin appeared and the pain was described as persistent, aching or tangling (Fig. 3).

In stage III, bluish discoloration of the skin on the toes or fingers occurred on the dorsal and plantar surfaces of the foot, and some patients presented with skin cyanosis in patches involving the lower third of the shin bone or the forearm (Fig. 4 and Fig. 5).

Loss of skin colour and the disappearance of pain in the fingers and toes were typical for stage IV (Fig. 6). The skin acquired a normal body colour with time.

The analysis of the capillary bed allowed registering the mesotype of the capillary loops on the fingers (n = 8). The study revealed tortuous capillary loops of small caliber with signs of spasm as well as capillary loops of medium caliber that had slightly expanded length and showed tortuosity with "paragraphs" and spiral shapes. The proportion of the capillaries was not reduced. The density of capillary loops was 12-18 capillaries per 1mm^2. Capillary blood flow rate was moderately reduced; the index of capillary tortuosity was 28-32%. Patients had a normocirculatory type of blood flow with elements of deceleration and spastic type of microcirculation (Fig. 7).

The mesotype of capillary loops was registered on the toes (n = 12). Tortuosity of capillaries in the form of paragraphs with signs of a spasm and venular stagnation was also noted. The index of tortuosity of capillaries was 47-48%, and the density of capillary loops was 8-11 capillaries per 1mm^2. Patients had a spastic type of blood flow with signs of stagnation in the microcirculatory tract (Fig. 8).

COVID-19 treatment was administered according to the accepted protocols and depending on the severity of the disease and the presence of concomitant pathology [18].

Identical treatment was prescribed to patients with COVID fingers in both groups (n = 20). Given the nonspecificity of symptoms, the absence of visible skin manifestations in the first stage of the disease, no specific treatment was provided to these patients, except for subcutaneous administration of nadroparin or enoxiparin sodium according to the treatment protocol for COVID-19 [18].

In stage II characterized by the appearance of clinical manifestations of COVID toes and fingers, pentoxifylline infusion at a dose of 600 mg for the group without concomitant pathology (n = 17) and 300 mg for the group with concomitant pathology (n = 3) was administered intravenously daily. Due to its pharmacodynamics and pharmacokinetics, it inhibits the aggregation of platelets and erythrocytes, increases their elasticity, reduces the increased concentration of fibrinogen in blood plasma and enhances fibrinolysis, which reduces its viscosity and improves rheological properties. In addition, pentoxifylline has a myotropic vasodilating effect and reduces the total peripheral vascular resistance and thus improves microcirculation and tissue oxygen supply. The observation of the patients showed that on the 4th or 5th day of the therapy administration, they experienced less pain in their fingers and toes and had less severe skin cyanosis at rest. The course of vascular infusion therapy lasted from 10 to 20 days, depending on the positive response to treatment, which was characterized by less intensive pain on exertion and marbled skin with vague signs of cyanosis. After a course of infusion therapy, patients were transferred to tablet forms of the drug, discharged from the hospital after complete recovery from the underlying disease, and provided with further outpatient follow-up. It should be noted that in the group of patients without concomitant pathology (n = 17) the response to specific treatment was better, the duration of stage III and IV was reduced. In all patients with concomitant pathology, the duration of infusion therapy was 20 days.

In one patient with diabetes mellitus, despite specific treatment, on day 14 (stage III of COVID toes and fingers) the process turned into wet gangrene of the distal part of the foot, which necessitated an amputation of the upper third of the right shin bone. The patient was discharged on the 7th day after surgery with a negative PCR test SARS-CoV-2 and in satisfactory condition for outpatient treatment.

In the group, 1 patient with abdominal syndrome died. The cause of death was the underlying disease.

Therefore, in patients with confirmed COVID-19 and ischemic manifestations on the fingers or toes, it is necessary to use a differentiated approach in view of COVID-19 chilblain-like lesions, which do not require active surgical tactics.

DISCUSSION

In both groups (Table II), there were changes in the leukocyte formula, which were mainly manifested by a sharp decrease in the number of platelets and lymphocytes. This could most likely be due to the viral etiology of the disease and it is consistent with the literature [8, 9, 10, 11, 12]. No statistically significant difference was found (P> 0.05). Both groups demonstrated a significant increase in C-reactive protein, which is characteristic of patients with SARS-CoV-2. In the group of patients with surgical pathology, it was statistically significantly higher than

in the group without surgical pathology (P <0.001). The data obtained are typical for the inflammatory process. In both groups, there was an increase in D-dimer, in some cases up to 8 μg / ml, due to vascular endothelial damage, blood clotting and thrombosis and it is consistent with the literature [13, 14]. No statistically significant difference was found (P> 0.05). In both groups, there was also an increase in procalcitonin, and in the group with surgical pathology, this result was statistically significantly higher (P <0.001), indicating a high risk of the development of secondary bacterial infection concomitant to the underlying condition. The patients had elevated levels of interleukin-6 (IL-6), which may be due to the bodily response to the SARS-CoV-2 virus and it is consistent with the literature [15-17]. No statistically significant difference was found (P> 0.05).

Changes in laboratory findings in COVID-19 patients with surgical pathology depending on the severity of the underlying condition were more significant (Table III). Both groups were characterized by lymphopenia, but it was more pronounced in the group of patients with severe course of the disease and reached proper statistical significance. The obtained data are comparable with the literature data. Thrombocytopenia was observed in both groups of patients, but had no significant statistical differences [8-12]. C-reactive protein was significantly elevated in both groups, despite a higher mean value in the group of patients with severe COVID-19. When compared, its level was not statistically significant, which may be due to insufficient sample of patients. According to other authors, C-reactive protein levels were elevated and correlated with the severity of the disease [19, 20]. The D-dimer index was elevated in both groups, reaching 8 μg / ml in the group with the severe course of the disease, and was statistically significantly different from the group with the moderate course of the underlying disease. We believe that it can be explained by an intensive inflammatory process associated with a massive viral attack of the macroorganism. Elevated levels of procalcitonin in both groups indicated the development of the bacterial infection, and in patients with the severe course of the disease, this parameter was statistically significantly higher.

CONCLUSIONS

1. Surgical ischemic manifestations were observed in 8.04% of all patients with COVID-19, of which 86.48% presented with ischemic abdominal syndrome and 13.52% with COVID toes and fingers.
2. C-reactive protein and procalcitonin are the markers that may indicate the development of ischemic surgical problems. A direct statistically significant linear correlation was found between the severity of the underlying disease and the mean D-dimer (r = 0.815; p = 0.01).
3. The confirmed phenomenon of COVID toes and fingers does not require active surgical tactics. It is necessary to conduct pathogenetic treatment of COVID-19 and dynamic monitoring of its clinical course.

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ORCID and contributionship:
Oleksandr Yu. Ioffe: 0000-0002-1306-7920 [A, F]
Stepan L. Kindzer: 0000-0002-4136-9299 [D]
Mykola S. Kryvopustov: 0000-0003-4978-4873 [C, D]
Yuri A. Dibrova: 0000-0002-2833-1667 [A,E]
Yuri P. Tsiura: 0000-0001-6651-8564 [B]
Mykhailo O. Havrylchenko: 0000-0003-4564-0303 [B]
Oleg V. Lobanov: 0000-0003-1056-0709 [B]

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CORRESPONDING AUTHOR
Mykola S. Kryvopustov
Bogomolets National Medical University
13 Taras Shevchenko Boulevard, 01601 Kyiv, Ukraine
tel: +38(066)3916946
e-mail: mykola.kryvopustov@gmail.com

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ORIGINAL ARTICLE

PHYSICAL DEVELOPMENT OF STUDENTS AS AN INDICATOR OF THE PHYSICAL EDUCATION SYSTEM FUNCTIONING IN THE EDUCATIONAL INSTITUTION

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Grygoriy P. Griban[1], Olena O. Kosheleva[2], Olena O. Mitova[2], Alla M. Harlinska[1], Olena V. Solodovnyk[1], Bogdan S. Semeniv[3], Kostiantyn V. Prontenko[4]

[1]ZHYTOMYR IVAN FRANKO STATE UNIVERSITY, ZHYTOMYR, UKRAINE
[2]PRYDNIPROVSK STATE ACADEMY OF PHYSICAL CULTURE AND SPORT, DNIPRO, UKRAINE
[3]STEPAN GZHYTSKYI NATIONAL UNIVERSITY OF VETERINARY MEDICINE AND BIOTECHNOLOGIES LVIV, LVIV, UKRAINE
[4]S. P. KOROLIOV ZHYTOMYR MILITARY INSTITUTE, ZHYTOMYR, UKRAINE

ABSTRACT

The aim: To investigate the impact of organizational and methodological conditions of physical education system in higher educational institution on the students' physical development.

Materials and methods: The research involved 120 students of two higher educational institutions (30 men and 30 women each). Determination of physical development of students was carried out in the dynamics of learning from the first to the fourth instructional years in terms of 100 m run, 3000 m (boys) and 2000 m (girls) run, pull-ups on the crossbar (boys), push-ups (girls), 4 x 9 m shuttle run, standing long jump, lifting torso to the sitting position, torso leaning forward from the sitting position.

Results: The research determined organizational and methodological conditions of physical education system in two educational institutions, which differ in the duration of "Physical Education" academic subject depending on the instructional year, the number of academic hours provided for the subject mastery, approaches to the basic and elective components of the curriculum, organization of fitness and health recreation as well as sports events during extracurricular activities.

Conclusions: It was established that the level of students' physical development is better in the educational institutions where the physical education system functions more efficiently (compulsory physical education training sessions are held in the amount of 4 hours a week, more students are involved in educational and extracurricular physical education training sessions, where students' training motivation is higher).

KEY WORDS: physical education, organizational and methodological conditions, physical development, students

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INTRODUCTION

Student youth is a special social group, whose life-sustaining activities are characterized by high mental and emotional loads caused by intellectual work, which takes place in conditions of lack of time, nervous tension and stress [1, 2]. The analysis of the scientific literature shows that during the years of study at a higher educational institution (HEI) student youth tend not to increase health, but largely lose the reserve capacity of their body, which negatively affects active dispositive capacity and sharply reduces creative potential [3, 4]. To solve this problem, higher educational institutions need to make full use of the possibilities of physical education. Meanwhile, in the conditions of reforming higher education and granting autonomy to HEIs, the entire responsibility for the organization of physical education in HEIs rests with its administration. Unfortunately, according to the leading experts in the field of physical culture [5, 6], there is currently an underestimation of the importance of physical education for the preservation and strengthening of the health of student youth by representatives of HEI administrations. This leads to a decrease in the corresponding academic load, lack of quality control of students' physical condition. Currently, there is a reduction in the number of academic hours for the study of "Physical Education" academic subject in many HEIs of Ukraine [7, 8]. This situation has led to a decrease in motor activity and, as a consequence, deterioration of the indicators of physical development of students.

THE AIM

The aim is to investigate the impact of organizational and methodological conditions of physical education system in higher educational institution on the students' physical development.

MATERIALS AND METHODS

The research was conducted in 2017-2021 on the basis of the two higher educational institutions in Dnipro (Ukraine):

Oles Honchar Dnipro National University (DNU), Prydniprovska State Academy of Civil Engineering and Architecture (PSACEA). The research involved 120 students (30 men and 30 women each) of the main educational department.

The following tasks were identified to achieve the aim of the research: 1) to analyse the effectiveness of the physical education system in each HEI; 2) to study the attitude of students to the existing system of physical education in HEI; 3) to investigate the dynamics of indicators of physical development of students of each HEI.

To implement the first task, we analysed the content of the working educational documentation of the departments of physical education of the two HEIs. The attitude of students to the organization of physical education in HEI, their motivation for physical education training sessions were assessed by the authors' questionnaire. The questionnaire included 15 questions and was developed in compliance with all necessary requirements for sociological research and was approved by the Academic Council of the Dnieper State Academy of Physical Culture and Sports before its application. Determination of physical development of students was carried out in the dynamics of learning from the first to the fourth instructional years in terms of 100 m run, 3000 m (boys) and 2000 m (girls) run, pull-ups on the crossbar (boys), push-ups (girls), 4 x 9 m shuttle run, standing long jump, lifting torso to the sitting position for 1 minute, torso leaning forward from the sitting position.

Scientific methods: theoretical analysis and generalization of scientific and methodical literature, documentary method, questionnaires, testing, methods of mathematical statistics. Study results were processed using the "Data Analysis" package of Microsoft Excel spreadsheets. Descriptive statistics (mean and standard deviation) were determined. The reliability of the differences in average values was estimated by the Student's t-test; the difference was considered to be reliable at $p<0.05$

This research has been complied with all the relevant national regulations and institutional policies, and has followed the tenets of the World Medical Association Declaration of Helsinki – ethical principles for medical research involving human subjects. All participants agreed to participate in the research.

RESULTS

The analysis of the working educational documentation of the departments of physical education of DNU and PSACEA shows that the organizational and methodological conditions for building a system of physical education of students in these HEIs have significant differences regarding the duration of "Physical Education" academic subject depending on the instructional year, the number of academic hours provided for the subject mastery, approaches to the basic and elective components of the curriculum, sports as well as fitness and health recreation systems presented in the curriculum, organization of fitness and health recreation as well as sports events with students during extracurricular activities (Table I).

The most important fundamental peculiarity of the system of physical education in DNU is that the study of "Physical Education" academic subject is carried out during the entire years of attendance, except for the final semesters, for 4 hours a week. In PSACEA compulsory training sessions are held during four semesters in the first and second instructional years for 4 hours a week.

We conducted a survey of graduate students of both HEIs (the fourth instructional year) to study the opinions of students on the effectiveness of the existing system of physical education in HEIs, to determine their attitude and motivation to physical education training sessions within academic and extracurricular hours. It was found that the vast majority of students (53.3 % of DNU students and 40 % of PSACEA students) indicated the lack of

Table I. Comparative analysis of the effectiveness of the physical education system in different HEIs

Researched indicators	HEI	
	DNU	PSACEA
Duration of "Physical Education" academic subject by semesters	7 semesters according to the level of education "Bachelor"	4 semesters according to the level of education "Bachelor"
Number of hours of training sessions a week	4 hours	4 hours
Sports as well as fitness and health recreation systems in the basic component of the curriculum	Track-and-field athletics, gymnastics, game-oriented sports (basketball, volleyball, football, badminton), swimming	Track-and-field athletics, gymnastics, game-oriented sports, swimming
Conditions for the implementation of the elective component of the curriculum	During extracurricular activities	During training sessions
Peculiarities of the implementation of theoretical and methodological training	During each training session	2 hours of training sessions and 4 hours of independent training in each module
Type of final academic assessment	Pass / fail exam	Pass / fail exam
Conditions for physical education training sessions during extracurricular activities	27 sections, free training sessions for students, 2 times a week	12 subscription sections, preferential terms of payment for training sessions, 2 times a week

Table II. Dynamics of indicators of physical development of male students during their study in the HEI (n = 60)

Instructional year	DNU (n=30)			PSACEA (n=30)			Significance of the difference	
	X	σ	m	X	σ	m	t	p
100 m run, s								
1st	14.4	1.41	0.13	14.6	1.27	0.15	1.01	>0.05
2nd	14.2	1.35	0.14	14.4	1.32	0.17	0.91	>0.05
3rd	14,0	1.29	0,12	14,5	1.29	0,14	2.71	<0.05
4th	14,0*	1.17	0,15	14,7	1.31	0,16	3.19	<0.01
3000 m run, min, s								
1st	14.14	0.59	0.21	14.15	1.03	0.27	0.03	>0.05
2nd	14.01	1.08	0.24	14.06	1.07	0.29	0.13	>0.05
3rd	13.46	1.05	0.31	14.11	1.12	0.21	1.74	>0.05
4th	13.38*	0.57	0.28	14.15	1.09	0.23	2.12	<0.05
4 x 9 m shuttle run, s								
1st	9.35	0.51	0.11	9.65	0.42	0.12	1.84	>0.05
2nd	9.20	0.48	0.09	9.56	0.58	0.14	2.14	<0.05
3rd	9.26	0.52	0.15	9.67	0.54	0.11	2.20	<0.05
4th	9.18	0.56	0.13	9.69	0.56	0.13	2.77	<0.05
Standing long jump, cm								
1st	218.5	19.84	2.17	220.5	19.21	2.15	0.66	>0.05
2nd	223.7	18.93	2.09	224.9	18.76	2.19	0.39	>0.05
3rd	228.2	19.16	1.98	223.5	18.39	2.08	1.62	>0.05
4th	231.3***	18.91	1.79	219.8	19.91	1.96	4.30	<0.001
Pull-ups on the crossbar, number of times								
1st	11.8	3.41	0.96	11.5	2.81	0.89	0.23	>0.05
2nd	12.5	3.48	1.07	12.7	4.43	0.83	0.15	>0.05
3rd	12.8	4.01	1.13	12.5	3.91	0.75	0.22	>0.05
4th	13.6	3.85	1.32	11.9	4.14	0.67	1.15	>0.05
Lifting torso to the sitting position for 1 minute, number of times								
1st	43.2	5.78	1.47	43.7	6.72	1.89	0.21	>0.05
2nd	45.6	6.37	1.48	46.0	6.29	2.01	0.16	>0.05
3rd	47.8	7.09	1.82	45.3	5.83	1.73	1.00	>0.05
4th	49.7**	6.96	1.67	44.2	6.08	1.86	2.20	<0.05
Torso leaning forward from the sitting position, cm								
1st	13.3	5.21	0.91	12.4	4.84	0.98	0.67	>0.05
2nd	14.2	5.67	1.30	12.6	4.91	1.32	0.86	>0.05
3rd	15.5	6.03	1.22	12.3	5.07	1.43	1.70	>0.05
4th	16.2*	5.85	1.09	11.9	4.95	1.51	2.31	<0.05

Notes: X – arithmetic mean, σ – mean-square deviation, m – error of the mean-square deviation, t – value of the Student's test, p – significance of the difference between the indicators of students of different HEIs, * – significance of the difference betweenthe indicators of the 1st and the 4th instructional years at $p < 0.05$, ** – at $p < 0.01$, *** – at $p < 0.001$

opportunities to engage in the chosen sport as the factor that causes dissatisfaction with the content of physical education training sessions. 43.3 % of DNU students and 56.6 % of PSACEA students are satisfied with the quality of organization of fitness and health recreation as well as sports events during extracurricular activities. According to the results of the survey, 43.3 % of DNU students and 33.3 % of PSACEA students regularly engage in physical

Table III. Dynamics of indicators of physical development of female students during their study in the HEI (n = 60)

Instructional year	DNU (n=30)			PSACEA (n=30)			Significance of the difference	
	X	σ	m	X	σ	m	t	p
100 m run, s								
1st	17.3	1.17	0.25	17.4	1.16	0.19	0.32	>0.05
2nd	17.1	1.21	0.31	17.1	1.13	0.21	0.01	>0.05
3rd	16.9	1.19	0.24	17.1	1.18	0.23	0.60	>0.05
4th	16.8	1.22	0.22	17.2	1.14	0.18	1.41	>0.05
2000 m run, min, s								
1st	11.55	0.59	0.35	11.57	1.01	0.26	0.05	>0.05
2nd	11.46	0.57	0.29	11.49	0.58	0.24	0.08	>0.05
3rd	11.32	0.54	0.27	11.55	1.04	0.27	0.60	>0.05
4th	11.24	0.56	0.28	11.59	1.02	0.31	0.84	>0.05
4 x 9 m shuttle run, s								
1st	11.1	0.53	0.13	11.0	0.48	0.11	0.59	>0.05
2nd	11.1	0.48	0.12	10.8	0.53	0.14	1.63	>0.05
3rd	11.0	0.46	0.16	11.1	0.58	0.15	0.41	>0.05
4th	10.8	0.51	0.14	11.2	0.61	0.13	2.09	<0.05
Standing long jump, cm								
1st	165.5	13.89	1.87	165.8	13.48	1.79	0.12	>0.05
2nd	169.8	14.01	1.93	170.7	13.76	1.86	0.34	>0.05
3rd	171.9	14.17	1.91	168.3	13.84	1.91	1.33	>0.05
4th	172.2*	14.28	1.89	166.1	13.65	1.94	2.25	<0.05
Push-ups, number of times								
1st	14.8	3.41	0.69	14.6	2.82	0.56	0.23	>0.05
2nd	15.6	5.54	1.01	15.3	4.39	0.81	0.24	>0.05
3rd	17.6	4.49	1.02	15.1	4.56	0.90	1.84	>0.05
4th	18.1*	5.38	1.10	14.2	4.18	0.89	2.76	<0.05
Lifting torso to the sitting position for 1 minute, number of times								
1st	35.7	6.59	1.76	37.8	6.97	1.69	0.86	>0.05
2nd	39.1	6.73	1.82	40.9	7.02	1.76	0.71	>0.05
3rd	44.7	6.91	1.78	40.3	6.89	1.74	1.77	>0.05
4th	48.8***	7.11	1.91	38.8	7.12	1.77	3.84	<0.01
Torso leaning forward from the sitting position, cm								
1st	14.3	5.13	0.93	14.2	4.67	0.81	0.08	>0.05
2nd	15.8	5.19	0.96	14.9	6.02	1.12	0.61	>0.05
3rd	17.3	6.11	0.91	14.9	5.97	1.08	1.70	>0.05
4th	18.9**	5.76	0.89	14.6	5.89	1.11	3.02	<0.01

Notes: X – arithmetic mean, σ – mean-square deviation, m – error of the mean-square deviation, t – value of the Student's test, p – significance of the difference between the indicators of students of different HEIs, * – significance of the difference betweenthe indicators of the 1st and the 4th instructional years at $p < 0.05$, ** – at $p < 0.01$, *** – at $p < 0.001$

exercises and sports during extracurricular activities. At the same time, the majority of students of DNU and PSACEA prefer independent physical exercises (50 % and 43.3 %, respectively), and only a small part of students prefer to engage in physical exercises during training sessions and on the basis of their HEI during extracurricular activities. These results indicate the need on the one hand to improve the system of fitness and health recreation as well as sporting and mass participation events during extracurricular activities, and on the other – to pay more attention to the issues of rational planning of independent physical exercises during extracurricular activities. The most important

reasons that motivate students of both HEIs to exercise include strengthening health, improving appearance and knowledge of the benefits of training sessions. However, the number of DNU students who indicated that they were motivated to exercise by knowledge about their benefits significantly exceeds the number of PSACEA students (63.3 % compared to 43.3 %). This fact indicates that DNU gives more attention to the formation of knowledge about the benefits of exercise. The need to take a pass / fail exam in physical education also stimulates students of DNU to a greater extent than students of PSACEA (66.6 % and 38.3 %), which indicates higher requirements for students.

The results of the comparative analysis of indicators of physical development of students of both HEIs for the period of their study are given in Table II (men) and Table III (women).

The analysis of indicators shows that there were no statistically significant differences in physical development indicators for all tests ($p > 0.05$) during the first instructional year of male students of DNU and PSACEA. At the beginning of the research, the development of strength, agility and flexibility of students in both HEIs corresponded to the average level, and endurance and speed – low. During the period of study, there were some changes in the indicators of physical development of students of both HEIs, but the nature of these changes differs significantly depending on the organizational and methodological conditions of building a system of physical education in each of the HEIs. Thus, DNU students showed a significant ($p < 0.05$-0.001) improvement in most of the studied indicators in the learning process, and PSACEA students found no statistically significant changes in test results during their study period ($p > 0.05$), and even from the third instructional year there is a tendency to deterioration of the results of all tests that were determined during the study. The analysis of the results of the 100 m run showed that the students of DNU showed a significant improvement in the results of the 100 m run by 0.4 s ($p < 0.05$) during the period of their study. At the same time, the level of speed qualities of DNU students was significantly better than in the students of PSACEA by 0.5 ($p < 0.05$) and 0.7 ($p < 0.01$) seconds during the third and the fourth instructional years. The results of the 3000 m run for DNU students significantly improved from the first to the fourth instructional year by 36 seconds ($p < 0.05$). There was also a significantly better level of endurance during the fourth instructional year in DNU students compared to PSACEA students by 37 seconds ($p < 0.05$). The level of agility, which was assessed by "4 x 9 m shuttle run" test, was also significantly better in DNU students at the end of the research than in PSACEA students by 0.51 seconds ($p < 0.05$). The difference between the indicators of the development of speed and strength qualities of the students of the two HEIs, which were tested by standing long jumps, results in 11.5 cm in favour of DNU students and is significant ($p < 0.001$). No significant difference was found ($p > 0.05$) in the pull-ups on the crossbar during any of the instructional years. The results of lifting torso to the sitting position for 1 minute during the fourth instructional year showed that the level of development of the strength of the abdominal muscles was significantly better in DNU students than in the students of PSACEA, by times ($p < 0.05$). According to the indicators of flexibility tested by "Torso leaning forward from the sitting position" exercise, the students of DNU showed significantly better indicators than the students of PSACEA during the fourth instructional year, by 4.3 cm ($p < 0.05$).

Similar trends were observed in the indicators of physical fitness of female students (Table III). As in men, the groups of female students of different HEIs did not have statistically significant differences in the indicators of physical development ($p > 0.05$) during the first instructional year. According to the obtained data, there were no statistically significant changes in the indicators of development of speed, endurance and agility in the girls of both HEIs from the first to the fourth instructional years ($p > 0.05$). An increase in performance was determined in DNU female students according to such tests as "Standing long jump", "Push-ups", "Lifting torso to the sitting position for 1 minute" and "Torso leaning forward from the sitting position", which turned out to be significantly better during the fourth instructional year than the first one ($p < 0.05$-0.001). PSACEA students did not show statistically significant differences in the studied indicators ($p > 0.05$) during the entire study period, with some tendency to deteriorate in all tests used in our research.

The comparative analysis of the indicators of physical development of students of the studied HEIs shows that the results in the 100 m and 2000 m run during the fourth year of DNU students were better compared to the results of PSACEA students by 0.4 seconds and 25 seconds, respectively, but no significant difference was found ($p > 0.05$). The indicators of development of agility ("4 x 9 m shuttle run") and speed and strength qualities ("Standing long jump") of the students of DNU during the fourth instructional year turned out to be significantly better than in the students of PSACEA, by 0.4 seconds and 6.1 centimetres, respectively. $p < 0.05$). DNU students of the fourth instructional year also showed significantly better results than PSACEAstudents according to the strength exercises ("Push-ups" and "Lifting torso to the sitting position for 1 minute"), by 3.9 times ($p < 0.05$) and 10 times ($p < 0.01$), respectively. DNU students also showed better results compared to the students of PSACEAat the end of their study in terms of the indicators of flexibility ("Torso leaning forward from the sitting position"): the difference is 4.3 cm and is significant ($p < 0.01$).

DISCUSSION

The main task of the system of physical education in the HEI is the formation of students' motivational and value attitude to physical culture, the need for regular exercise and sports. Health is the priority of physical education training sessions with students [9, 10]. However, many studies have shown a significant deterioration in the health, physical development

and physical fitness of Ukrainian students [11, 12]. In addition, many scientists [13, 14] point to a direct relationship between an increase in the number of students with a low level of physical fitness (physical development) and a deterioration in their physical health, especially in endurance tests. Thus, according to scientists, 100 % of students who have a low level of physical development, such motor skills as general endurance, speed, agility, strength endurance and flexibility are outside the safe level of physical health, which indicates a direct relationship between the state of health and the level of physical development and fitness of students [15].

During the period of students' study the HEI should be one of the systems of purposeful influence on solving the problem of reducing diseases and ensuring a high level of health and physical development of student youth. Therefore, it is necessary to create and maintain such an environment, such organizational and methodological conditions in the HEI that will promote the formation of goals, values, principles of healthy lifestyles and control over the factors that determine or affect the student's health as well as his / her physical development and fitness.

Our analysis of the dynamics of the indicators of physical development of students of the two HEIs, which organizational and methodological conditions for building a system of physical education have some differences, showed that the students of DNU (both men and women), where physical education training sessions are held throughout the entire period of study, revealed better indicators of physical development at the end of their study (during the fourth instructional year) than the students of PSACEA, according to all tests. At the same time, the dynamics of all studied indicators of DNU students is positive during their study in the HEI (from the first to the fourth instructional year), and the indicators of PSACEA students improve up to the second instructional year, and deteriorate from the third to the fourth instructional year occasionally even to the ones of first instructional year. All this testifies to the significant influence of organizational and methodological conditions of the functioning of the system of physical education in the HEI on the indicators of physical development of students in the learning process. Our research confirms the scientific achievements of many scientists [16-18] and expands them.

CONCLUSIONS

1. The efficiency of the functioning of the system of physical education in each of the two HEIs was analysed and it was found out that the organizational and methodological conditions of each of them differ in the duration of "Physical Education" academic subject depending on the instructional year, the number of academic hours provided for the subject mastery; approaches to the basic and elective components of the curriculum; sports as well as fitness and health recreation systems presented in the curriculum; organization of fitness and health recreation as well as sports events during extracurricular activities.
2. The attitude of students to the existing system of physical education in the HEI was studied and the level of their motivation to engage in physical exercises and sports within academic and extracurricular hours was determined. It was found that among the factors that motivate students to exercise, the most important for students of both HEIs are: strengthening health, improving appearance and knowledge of the benefits of training sessions. The opportunity to engage in the chosen sport was among the factors that cause dissatisfaction with the content of physical education training sessions. 43.3 % of DNU students and 33.3 % of PSACEA students regularly engage in physical exercises and sports during extracurricular activities. The need to take a pass / fail exam in physical education also stimulates students of DNU to a greater extent than the students of PSACEA (66.6 % and 38.3 %), which indicates higher requirements for students.
3. The dynamics of the indicators of physical development of students of the two HEIs was studied and it was established that the level of physical development of students (both men and women) is better in the HEI where "Physical Education" academic subject is studied during the entire instructional period (DNU), unlike PSACEA where training sessions are held only during the first and the second instructional years. According to the majority of the studied indicators, the indicators of DNU students were significantly ($p < 0.05$-0.001) better than those of PSACEA students at the end of the research.

Prospects for further research are to study the health indicators of HEIs students with different organizational conditions for the functioning of the physical education system.

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ORCID and contributionship:
Grygoriy P. Griban: 0000-0002-9049-1485[A]
Olena O. Kosheleva: 0000-0002-9085-6800[B,D]
Olena O. Mitova: 0000-0002-4309-9261[B,F]
Alla M. Harlinska: 0000-0001-7859-8637[C]
Olena V. Solodovnyk: 0000-0001-6151-4353[D]
Bogdan S. Semeniv: 0000-0002-8302-1389[F]
Kostiantyn V. Prontenko: 0000-0002-0588-8753[E]

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CORRESPONDING AUTHOR
Grygoriy P. Griban
Zhytomyr Ivan Franko State University
40 Velyka Berdichivska St., 10002 Zhytomyr, Ukraine.
tel: +380973341092
e-mail: gribang@ukr.net

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ORIGINAL ARTICLE

EPIDEMIOLOGICAL SITUATION OF PRE-CANCER DISEASES OF THE ORAL MUCOUS IN UKRAINE

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Yulia G. Kolenko, Tetiana O. Timokhina, Olesya V. Lynovytska, Konstantin O. Mialkivskyi, Nina S. Khrol
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To conduct a prospective clinical study to assess the prevalence, structure, risk factors and features of clinical manifestations of precancerous diseases of oral mucosa and red lip in Kyiv residents and to analyze opportunities to improve the quality of their primary diagnosis.

Materials and methods: The examination of 423 patients with precancerous diseases of oral mucosa and red lip included clarification of the main complaints and anamnesis of the disease, objective assessment of the state of oral mucosa and red border of the lips according to visual, stomatoscopic, luminescent analysis, cyto-, histological studies.

Results: Attention is drawn to the prevalence among precancerous diseases of patients with leukoplakia - 41.37% and lichen planus - 44.21%. The levels of detection of precancerous diseases of the oral mucosa due to the current and preliminary history for individual nosological forms are almost identical, which indicates the reliability of the above indicators.

Conclusions: Promotion between the people about timely dental treatment for precancerous diseases of the oral mocosa and the use of radical technologies in their treatment will not only increase the effectiveness of treatment, but significantly limit the malignancy of these diseases.

KEY WORDS: oral mucosa, red border of the lips, precancerous diseases, primary diagnosis

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INTRODUCTION

The fight against malignant neoplasms is currently not only one of the most important problems of medicine, but also a very topical issue of the social life of society, since among the causes of death of the population in industrialized countries, malignant neoplasms occupy the 2nd–3rd place [1, 2].

Oral mucosal (OM) cancer accounts for 40% of all head and neck variations cancers [3] and 1–3.5% of all malignant tumors, and takes second place after laryngeal cancer [3, 4]. Latest figures show that around 6,000 new cases of mouth cancer a year are diagnosed in the Ukraine, 360 to 400 of which in Kyiv.

The standardized incidence rate per 100,000 population in Ukraine in 2007 was 2.7, including 2.4 in Kyiv. At first glance, the incidence rate is relatively low. At the same time, over the past 15 years, the number of patients with OM tumors has more than doubled, and exceeding 5–7 cases per 100,000 population [5]. However, it should be taken into account that in most patients, cancer of the oral mucosa and otolaryngeal region is diagnostic on late stages - for example, cancer of the oral mucosa, according to some reports diagnostic on late stage in more than 70% of cases. Such late diagnosis, as a rule, requires treatment in the form of complex traumatic surgical interventions, the results of which remain unsatisfactory, since the incidence and mortality from malignant neoplasms of the oral mucosa have a steady upward trend [6, 7].

Therefore, the actual task of dentistry is to increase the effectiveness of measures for the prevention and early diagnosis of cancer of the oral mucosa. In particular, early detection and adequate treatment of diseases such as benign tumors and precancerous diseases of the oral cavity are central [8; 9].

THE AIM

The main objective of the study is to conduct a prospective clinical study to assess the prevalence, structure, risk factors and features of clinical manifestations of precancerous diseases of OM and red lip in Kyiv residents and to analyze opportunities to improve the quality of their primary diagnosis.

MATERIALS AND METHODS

In the period from 2015 to 2020 on the basis of the Department of Therapeutic Dentistry of the National Medical University named after O.O. Bogomolets conducted a comprehensive dental examination and treatment of 423 patients aged 20 to 87 years with precancerous diseases of OMC and red lip.

The clinical examination of OM was performed in accordance with WHO recommendations (Kraemer J.R. et al., 1980). The examination included clarification of the main complaints and anamnesis of the disease, objective assessment of the state of OM and red border of the lips according to visual, stomatoscopic, luminescent analysis, cyto-, histological studies.

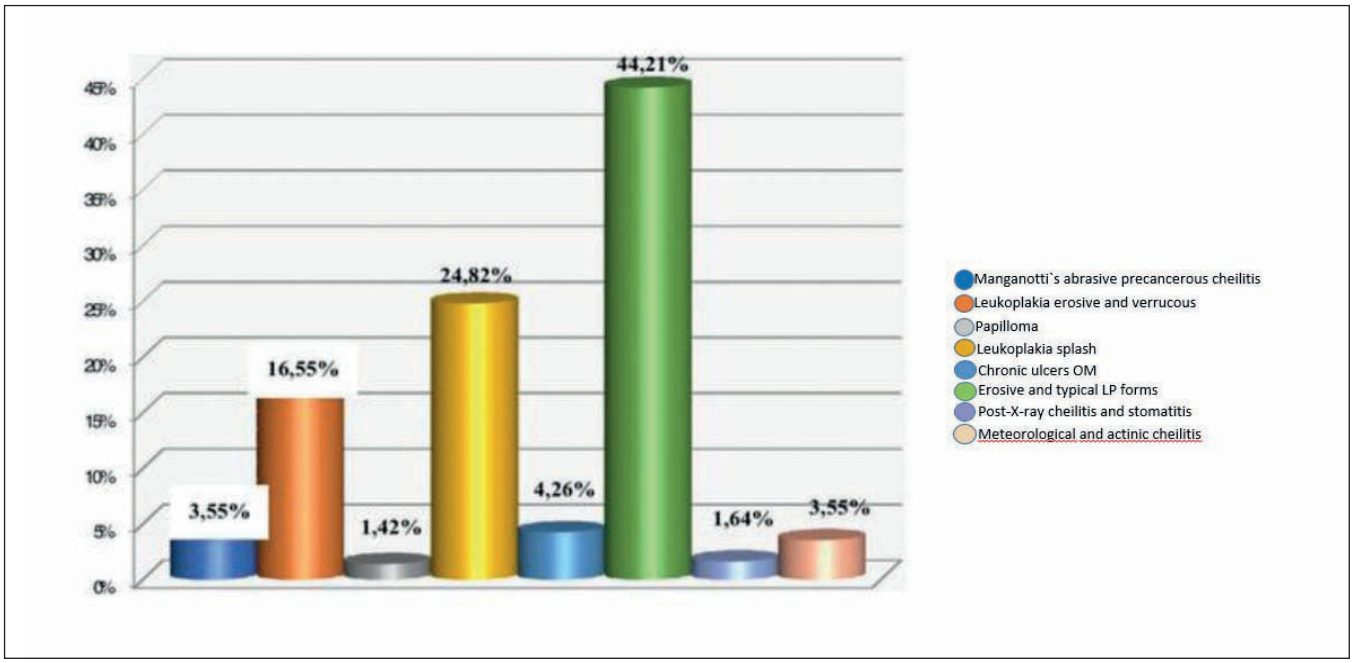

Fig. 1. The frequency of manifestation of precancerous lesions of the oral mucosa

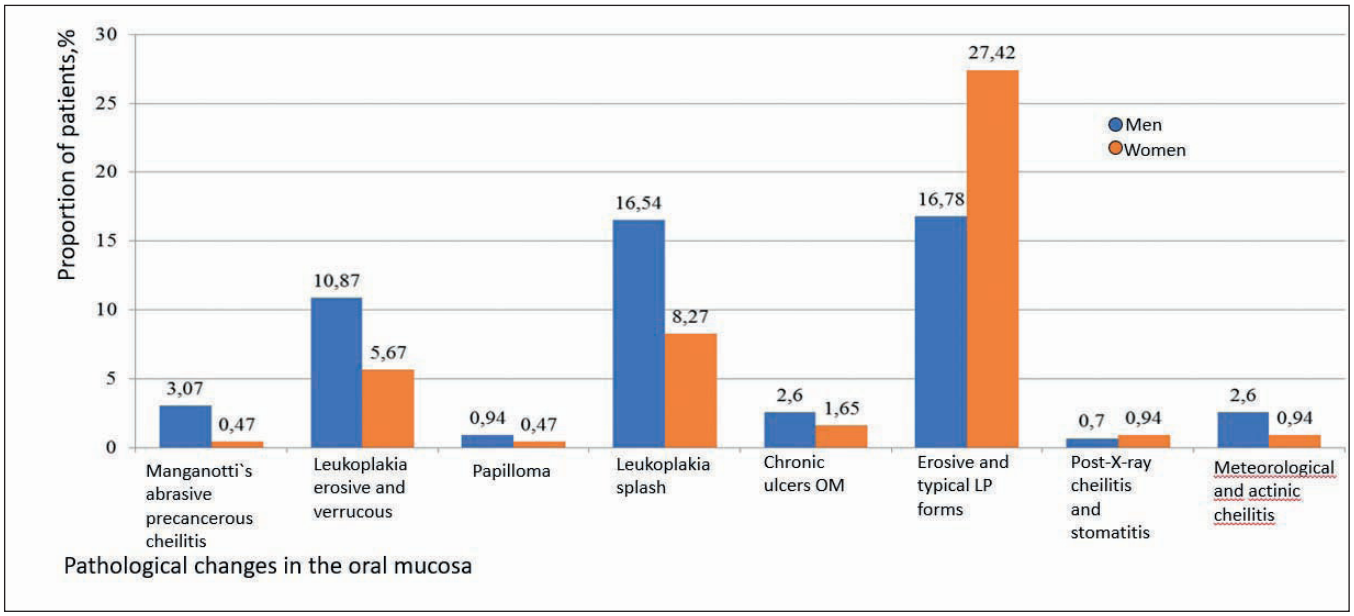

Fig. 2. Distribution of patients with precancerous diseases of oral mucosa by sex

The assessment of the quality of the primary diagnosis of the disease of oral mucosa was carried out by dropping a dental patient from the case histories, referrals from dentists and/or internists, and anamnesis data. Were determined the level (I-IV) of the primary diagnosis of the disease (B. Bates et al., 1997) and completeness of the formulation of the clinical diagnosis, that reflecting the whole variety of diseases of the oral cavity, maxillofacial area and dental diseases that were detected in the patient; was calculated the percentage of under examined patients, cases of overdiagnosis and direct diagnostic errors. Were analyzed the answers from the questionnaires with following blocks of questions: dental turnover, adherence to treatment and attitude to dental care; clinical manifestations of precancerous diseases of oral mucosa; the presence and types of orthopedic structures in the oral cavity; food texture and temperature; nature of brushing teeth; bad habits; the level of knowledge on the prevention of dental diseases.

The results of the study were processed by the method of variation statistics using the indicator by the method of Fisher's angular transformation.

RESULTS

Residents of Kyiv city prevailed (79.5%) among the surveyed, 20.5% of patients lived in different regions of Ukraine. Public dentists (45.5%) or private (23.9%) dental clinics (offices) and specialists from medical institutions (15.3%) were sent for consultations with patients; 15.3% of

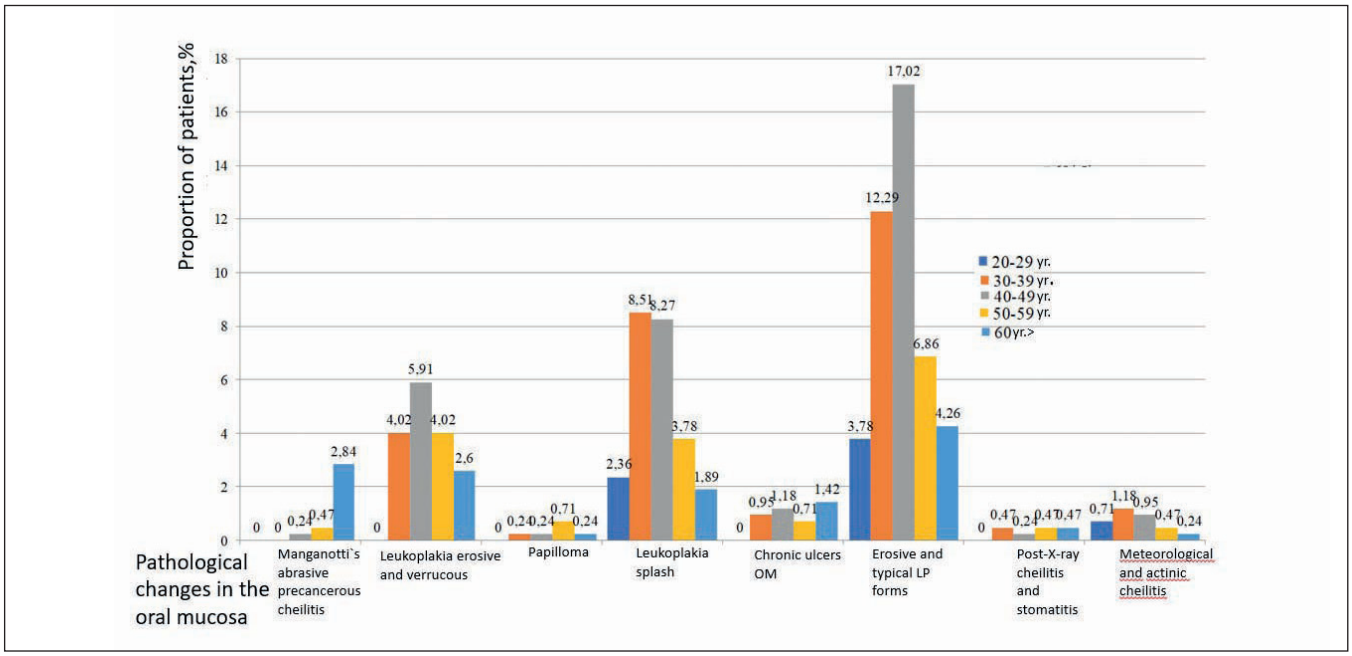

Fig. 3. Distribution of patients with precancerous diseases of oral mucosa by age

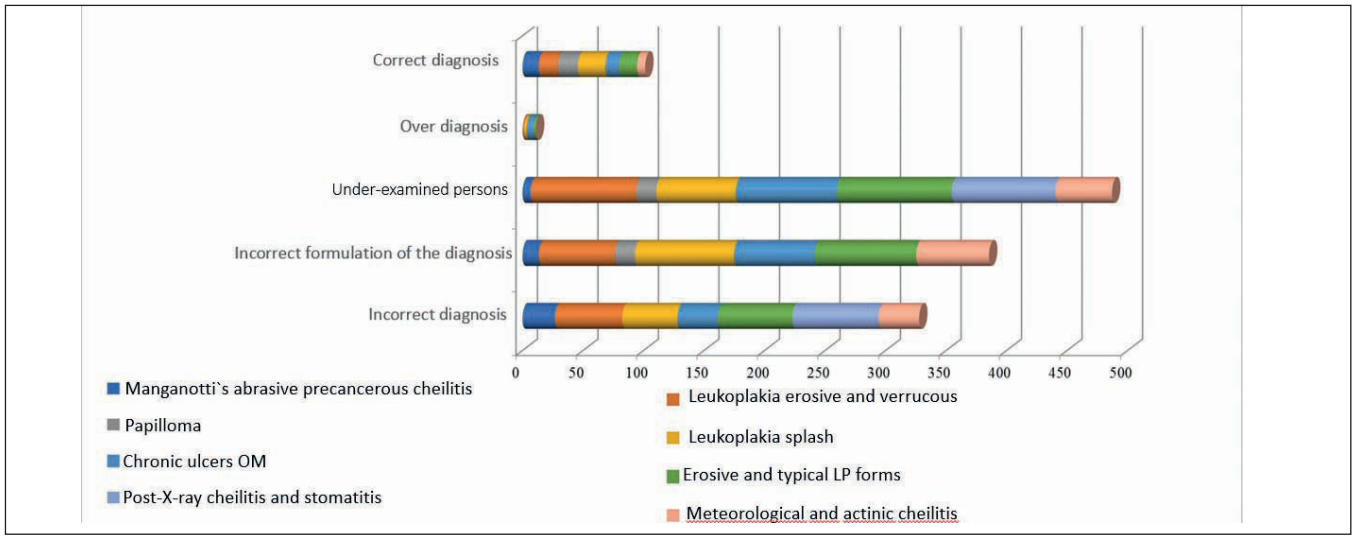

Fig. 4. Indicators that characterizing the level of diagnosis of precancerous diseases of the oral mucosa in dental institutions that referred patients for consultation

patients independently applied for medical and advisory assistance.

The structure and prevalence of precancerous diseases of the oral mucosa, identified as a result of a comprehensive examination of 423 patients, was as follows: erosive and hyperkeratotic (typical) forms of lichen planus - in 187 patients (44.21%), a flat form of leukoplakia - in 105 patients (24.82), erosive and warty (verrucous) leukoplakia - in 70 patients (16.55%), chronic mucosal ulcers - in 18 patients (4.26%), Manganotti's abrasive precancerous cheilitis - in 15 patients (3.55%), meteorological and actinic cheilitis - in 15 patients (3.55 %), post-X-ray cheilitis and stomatitis - in 7 patients (1.64%), papilloma - in 6 patients (1.42%) (Fig. 1). 20 patients (4.51%) were diagnosed with OM cancer.

Prevalence of precancerous diseases of the oral mucosa averages 29.2±1.0%. These diseases have an adverse effect on the dental status of urban residents. In particular, without causing any particular concern, OM diseases had a mild course in 118 out of 423 respondents (28.4 ± 1.8%). They did not seek dental care and self-treated with various dental rinses. In the remaining 305 surveyed diseases, OM had a course in clinical forms, accompanied by various ailments (soreness, mucosal roughness, dryness, etc.), difficulty in chewing food, difficulties in maintaining oral hygiene, and a long course of diseases (up to 14 days). All respondents applied for dental care, but, as a rule, it was already too late. This is probably why 224 out of 423 respondents (52.7 ± 2.4%) were dissatisfied with the quality and effectiveness of their treatment, since subsequently they experienced relapses of the OM, or the formation of new foci in other parts of the mucosa. This led to repeated dental visits and disability.

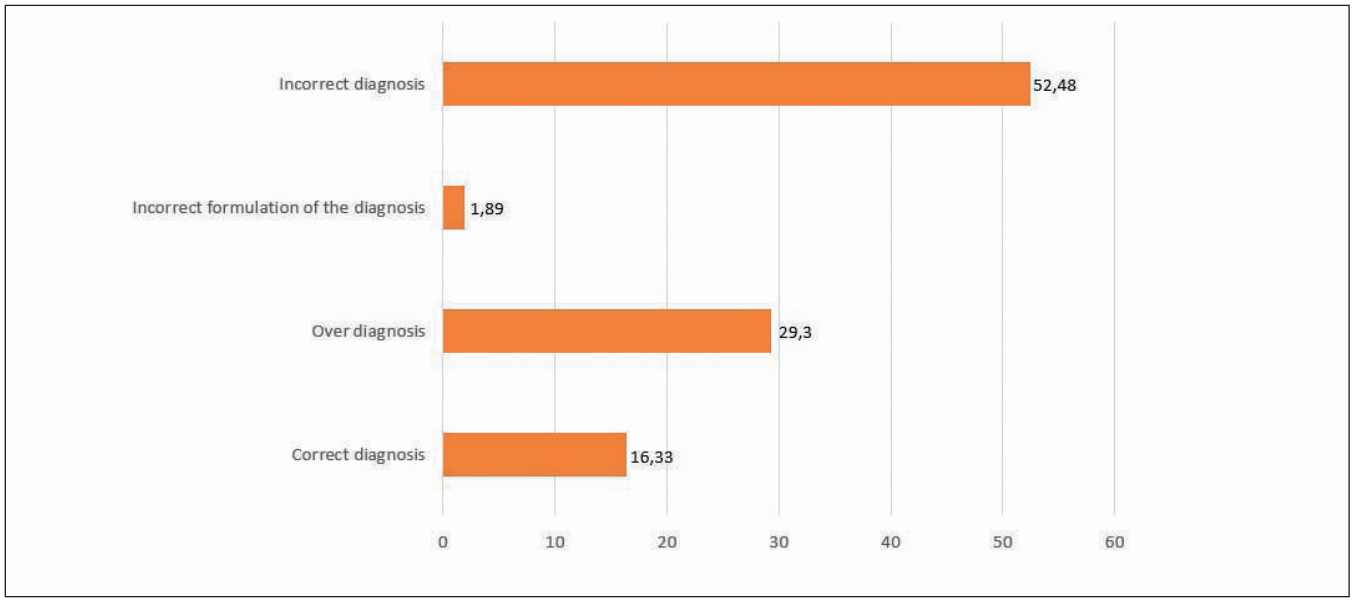

Fig. 5. Indicators that characterizing the general level of diagnosis of precancerous diseases of the OM in dental institutions that referred patients for consultation

There is a pronounced positive correlation between the age of the respondents and the level of OM disease (r=+0.95±0.04). So, if in the group of respondents, whose age did not exceed 20 years, the indicator of the level of OM disease was 16.3 ± 2.5%, then as the age of the respondents increases, it consistently grows and reaches 37.7 ± 4.0% for respondents of age older than 60 years (t=4.53; p<0.001).

Analysis of all the data obtained by questioning allows us to deduce some regularities. The first of them is related to the fact that in 266 out of 423 patients, were found various types of orthopedic structures during examination of the oral cavity (62.6±1.0%). The remaining 157 cases were observed precancerous diseases of the oral mucosa in patients who did not have orthopedic structures (19.3±1.4%; t=8.22; p<0.001). Therefore, with all probability, can be assume that orthopedic constructions injure the oral mucosa, violate its integrity and thereby create the possibility of developing precancerous diseases.

The second pattern is related to the fact that although among men and women with increasing age the level of precancerous diseases of the oral mucosa increases equally, the incidence rate in total among the former is significantly higher than among the others. Thus, cases of precancerous diseases of the oral mucosa were detected in 229 men (54.1±1.4%) and in 194 women (45.9±1.4%; t=4.65; t=4.65; p<0.001) out of 423 examined.

In a comparative analysis of the frequency of detection of precancerous diseases of the oral mucosa, depending on gender, it was found that significantly more often in men were found: leukoplakia (27.70% versus 13.95% in women, p<0.05), abrasive pre-cancerous cheilitis Manganotti (3 08) % versus 0.24% in women, p<0.05), chronic ulcers of the oral mucosa (2.60%, p<0.05). In women, erosive and hyperkeratotic (typical) forms of lichen planus are significantly more common (27.42% versus 16.78% in men, p<0.05) (Fig. 2).

Analysis of the incidence of OM, depending on age, gave the following results. In the group of patients aged 40–49 years, the incidence of erosive and warty forms of leukoplakia was 5.91±0.08%, while among patients aged 50–59 and 30–39 years this figure was 4.02±0. 09%. (p<0.05). Also, the prevalence of erosive and hyperkeratotic (typical) forms of lichen planus was noted in the age group of 40-49 years compared with patients aged 30-39 years, while there were no significant differences in the disease of chronic ulcer of the oral mucosa (Fig. 3).

According to picture 4, most dentists who referred patients for medical counseling made direct errors in the diagnosis of post-X-ray cheilitis and stomatitis (71.43%), lichen planus (61.50%) and leukoplakia (55, 71%) OM. The greatest difficulties in diagnosis were caused by lichen planus (83.96% of misdiagnosis) and flat leukoplakia OM (81.90%). Less frequently, direct errors were made in the diagnosis of chronic ulcers OM (66.67%), erosive and warty (verrucous) leukoplakia (62.86%), meteorological and actinic cheilitis (60.0%). It should be noted the high percentage of under-examined patients (both in terms of dental status and the general condition of patients). Thus, 95.19% of patients with lichen planus were examined, 87.14% - with erosive and warty (verrucous) leukoplakia and 85.71% - with post-X-ray cheilitis and stomatitis. There is a fairly high percentage (5.56%) of cases of over diagnostic of chronic OM ulcers, verified as "new OM".

DISCUSSION

A special place among all diseases of the oral mucosa is occupied by precancerous diseases. Their prevalence is quite high and amounts to 12.5% of all diseases of the oral cavity and 26.6% of all neoplasms of the maxillofacial region [10, 11, 12]. According to WHO, the last decade has been marked by an increase in the prevalence of diseases in this

group and a change in the age structure of the incidence in the direction of increasing the group up to 35 years.

Precancerous diseases of the oral mucosa occur in 10–14% of outpatient dental patients, and the correct diagnosis detected in less than 45–65% of cases [13, 14, 15]. The variety of clinical manifestations of neoplastic diseases of the oral mucosa and the variability of signs of their transformation into a malignant tumor is a reason significant difficulties and errors in the diagnosis and correct choice of treatment tactics and clinical examination of patients [6, 16].

In general, in Ukraine there is a clear upward trend in the incidence of malignant neoplasms of oral mucosa, while detection at stages I-II is only 33.9% of those first registered. This indicates the low effectiveness of measures for the prevention and timely detection of cancer in the outpatient dental treatment network [5].

In this study, attention is drawn to the prevalence among precancerous diseases of patients with leukoplakia - 41.37% and lichen planus - 44.21%. The levels of detection of precancerous diseases of the oral mucosa due to the current and preliminary history for individual nosological forms are almost identical ($t = 2.03$; $p<0.05$), which indicates the reliability of the above indicators (Fig. 1).

Considering that usually precancerous diseases of the OM, as well as cancer in the early stages, have an asymptomatic course, the importance of an integrated approach to their diagnosis, which includes a number of modern planned and emergency types of examination, becomes obvious [7-9, 15]. At the same time, J. Epstein (2008) emphasizes the primary role of primary care physicians and their oncological alertness in screening for precancerous diseases of the oral mucosa and pharynx, which makes it possible to prevent the development of cancer at an early stage [1].

Any disease with damage to the oral mucosa or its change in combination with a long course must be perceived as a potentially dangerous development of cancer of the OM.

When diagnosing diseases of the oral mucosa and lips, only in 30–35% cases showing correct diagnosis [3].

Obtained data analysis showed that in 52.48% of patients with precancerous diseases of the OM, errors were made in the diagnosis (Fig. 4.5). The completeness and correctness of the formulation of the diagnosis, which included the nosological form of the disease, the prevalence of the process indicating the areas of involvement, the stage and nature of the course of the disease, as well as its clinical form, did not meet the necessary requirements in the vast majority of cases (73.52%). In addition, 79.91% of patients were unexamined directly by the dentists themselves and were not referred to doctors of other specialties - none of the referrals, none of the extracts from the case histories contained data on the examination of patients by internists at the time of the examination. The correct diagnosis was made only in 69 patients (16.33%) with precancerous diseases of the oral mucosa (Fig. 5).

Thus, the diagnosis of precancerous diseases of the oral mucosa, carried out in dental institutions, only in 47.52% of cases corresponded to the minimum acceptable (I and II) diagnostic levels, allowing, respectively, to determine the presence of a lesion of the oral mucosa and (or) identify the nosological form of the disease. Qualitative, according to III-IV levels, diagnosis of precancerous diseases of the oral mucosa with the formulation of a complete clinical diagnosis, form, topology, stage and nature of the process, caused difficulties in 73.52% of clinical situations. The low quality of diagnosis of precancerous diseases of the oral mucosa is also confirmed by the high number of unexamined patients (79.91%) and cases of over diagnosis (1.89%); The greatest difficulties in making a diagnosis were caused by post-X-ray cheilitis and stomatitis (71.43%).

CONCLUSIONS

Thus, using a number of diagnostic methods, were found a fairly high prevalence of precancerous diseases of the OM in residents of Ukraine. Among them, the erosive-ulcerative form of lichen planus and the erosive and warty forms of leukoplakia dominate. The prevalence of precancerous diseases, as well as cancer of the oral mucosa, increases with age. In general, it should be emphasized that the results obtained are obviously not conclusive. On the contrary, they indicate the need for a wider introduction into practice of new, modern screening methods for diagnosing precancerous and malignant diseases of the OM.

Presented data allow to recognize that precancerous diseases of the oral mucosa are one of the factors that worsen the dental status of the adult population. In the etiology of these diseases, an important role is played by the age and sex structure of the population, the presence of bad habits, as well as the technological quality of orthopedic structures and restorations.

Promotion between the people about timely dental treatment for precancerous diseases of the OM and the use of radical technologies in their treatment will not only increase the effectiveness of treatment, but significantly limit the malignancy of these diseases.

It was found that only in 16.33% of cases, the diagnosis of precancerous diseases of the oral mucosa, carried out in dental institutions, was of high quality, respectively, III-IV levels of diagnosis of precancerous diseases of the oral mucosa with the formulation of a complete clinical diagnosis, form, topology, stage and nature of the process. This indicates the lack of experience of doctors in the diagnosis of precancerous conditions of the oral mucosa. There are two main prerequisites for the late diagnosis of OM cancer. The first is due to the fault of the patient: delay in doctor visit, that is, only after the appearance of a pronounced pain symptom or after prolonged self-treatment and the absence of a positive effect; the second reason is due to the doctor's fault: the doctor's lack of alertness during the initial contact with the patient, and as a result, long-term treatment without identifying and eliminating the cause of the disease, which worsened the prognosis of treatment results in this situation.

Based on the study, we can conclude that for the early diagnosis of malignant tumors of the oral cavity, it is nec-

essary to carefully collect an anamnesis, focusing on the presence of risk factors for the development of precancerous diseases of the OM. A thorough history taking should be carried out even in the absence of complaints from the patient. Carrying out this stage of the clinical examination of a patient with a precancerous disease will allow early diagnosis of the first signs of its malignancy.

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ORCID and contributionship:
Yulia G. Kolenko: 0000-0003-1659-3333 [A, B, E, F]
Tetiana O. Timokhina: 0000-0002-0220-0220 [A, B, D]
Olesya V. Lynovytska: 0000-0001-6723-6921 [B, C, F]
Konstantin O. Mialkivskyi: 0000-0003-0437-167X [C, D]
Nina S. Khrol: 0000-0001-7317-6590 [E, F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Tetiana O. Timokhina
Bogomolets National Medical University
1 Zoologichna st., 03057 Kyiv, Ukraine
tel:+380961111122
e-mail: tanyatimokhina@gmail.com

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ORIGINAL ARTICLE

HYPERAMMONAEMIA AND COGNITIVE IMPAIRMENT IN EPILEPSY PATIENTS TREATED WITH VALPROIC ACID – PRELIMINARY STUDY

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Elżbieta Ewa Szczygieł-Pilut[1], Anna Zajączkowska-Dutkiewicz[2], Daniel Pilut[3], Jarosław Dutkiewicz[4]
[1]DEPARTMENT OF NEUROLOGY WITH STROKE AND NEUROLOGICAL REHABILITATION SUB-UNIT, JOHN PAUL II SPECIALIST HOSPITAL, CRACOW, POLAND
[2]JOHN PAUL II SPECIALIST HOSPITAL, CRACOW, POLAND
[3]INDIVIDUAL MEDICAL PRACTICE, CRACOW, POLAND
[4]STANISŁAW WYSPIAŃSKI, HIGH-SCHOOL № 8, CRACOW, POLAND

ABSTRACT

The aim: To determine whether VPA pharmacotherapy, mainly in the group of patients using subtherapeutic doses of VPA, could contribute to the occurrence of cognitive impairment.

Materials and methods: The study involved 14 patients: six women and eight men, aged 24 - 77 years (mean SD ± - 52.36±13.71) diagnosed with epilepsy in accordance with the ILAE criteria (International League Against Epilepsy), in whom the main clinical complaint, in addition to poor control of epileptic seizures, were impaired concentration, attention and memory impairment.

Results: Mild cognitive impairment - MCI was diagnosed in 4 patients (28.57%) (3 with elevated ammonia levels, 1 without), in 1 patient (7.14%) there was a mild level of dementia. In only one MCI case, elevated serum concentrations of valproic acid were also recorded. It is very important to highlight that cognitive impairment has never been diagnosed before (prior to VPA therapy) in this group. Of these 5 patients, in four cases, after discontinuation of the drug, an improvement in the clinical condition was achieved. In a patient with mild level dementia, the termination of therapy did not give a similar effect. This proves the possibility of other mechanisms responsible for generating these sometimes irreversible disorders.

Conclusions: Regardless of the dose and concentration of ammonia in blood serum of patients diagnosed with epilepsy, VPA therapy may cause various, significant dysfunctions that significantly impair quality of life.

KEY WORDS: epilepsy, mild cognitive impairment, hyperammonemia

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INTRODUCTION

Hyperammonemia is defined as an increase in the level of ammonia in the blood, without any change in liver enzymes. One of the possible and at the same time relatively common causes of this condition is the use of antiepileptic pharmacotherapy, i.a. valproic acid (VPA). It is estimated, that as much as 25% of adult patients using VPA chronically show isolated and elevated blood ammonia levels [1].

Phenotypically, in hyperammonemia induced by the use of valproic acid, we can deal with various conditions, anywhere from clinically asymptomatic form with subtle deficits of cognitive functions, up to full-blown hyperammonemic encephalopathy manifested by: confusion, disorientation, agitation, irritability, delirium, lethargy, coma or even death. Hyperammonemic encephalopathy is a rare but serious adverse reaction induced by this drug [2, 3]. This idiosyncratic symptomatic dysfunction in most cases is completely reversible after discontinuation of this form of pharmacotherapy [3-6]. However, if it is not detected in a timely manner, it can lead to dramatic consequences [7-10]. The possibility of its occurrence should be taken into account in all patients taking VPA in a situation where the following symptoms occur: drowsiness, lethargy, generalized psychomotor retardation, focal neurological signs (including disturbances in the state of consciousness), or gastrointestinal symptoms.

The clinical picture in the course of hyperammonemia may be difficult to interpret in a group of patients with accompanying behavioral disorders, mental disorders or mental retardation.

In a screening cohort study in adult patients diagnosed with mental retardation, Williams et al. found that 11 out of 19 (58%) patients treated with VPA had different disorders (from mild dysfunctions to lethargy, which was observed in two patients) not previously assigned to this substance [11, 12].

A retrospective analysis of 2700 patients treated with VPA shows that ammonia in the blood increases depending on the dose of the drug and is elevated in patients when used simultaneously with liver enzyme inducers (phenytoin, phenobarbital, carbamazepine) [13]. It is also worth paying attention to the standard level ranges of ammonia, which are still being discussed. Some experts give acceptable levels as low as 30 μmol/L and as high as 60 μmol/L,

in spite of the clinical manifestation possibly remaining undetectable at higher values. With regard to hepatic encephalopathy, the predominance of arterial ammonia over venous ammonia was confirmed. Ammonia concentrations in the arteries are higher than in the veins, which translates into different reference values [14].

Such a compound freely penetrates the blood-brain barrier using glutamine synthetase, available only for glial cells. Ammonia has a toxic effect on the central nervous system, the brain is only to a negligible extent involved in its metabolism [15]. The concentration of ammonia in the brain is usually two times higher than in arterial blood [16]. Central nervous system inflammation, noted in hyperammonemia is associated with osmotic oedema of astrocytes, secondary to intracellular accumulation of glutamine. In most patients with suspected hyperammonemic encephalopathy, serum glutamine levels or cerebrospinal fluid are elevated (especially initially), sometimes this condition is noted even in the absence of an elevation of concentration in serum ammonia. The level of glutamine in serum or cerebrospinal fluid may therefore be a useful and an additional laboratory test in the diagnosis of this encephalopathy [17].

High doses of VPA can also increase GABA levels in the brain, disrupting indirect metabolism, possibly at the level of medium-chain acetyl-CoA. Mitochondrial acetyl-CoA depletion and reduced production of N-acetylglutamate, a mandatory activator of the first urea cycle enzyme, carbamyl phosphate I (CPS1) synthetase, occurs. Inhibition of N-acetylglutamate leads to systemic disturbances and increase in the level of ammonia in the blood [18]. Changes in GABA levels in the brain, however, do not correlate with anticonvulsant activity [19].

A positive correlation between plasma VPA was also found relative to total bilirubin levels, which increased mainly in the first four months of treatment [19].

Hyperammonemic encephalopathy associated with VPA therapy may appear at normal (venous) ammonia levels [14]. In this group of patients, the increase in serum glutamine levels or cerebrospinal fluid is similar to that observed in patients with hyperammonemia and indicates a similar metabolic mechanism [14].

Risk factors for VPA-induced hyperammonemia include: concomitant use of topiramate, polypragmasia (including psychotropic drugs), drug interactions, urea cycle disorder, intellectual disability, VPA dose size (> 20 mg/kg body weight/day), patient age, alcohol, poor nutritional status leading to L-carnitine deficiency, general catabolic status, comorbid medical problems [13, 20-23]. These factors have been divided into genetic and acquired.

Among the genetic factors in the population of patients with epilepsy, both carriers of the rs1047891-A allele and independent levels of HDL, cholesterol and homocysteine have a negative impact on its development [24].

The association between the T1405 polymorphism was also documented in Caucasian patients diagnosed with epilepsy, in whom the duration of VPA therapy was at least 1 year, while liver tests and plasma levels of the drug were adequate [21].

The genetic basis of this disease entity was also noticed by the Japanese researcher Yagi M et al. in 2010, who in addition to emphasizing the fact of a possible notable increase in serum ammonia levels correlated with an increase in aspartate aminotransferase levels, also drew attention to the fact that the addition of two or more antiepileptic drugs with VPA and the heterozygous or homozygous carrier state of allele A of the CPS 14217 C> A polymorphism are independent risk factors for the development of this disease [20].

Termination of VPA therapy is the primary treatment for drug-induced hyperammonemic encephalopathy, although L-carnitine, lactulose, citrulline, metronidazole or neomycin have also been successfully used [21-23, 25].

Recognized as two of the most common drugs in its treatment are: lactulose and L-carnitine. Lactulose improves the diffusion of ammonia (NH_3) from the blood to the intestines, where it is converted to ammonium (NH_4^+ occurs), which causes an osmotic effect in the colon, conducive to the removal of unnecessary substances from the body [21].

L-corinth is often considered an antidote to acute or chronic valproic acid poisoning, but it is not a therapeutic option for the treatment of adults with adverse effects resulting from the use of this substance.

In relation to lactulose and L-carnitine, there have been repeated attempts to determine the superiority of the use of one substance over another, but reports on this issue are inconclusive [14, 20, 26].

THE AIM

The aim of the study was to determine whether the pharmacotherapy of VPA, mainly in the group of patients using its subtherapeutic doses, could contribute to the occurrence of cognitive impairment.

MATERIALS AND METHODS

This study was completed in a community hospital, and patients were retrospectively identified from June 1, 2011 to June 30, 2016, and accounted for whether they had been admitted to a psychiatric ward, received at least 1 dose of VPA, and had at least 1 level of ammonia taken at admission. Hyperammonemia was defined as greater than 47 μmol/L, and symptomatic hyperammonemia was defined based on specific symptoms. The treatment method was successful if the ammonia level was within the normal range at discharge. The result of the 357 patients studied, 347 patients met all the criteria for inclusion in the analysis. The reported incidence of hyperammonemia was 36%, with 43.2% of patients with symptoms. Lactulose initiation was the most frequently chosen treatment method (48.7%). VPA discontinuation was the most effective treatment (success rate 56.3%).

We present an analysis of 14 patients hospitalized in the Department of Neurology of the John Paul II Specialist Hospital in Cracow, including six women and eight men, aged 24-77 years (average ± SD - 52.36±13.71) with diag-

nosed focal epilepsy (8 patients) and generalized epilepsy (6 patients), according to the ILAE criteria (International League Against Epilepsy), over at least 12 months period. In the study that has lasted 12 months, patients were recruited from a larger pool of subjects diagnosed with epilepsy, were later admitted to the Department of Neurology and taking VPA in mono or polytherapy in the ranges between 900 mg and 2000 mg (mean ± SD- 1292.86±412.24) and L-carnitine in the ranges between 300mg and 900 mg, in whom the main clinical complaint in addition to poor control of epileptic seizures, were impaired concentration and attention and memory impairment (Table I).

The main criterion qualifying patients for the study was the diagnosis of epilepsy and a positive history of impaired concentration, attention and memory impairment.

Patients hospitalized in the ward with diagnosed epilepsy and a negative history of cognitive disorders, were initially excluded from the study. Based on an interview with patients and their families, each patient was initially qualified for the study as a patient with a positive history of cognitive dysfunction. Each of these patients were examined by a clinical neuropsychologist for the purpose of medical verification of this diagnosis.

Patients with renal insufficiency, liver failure, malignant neoplasms of the brain and meninges, infectious diseases transmitted by droplets, severe intellectual disabilities 34-20 Weschsler IQ and with severe psychotic disorders, pregnant women, breastfeeding and planning pregnancy, were excluded from the study. The study also excluded all patients who, in the neuropsychologic study preceding the implementation of VPA treatment, were diagnosed with cognitive impairment or dementia of any degree.

The following criteria were used in the assessment of patients' cognitive dysfunction: Mini Mental State Examination Test, J. Stroop's Color Word Test, Rey Complex, Figure Test, Wechsler Memory Scale, WCST: (Wisconsin Card Sorting Test), ACER screening test. Tests were performed by a clinical neuropsychologist.

In all patients, brain imaging was performed, i.e.: computed tomography (CT), magnetic resonance imaging (MRI), electroencephalographic examination (EEG) while the patients were alert, neuropsychological examination.

Each patient gave informed and voluntary consent to participate in the study. 5 ml of venous blood was drawn from each patient to analyse the concentration of ammonia and valproic acid. Blood samples were taken from the cubital fossa 0.5 hours before administration of the next morning dose. The study was not presented at the Bioethics Committee meeting.

The lack of this procedure was due to the fact that these procedures were performed as part of a standard procedure during hospitalization in the department of neurology.

VPA concentration determinations were performed using the spectrophotometric method in the commercially available CEDIA® Valproic Acid II Assay test (Thermo Scientific company) in the analytical laboratory of the John Paul II Specialist Hospital in Cracow. The sensitivity of the CEDIA VPA test was 3.0 μg/ml (20.8 μmol/L). The range of therapeutic concentrations of VPA in plasma at steady state was assumed at the level of 50-100 mg / L.

The range of ammonia concentrations in women was assumed 10 – 50 μg / ml and in men 15 – 60 μg / ml.

Distribution of antiepileptic drugs in the study group is presented in table II.

RESULTS

In the study group, seven patients (50%) had a serum VPA level within normal limits, one patient (7.14%) had elevated levels, and in other cases (42.86%) it was reduced. The VPA level was in the range of 16.9 - 104 μg/mL (mean ± SD - 61.13±23.14). Ammonia concentrations ranged from 31 to 100 umol/L (mean SD ±, 53.42±16.80), 6 patients (42.85 %: 4F-28.57%, 2M-14.28%) had elevated levels, in 1 case also correlated with elevated serum concentration of VPA.

In the neuropsychological examination, mild cognitive impairment was found in 4 patients (28.57%) (3 with elevated ammonia levels, 1 without), while 1 patient (7.14%) was found to have a mild degree of dementia (Fig. 1, 2). In a patient with toxic serum VPA concentrations, a decision was made to gradually discontinue it, most likely resulting in an improvement in cognitive functions in a controlled neuropsychological examination (postponed by 6 months from the discontinuation of the drug). However, in a patient diagnosed with mild dementia after discontinuation of VPA and switching to LEV, no improvement was achieved in a controlled neuropsychological examination. In the remaining 3 cases, the VPA dose was reduced, which in turn, resulted in delayed response of normal serum ammonia concentration and cognitive improvement, confirmed in a controlled neuropsychological examination.

Electroencephalographic examination for all patients with cognitive decline and dementia, showed a slight generalized decrease in baseline rhythm. In the remaining patients, the baseline activity was within the limits of the norm (Fig. 3).

In laboratory studies, two patients with mild cognitive impairment, were found to have liver tests at the upper limit of norms.

DISCUSSION

VPA-induced hyperammonemia is a common, unfavorable phenomenon that every physician using this drug should take into account. Despite many years of experience, the mechanism of its generation is still not fully understood. Similar difficulties will also appear in the case of encephalopathy. It is not always a consequence of the increase in ammonia levels alone. Studies indicate the presence of non-hyperammonemic causes leading to encephalopathy, as in the case with a 21-year-old man receiving sodium valproate, clobazam and phenobarbital to control generalized tonic seizures. Two weeks after the VPA dose escalation, the patient experienced generalized psychomotor slowdown accompanied by gait disorders. The EEG scan recording confirmed encephalopathy. The level of valproate in the

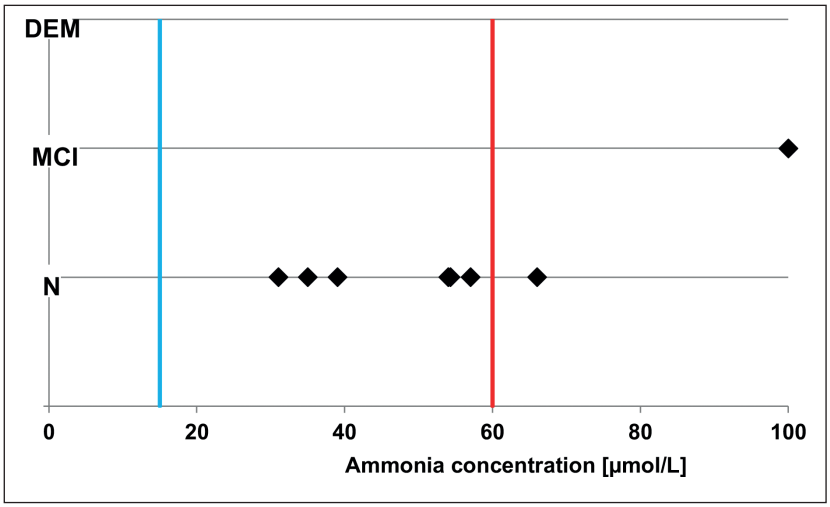

Fig. 1. Dependence of ammonia concentration on cognitive impairment in the group of male patients.
N- Normal
MCI - Mild cognitive impairment
DEM- Dementia

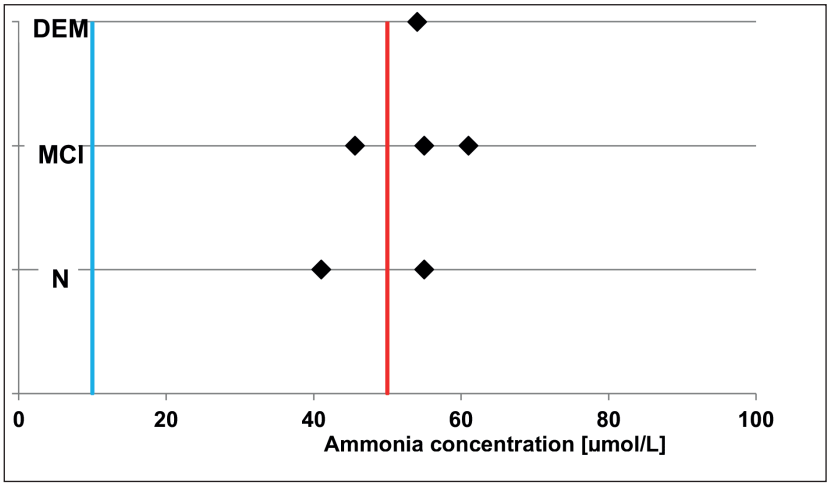

Fig. 2. Dependence of ammonia concentration on cognitive impairment in the group of female patients.
N - Normal
MCI - Mild cognitive impairment
DEM - Dementia

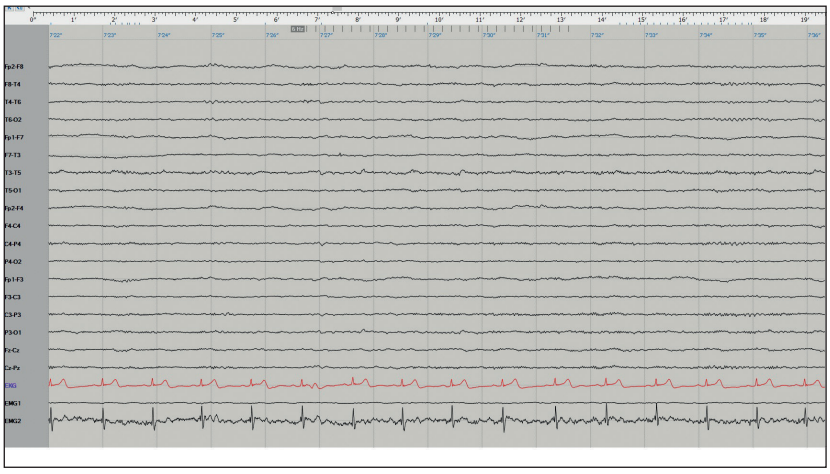

Fig. 3. Electroencephalographic recording in a patient with a slight generalized deceleration of the baseline rhythm

serum was elevated, the level of ammonia was within the limits of the norm. In the patient, the potential causative agent of this VPA dysfunction was discontinued, obtaining an improvement in the clinical condition with simultaneous normalization of the EEG recording. Eventually, the boy was diagnosed with non-hyperthemaemic valproate encephalopathy [27]. In our study, four patients with mild cognitive impairment took similar therapeutic steps to reduce the VPA dose to the one that resulted in normal (necessary in all three cases) serum ammonia concentrations. It also contributed to the achievement of clinical success, i.e. the improvement of cognitive functions. Analyzing these cases from a clinical standpoint, one gets the impression that therapeutically, these decisions were right. In the literature, however, attention is paid not only to the clinical aspect, but also to ammonia levels that significantly exceed the upper limit of the norm. Another study described five adult patients with frontal lobe epilepsy (FLE) who had VPA adverse effects in the form of gate instability accompanied by falls and mild encephalopathy. These symptoms

Table I. Characteristics of the study group.

Patients		
	Mean SD ±	Range
Gender [F/M]	6/8	
Age [years]	52.36±13.71	24-77
Ammonia concentration [µmol/L]	53.42±16.80	31-100
VPA level [µg/mL]	61.13±23.14	16,9-104
VPA p.o. dose [mg/day]	1292.86±412.24	900-2000

LTG - lamotrigine,
LEV - levetiracetam,
TPM - topiramate,
CLN - clonazepam,
PGB - pregabalin,
CBZ - carbamazepine.
Statistical analysis performed with nonparametric tests - chi-square test.

Table II. Distribution of antiepileptic drugs in the study group.

Epilepsy	Medicines
Focal epilepsy	LTG
Generalized epilepsy	-
Generalized epilepsy	-
Focal epilepsy	LEV
Focal epilepsy	TPM, PGB
Generalized epilepsy	-
Focal epilepsy	LEV, CLN
Focal epilepsy	CBZ
Generalized epilepsy	PGB
Focal epilepsy	CBZ
Generalized epilepsy	-
Generalized epilepsy	LEV, CLN, PGB
Focal epilepsy	TPM, LEV, LTG, CLN
Focal epilepsy	-

LTG - lamotrigine,
LEV - levetiracetam,
TPM -topiramate,
CLN - clonazepam,
PGB - pregabalin,
CBZ - carbamazepine.
Statistical analysis performed with nonparametric tests - chi-square test.

developed either after the implementation of the drug (three patients) or after its addition to other antiepileptic drugs (two patients). In all subjects, VPA was within the therapeutic concentration range, serum ammonia levels were significantly elevated (291–407 µmol/l, range 20–85 µmol/l) with normal or slightly higher liver enzymes. Dose reduction or discontinuation of VPA led to a return of ammonia to normal and cessation of clinical symptoms [23].

In May 2019, on the pages of the Japanese magazine Rinsho Shinkeigaku Yamada H et al., published a case report of a 79-year-old female patient treated in antiepileptic monotherapy with valproic acid in a total daily dose of 800 mg, who on the 6th day after the implementation of the drug developed impaired consciousness, cerebral oedema and status epilepticus. The concentration of valproic acid in serum was 128.3 µg/ml and the serum ammonia concentration was 404 µmol/l. In the wake of the above results, the patient underwent continuous hemodiafiltration in combination with L-carnitine for complete clinical improvement [2].

Another example of a 78-year-old woman taking valproate at a dose of 1,000 mg/day for 10 months to treat tonic- clonic seizures was reported in the Epilepsy journal in 2002. In the mentioned patient, the level of ammonia in the blood was 123 microg / dl (norm: 15-50 microg / dl). Due to the possibility of hyperammonemic encephalopathy secondary to VPA, the drug was discontinued, and oral lactulose along with intravenous L-carnitine in a dose of 1 g / day were implemented for treatment. The pharmacotherapy used, resulted in full patient recovery within 48 hours [26].

In 2018, De Michele G et al., published a case of a patient with subacute encephalopathy in the course of 3-month VPA therapy at a relatively low dose of the drug

(800 mg per day). In the neurological examination, the patient was found to have disorders of cranial nerves, impaired gait coordination, increased deep tendon reflexes in four limbs. On the other hand, the MRI examination of the brain depicted subcortical atrophy with features of leukoencephalopathy. The patient's clinical condition improved significantly after discontinuation of this pharmacotherapy [3]. The three studies cited above, as well as our experience, highlight the fact that significant adverse effects of VPA can occur even at subtherapeutic doses.

Regarding clinical approach, the findings of the final treatment of Baddour E et al. in the March 2018 issue of the Journal Mental Health Clinician report, on the analysis of 347 patients treated with VPA, in whom hyperammonemia occurred in 36% of the subjects, from which more than 43% were symptomatic. It is a common agreement that discontinuation of VPA therapy is the most effective treatment method of hyperammonemia, giving an improvement in clinical status in more than half (in 56.3%) of cases [15].

Nakamura et al., however, are of a different opinion. In a prospective analysis of 22 psychiatric subjects treated with VPA continuously, for more than 3 months, with high plasma ammonia concentrations (> 86 µg / dl or 61 µ mol / l) with simultaneous administration of L-carnitine in fixed oral doses, depending on body weight, they have noticed an increase in the level of free carnitine, acylcarnitine and carnitine in general, in the study population. They also noted a statistically insignificant improvement in serum ammonia levels with this pharmacological combination. In summary, they recommended that ammonia levels be measured only in patients treated with VPA with clinical manifestation of the disease and that VPA therapy be discontinued only if the benefits of this effect outweigh the risk of discontinuation of treatment [22].

Chicharro et al. conducted a meta-analysis of 24 studies to review the incidence and association between

VPA-induced hyperammonemia and clinical symptom presentation. The study confirmed that the incidence of hyperammonemia among patients receiving VPA (16% to 100%) varies widely. The authors, just like Nakamura et al. suggested that measuring serum ammonia levels in asymptomatic patients taking VPA is unnecessary and could lead to diagnostic errors. The researchers concluded that VPA therapy should not be discontinued on the basis of isolated hyperammonemia [14].

However, the results of our study are not so promising. Despite five subjects being diagnosed with MCI or mild dementia during VPA therapy, in no case were the measurements of valproic acid or ammonia significantly increased. Nevertheless, not in all cases after VPA treatment discontinuation, clinical improvement was achieved.

This calls into question the mechanism that caused this pathology. Of course, it is worth emphasizing that we excluded the internist-metabolic- endocrine causes of these abnormalities; these patients also did not have a modified combined pharmacotherapy, hence why this data does not evoke full enthusiasm.

The patient diagnosed with mild dementia still remains in our clinical follow-up, and perhaps, a scheduled neuropsychological reassessment in a deferred mode from the end of treatment, will give better test results. In the study group, however, it is worth emphasizing the fact that all the decisions made therapeutically did not contribute to the increase in frequency of epileptic seizures.

Based on this analysis and the studies cited, many issues concerning both the dosage of valproic acid and the determination of its concentration and serum ammonia concentration are still under consideration, it is worth emphasizing the need to unify the procedure on this topic [28, 29]. VPA is a drug known in medicine since the 60s of the last century, widely used not only in neurology, but also in psychiatry, and our knowledge of the potential mechanisms of adverse effects still remains incomplete. Standards of conduct should therefore be established to determine the advisability of carrying out determinations of serum concentrations of ammonia and valproic acid. These measurements, as shown by data from the literature, may help in the interpretation of the clinical condition of many patients with cognitive dysfunctions or gastrointestinal dysfunctions. Regardless of their acute, subacute or chronic nature.

CONCLUSIONS

The results show that many patients with elevated ammonia levels are asymptomatic and therefore, based on findings in the literature, may not require treatment. Although lactulose was found to be the most common initiated treatment, the most effective was the interruption of VPA.

Regardless of the dose and concentration of ammonia in blood serum of patients diagnosed with epilepsy, VPA therapy may cause various, significant dysfunctions that significantly impair quality of life.

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ORCID and contributionship:
Elżbieta Ewa Szczygieł-Pilut: 0000-0002-9290-9312 [A-F]
Anna Zajączkowska-Dutkiewicz: 0000-0002-1303-2074 [C-F]
Daniel Pilut: 0000-0002-8917-6787 [D-F]
Jarosław Dutkiewicz: 0000-0001-6457-6859 [C]

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CORRESPONDING AUTHOR
Elżbieta Ewa Szczygieł-Pilut
Department of Neurology with Stroke and Neurological Rehabilitation Sub-Unit, John Paul II Specialist Hospital, Crakow
Prądnicka 80, 31-202, Cracow, Poland
tel: +48 12 614 20 00
e-mail: eszczygiel@vp.pl

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ORIGINAL ARTICLE

THE FEATURES OF THE NORMAL ULTRASTRUCTURE OF THE RAT DUODENUM AND UNDER THE COMBINED EFFECT OF THE FOOD ADDITIVES COMPLEX

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Galina A. Yeroshenko[1], Alona S. Grygorenko[1], Kostyantyn V. Shevchenko[1], Olga D. Lysachenko[2], Nataliia T. Maksymenko[1], Angela V. Vatsenko[1], Olena V. Klepets[1]

[1]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

[2]POLTAVA V.G. KOROLENKO NATIONAL PEDAGOGICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: Investigation of ultrastructural changes in the elements of rats' duodenal mucosa in norm and exposed to a complex of food additives (monosodium glutamate, sodium nitrite and Ponceau 4R).

Materials and methods: 70 rats of the experimental groups was administered 0.6 mg/kg of sodium nitrite, monosodium glutamate at a dose of 20 mg/kg, Ponceau 4R at a dose of 5 mg/kg in 0.5 ml of distilled water once daily per os. The doses of food additives were twice lower the allowable normal rate in food products. Animals were removed from the experiment at 1, 4, 8, 12 and 16 weeks.

Results: The effect of the complex of food additives on the mucous membrane of the duodenum was manifested by the development of edema and increased local immune response. In the later stages of observation, dystrophic changes in epithelial cells were determined. Vacuoles were found in the cytoplasm.

Conclusions: The use of a complex of food additives led to general ultramicroscopic changes in the mucous membrane of rats' duodenum, triggering the morphological mechanisms of nonspecific inflammation in the form of dystrophic changes and the development of apoptosis.

KEY WORDS: food additivess, duodenum, electrogram, rats

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INTRODUCTION

Food additives are not commonly considered as a food product, though they are supplemented for technological purposes in the production process and as a result become an integral part of them. Adverse reactions to food additives in children have been reported [1], as well as the impact of food additives, artificial sweeteners on the human intestinal microbiome and its ability to ferment fibers [2]. The findings of our study on the content of food additives in domestic and foreign products showed that the most commonly used food additives were monosodium glutamate, sodium nitrite and Ponceau 4R. Recently, the growing use of monosodium glutamate, a well-known food additive (also used in baby food product) and a component of some vaccines is a cause for concern due to its potential impact on human health [3]. It is difficult to find semi-finished or finished products made industrially, which would not have the above additive [4]. A group of Ukrainian researchers have studied the structural and functional changes in the rat large intestine wall under the effect of monosodium glutamate. The findings of the studies have shown that long-term daily consumption of monosodium glutamate, even in safe doses, leads to morphological changes in the colon wall in the form of focal inflammatory changes of the mucous membrane, blood circulation disorders in the intestinal wall, occurrence of erosive ulcers and dysplastic changes [5].

In Ukraine, the food additive E-250 (sodium nitrite) is widely used as a color retainer in the manufacturing of meat products [6]. Chronic exposure to sodium nitrite provokes the development of oxidative stress (increased 2,3-bisphosphoglyceric acid), inflammation (elevated interleukin-1-beta, which, in turn, causes a dramatic rise of iNOS activity), the development of endothelial dysfunction (increased von Willebrand factor) [7].

Ponceau 4R is a colorant of synthetic origin, which has a bright red color. It opens a whole palette of shades: yellow mixed with orange colorants gives brown, and when mixed with blue colorant, Ponceau gives a purple color [8]. No natural colorant has been found to date, demonstrating a problem to be investigated in the future. Noteworthy, although necessary, these substances are responsible for the high frequency of allergic reactions [9, 10].

Current scientific publications elucidate the outcomes of the effects of various food additives on organs and systems; however, insufficient data have been found to date, as previous studies were based on the effects of food additives alone, which does not reveal the full picture, as in practice manufacturers use them in combination.

THE AIM

The paper was aimed at the study of the ultrastructural changes in the elements of the rat duodenal mucosa in normal condition and under the effect of the complex of food additives (monosodium glutamate, sodium nitrite and Ponceau 4R).

MATERIALS AND METHODS

Outbred mature male rats (n=84) were involved into the experiment. The rats of control group consumed drinking water and received saline per os. The rats of the experimental group, with access to water ad libitum, were administered with 0,6 mg/kg sodium nitrite, 20 mg/kg monosodium glutamate and 5 mg/kg Ponceau 4R in 0.5 ml of distilled water once daily per os. The doses of food additives were twice lower the allowable normal rate in food products. The "open field" test was used to evaluate the rats' adaptive behavior [11]. The animals were sacrificed within 1, 4, 8, 12 and 16 weeks under thiopentone anesthesia overdose. After euthanasia, the fragments of the duodenal wall were fixed in 2.5% glutaraldehyde solution. Subsequently, the pieces of the duodenal wall were embedded into epon-12 in compliance with the conventional technique [12]. Electron microscopy study was made in the electron microscopy laboratory of the Institute of Morphology at I. Horbachevsky Ternopil National Medical University. The ultra-thin sections were made using the ultramicrotome LKB–3 (Sweden). Contrasting of sections was performed first in 1% uranyl acetate solution in methanol and then in Reynolds lead citrate [13]. The follow up analysis was made using the electron microscope PEM - 125 K (serial number 38-76, TU 25-07-871-70) at an accelerating voltage (50 - 75) kW. The housing of the animals and experimental part of the study has been carried out in compliance with the "General ethical principles used for animal experiments", adopted at the First National Congress on Bioethics and requirements of the international principles of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" [14].

RESULTS

Electron microscopy study of the duodenum of control rats showed that the rat mucous membrane had a typical structure, forming villi and crypts, the surface of which was covered with a single layer of prismatic microvilli epithelium, with different cellular representation (Fig. 1a, 1b). The glycocalyx, which was represented by glycoproteins and lipoproteins, was located on the surface of the microvilli. On the lateral surface of the apical part of the cells, due to microfilaments combined with intercellular contacts, enterocytes were conjoined and closed the connection between the intestinal lumen and the intercellular space. The epithelial cells of the villi consisted mainly of enterocytes with a brush border and goblet cells.

Prismatic enterocytes contained the ovoid nuclei in their basal portion. Euchromatin predominated in the nuclei and several nucleoli were visualized. Peripheral condensed heterochromatin was revealed in the form of lumps, located circularly on the periphery of the nucleus. A granular endoplasmic reticulum was located near the nucleus. The Golgi complex was located above the nucleus, and its cisterns lay vertically relative to the enterocyte. Numerous mitochondria were located around the perimeter of the cell. Bumps of smooth endoplasmic reticulum, lysosomes and vesicles were displaced to the apical part of the cells and localized near their terminal part. Among the enterocytes with a brush border in the villi and poorly differentiated enterocytes without a brush border in the crypts, the goblet cells, which are mucosal cells whose function is cyclical and associated with the accumulation and excretion of the secretory products into the intestinal lumen, were located. Goblet cells at different stages of the secretion had different structure and location of organelles. During the secretion phase, the nucleus with organelles was pressed against the basal surface of the cell. The Golgi complex and mitochondria were located near the nucleus; mitochondria were enlarged, light, with short cristae. During the excretion phase, the cell became narrow, its nucleus was diminished, and accordingly the cytoplasm was free from the granules of secretion. EC, ECL and P-cells were found in the epithelium of the duodenal mucosa. Notably, the electron microscopy study showed that endocrinocytes of the duodenum had a number of common features, which was expressed by the accumulation of secretory granules in the basal cytoplasm and the location of the Golgi complex in the supranuclear part, which primarily determined the morphological polarity of the endocrine cells. Endocrinocytes did not reach the lumen of the duodenum. They were located near the vessels of the blood microcirculatory bed, which determined the excretion through the basal or basal-lateral surface, which affected adjacent components.

On week 4 of the consumption of the complex of food additives, namely, monosodium glutamate, sodium nitrite and Ponceau 4R, edema was observed in the crypts, which led to dilatation of the venules of the mucous membrane, the wall of which was thinned; almost no blood corpuscles were determined in the lumen, endotheliocytes were flattened; on the adluminal surface the phenomenon of adhesion of leukocytes to the vascular wall was observed, blood plasma formed electronically transparent vacuole-like structures. The lumens of the capillaries were also dilated, with no blood corpuscles found. The vast majority of poorly differentiated exocrinocytes were identified in the crypts, the nuclei of which were mostly ovoid, sometimes with sporadic invaginations. The Golgi complex was poorly differentiated; it was located above the nucleus, surrounded by lysosomes and secretory vesicles, which moved closer to the nucleus. Cells were at the stage of differentiation into the Paneth cells. The Paneth cells were located at the bottom of the crypt sporadically or in clusters. They were characterized by a large orbicular nucleus with mitochondria located nearby; the Golgi complex was shifted to the basal part of the cell, the cisterns of the endoplasmic reticulum were dilated in the basal parts of the cell. EC-cells were located among the columnar epitheliocytes without a brush border in the crypt. The nucleus was orbicular. The

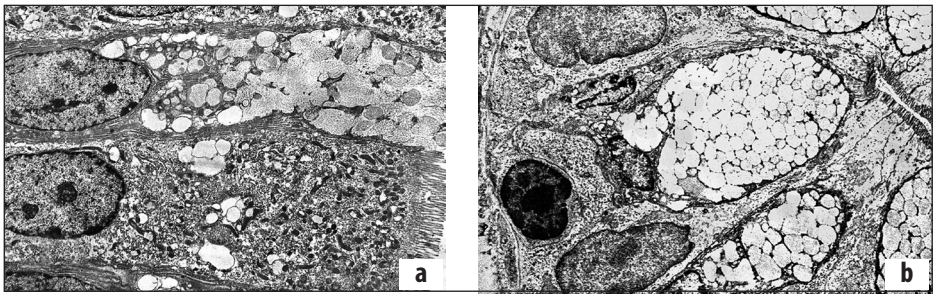

Fig. 1a and 1b. Goblet cells, endocrinocytes and enterocytes with a brush border in the epithelium of villi and crypts of control rats. Electronogram. ×8000 magnification.

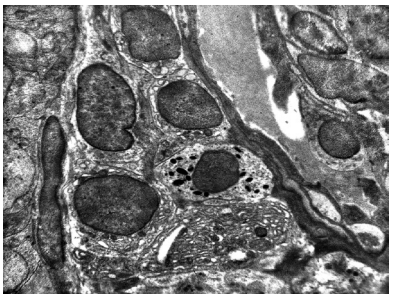

Fig. 2. The development of edema in the crypts of the mucous membrane of the rat duodenum after consumption of the complex of food additives. Electronogram. ×6000 magnification.

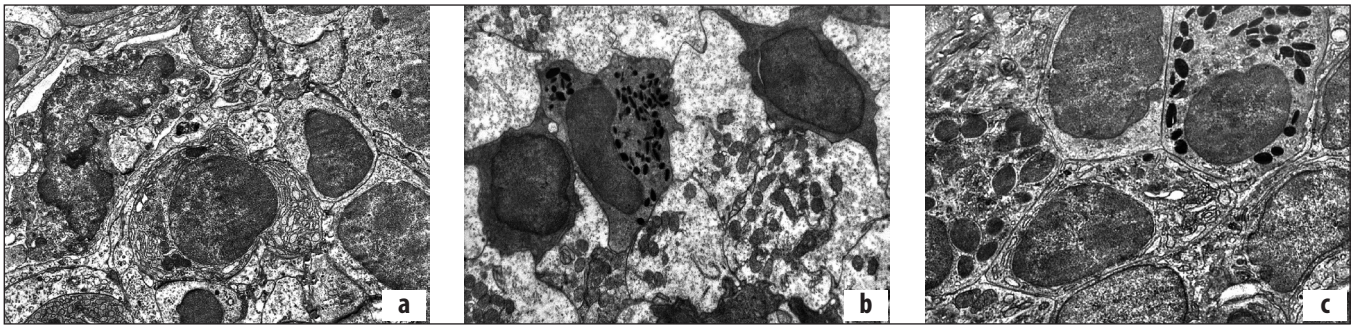

Fig. 3: a. Lymphocyte in the epithelium of the crypt of the rat duodenum on week 8 of the experiment. Electronogram. ×6000 magnification; b. Macrophages and EC-cell in the crypts on week 8 of consumption of the complex of food additives. Electronogram. ×6000 magnification; c. Eosinophil next to the P-cell in the epithelium of crypts on week 8 of the experiment. Electronogram. ×6000 magnification.

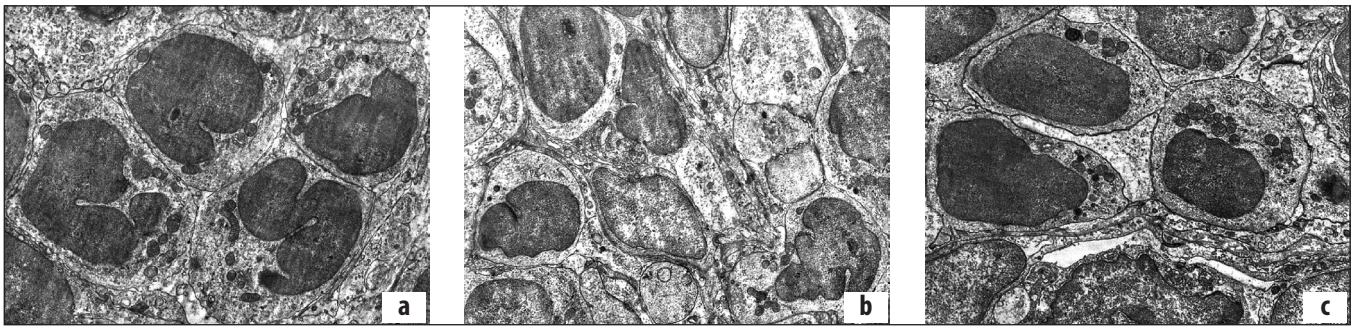

Fig. 4: a. Phenomena of apoptosis and segmentation of nuclei in the enterocytes of the epithelium of the crypts of rat duodenum on week 12 of the experiment. Electronogram. ×6000 magnification; b. P-cells next to the enterocytes with deformed nuclei on week 12 of consumption of the complex of food additives. Electronogram. ×6000 magnification; c. Differentiation of crypt epithelial exocrinocytes on week 16 of consumption of the complex of food additives. Electronogram. ×6000 magnification.

endoplasmic reticulum had dilations and ruptures in some places, and the tubules were branched. The Golgi complex was located near the wall. Granules with endocrine secretion were deformed, of different diameters, in some granules a slight desolation was noted (Fig. 2).

From week 8 to week 12 of the experiment, local immunity was intense that was manifested by the appearance of numerous lymphocytes (Fig. 3a), macrophages (Fig. 3b) and eosinophils (Fig. 3c) among the epithelial cells of the duodenum mucosa for the immune response and nonspecific inflammatory reactions. The Golgi complex with unchanged structure and large and orbicular nucleus was found among the Paneth cells above the nucleus, near which mitochondria were located; the endoplasmic reticulum was unchanged and evenly surrounded the nucleus; the Paneth cells with apoptosis were also noted. The nuclei of these cells were deformed, s-shaped, were at different stages of karyopyknosis, the lumps of heterochromatin were large and located on the periphery of the nucleus. Numerous vacuoles were observed in the heterogeneous cytoplasm; dilatation and destruction of cisterns of the granular endoplasmic reticulum was observed (Fig. 3a).

EC-cells were elongated. Their nuclei were dark, bean-shaped and reached the basal part of the cytoplasm. Secretory granules were unevenly distributed, formed aggregations and had a variety of shapes: from a bean-shaped to elongated oval.

The cytoplasm showed high electron density. According to all available indicators, the cells were at the stage of hypertrophy and hypersecretion, because due to the negative effect of the complex of food additives, the intestine responded by releasing large amounts of mucus as a protective reaction to the direct action of chemicals on the mucous membrane affected by serotonin produced by EC -cells. Exocrinocytes had an electronically transparent cytoplasm and showed no granules with secretory products; mitochondria were diminished and arranged in clusters (Fig. 3b).

On week 12, the electron microscopy study of exocrinocytes of the intestinal glands showed signs of apoptosis at different stages of manifestation. The nuclei were deformed, in some cells segmentation of nuclei and disappearance of nucleoli was observed. The cytoplasm was granular and contained a large number of electron-transparent vacuoles. The number of mitochondria was reduced, they showed polymorphism and were diminished (Fig. 4a). The findings of the electron microscopy study showed that on week 12 of the experiment, an increase in the number of P-cells among the cellular representation of the crypts of the rat duodenum was noted. These cells were a population with small granules. In their cytoplasm, the nuclei were elongated, occupying almost the entire volume of cells. The granular endoplasmic reticulum was well developed, located in the supranuclear zone near the Golgi complex, with very small cisterns. In the cytoplasm, the fine orbicular granules, with a light border were found. These granules contained bombesin, which is known to affect the secretion and contraction of smooth myocytes (Fig. 4b).

At the end of the experiment, in the epithelial cells of the duodenal mucosa an increase in the differentiation of exocrinocytes due to compensatory-restorative responses of the body to the action of alternative factors was noted. The cells had orbicular nuclei, but with a predominance of heterochromatin in the nucleus; an increase in the number of mitochondria in the cytoplasm was detected, but they were small in size and located in clusters. Lysosomes and a small number of secretory granules were located around the nucleus. Polysomes were found in the cytoplasm, which indicated an increase in the protein synthesis to build structural components of cells; granular endoplasmic reticulum fine cisterns were located in the perinuclear space; the Golgi complex was located above the nucleus. It should be noted that at the electron microscopy level, the cells with deformed nuclei and areas of desolation in the cytoplasm were noted next to the cells at the stage of differentiation, which indicated parallel processes of dystrophic changes of crypt epithelial cells and apoptosis (Fig. 4c).

DISCUSSION

Thus, the findings of the study of the ultrastructural organization of the rat duodenal mucosa have been found that the epithelial cells of the villi consisted, in the vast majority, of prismatic enterocytes with a brush border. The cells with striated border with many microvilli were found on their apical surface. The goblet cells were located sporadically between the columnar epitheliocytes with and without a striated border. Columnar epitheliocytes without a brush border predominated in the epithelial lining of the crypts, at the bottom of which the Paneth cells were located. Sporadic endocrine cells were detected throughout the intestinal glands: EC, ECL, and P-cells, which had a number of common features, namely, aggregation of the secretory granules in the basal parts of the cytoplasm and the Golgi complex was located in the supranuclear part, which determined the morphological polarity of endocrinocytes. The nuclei were light, ovoid and reached the basal part of the cytoplasm. Secretory granules were evenly distributed and had a variety of shapes: from elongated oval to bean-shaped. The lamina propria is represented by loose fibrous unformed connective tissue with microcirculatory vessels, namely, arterioles, capillaries and venules, which allows us to conclude that the mucous membrane of the rat duodenum corresponds to that in humans and can be used in the experiments to obtain reliable findings. Consumption of the complex of food additives due to direct immediate action of chemicals at the early stages of the experiment led to the spasm of exchange and resistance sections [15], to which the mucous membrane responded by nonspecific inflammation with subsequent edema and electron microscopy study revealed the following signs: the nuclei of epithelial cells with striated border had an oval, sometimes irregular shape with invaginations, the endoplasmic reticulum was partially visualized, with a poorly pronounced Golgi complex. Secretory granules of goblet cells had desolations and deformations. The nuclei were displaced closer to the basement membrane, and the Golgi complex was located between the nucleus and the mucous secretion, the endoplasmic reticulum was compacted. The nuclei of endocrinocytes were more oval in shape and in the vast majority deformed. The Golgi complex was located closer to the basement membrane. The endoplasmic reticulum was enlarged and ruptured in some places, with branched tubules. The granules with the secretory products were deformed, in which a slight desolation was noted. Changes in the vessels of the blood microcirculatory bed were noted, manifested by dilation of the venules of the lamina propria of the mucosa, with the adhesion of leukocytes to the vascular wall, blood plasma formed electronically transparent vacuole-like structures, capillary lumens were also dilated, with no blood cells found. The above changes indicated the development of edema and the activation of the local protective barrier, which was confirmed on the electrograms by the presence of macrophages and lymphocytes among the epithelial cells, and the presence of eosinophils (Fig. 3c), indicating a nonspecific allergic immune response, apparently caused by the presence of the Ponceau 4R colorant. Subsequently, there were signs of dystrophic changes in the epithelial cells of the duodenal mucosa, which was manifested by destructuring of the cytoplasm of the cells, deformation of the nuclei and the presence of various vacuoles. The phenomena of karyopyknosis in the Paneth cells and invaginations in the nuclei of columnar epitheliocytes indicated the presence of apoptotic manifestations. At the end of the experiment, adaptive mechanisms did not lead to complete recovery, which on the electrograms was manifested by the phenomena of cell differentiation with adjacent cells at different phases of apoptosis.

CONCLUSIONS

Consumption of the complex of food additives led to general ultramicroscopic changes in the mucous membrane of the rat duodenum, triggering the morphological mechanisms of nonspecific inflammation in the form of dystrophic changes and the development of apoptosis. The adaptive mechanisms do not lead to complete restriction of the alternative and intensification of the reparative processes, which at the end of the experiment was expressed by the presence of dystrophic changes in the epithelial cells and the phenomena of apoptosis.

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ORCID and contributionship:

Galina A. Yeroshenko: 0000-0003-4279-485X [A,F]
Kostyantyn V. Shevchenko: 0000-0003-1665-3236 [D]
Alona S. Grygorenko: 0000-0003-2268-6384 [B,D]
Olga D. Lysachenko: 0000-0002-7351-9335 [E]
Nataliia T. Maksymenko: 0000-0002-2495-9289 [D]
Angela V. Vatsenko: 0000-0001-5989-9493 [B]
Olena V. Klepets: 0000-0001-6398-9459 [E]

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CORRESPONDING AUTHOR

Galina A. Yeroshenko
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
tel: +380997275424
e-mail: gala_umsa@ukr.net

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ORIGINAL ARTICLE

COMPREHENSIVE APPROACH IN CORRECTIONAL WORK WITH OLDER PRESCHOOL CHILDREN WITH SPEECH DISORDERS

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Inna V. Baranets[1], Nataliya G. Pakhomova[1], Ivan M. Okhrimenko[2], Olha H. Hubar[1], Valentyna S. Padun[1], Larysa V. Drozd[1], Iryna A. Holovanova[3]

[1]POLTAVA V. G. KOROLENKO NATIONAL PEDAGOGICAL UNIVERSITY, POLTAVA, UKRAINE
[2]NATIONAL ACADEMY OF INTERNAL AFFAIRS, KYIV, UKRAINE
[3]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate the effectiveness of comprehensive approach in correctional work with older preschool children with speech disorders.

Materials and methods: The research was conducted in 2018-2022. The research involved 250 children aged 5-7 years, who were divided into two groups. The experimental group consisted of 150 children with motor alalia (57 girls and 93 boys). The control group consisted of 100 children without speech disorders (48 girls and 52 boys).

Results: The analysis of outpatient cards of children with speech disorders of various aetiology was carried out. The main results of a comprehensive medical as well as psychological and pedagogical examination of children with motor alalia are highlighted. The result of the research revealed that organic lesion of the brain affects not only the clinical presentation of nonverbal symptoms, but also psychospeech development, in particular.

Conclusions: The expediency of using a comprehensive diagnostic methodology was proved, where the medical component consisted in studying the peculiarities of bioelectrical activity of the brain on electroencephalography, which reflects the process of its morphological maturation in ontogenesis.

KEY WORDS: correctional work, comprehensive approach, children with speech disorders, alalia, diagnostics

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INTRODUCTION

An important condition for ensuring high efficiency of correctional and developmental work is interdisciplinary assessment of speech development disorders in children and adolescents, which involves the specialist's specialized knowledge, including medical, psychological and pedagogical components [1-3]. Therefore, the use of specialized knowledge, namely their organic combination in practice is becoming increasingly important in the process of comprehensive integrative attention to children with speech disorders, including motor alalia.

Revealing the essence of the concept of "specialized knowledge", first of all, we should characterize the concept of "knowledge", which in pedagogy is defined as understanding, retention and the ability to reproduce the basic facts of science and relevant theoretical generalizations (concepts, rules, laws, etc.) [4-6]. Along with this, the concept of "knowledge" can be considered in a broad and narrow sense. Knowledge in a broad sense is a set of theoretical and practical knowledge and the ability to apply it in various fields of activities; knowledge in a narrow sense (in a separate field) is a conceptual and factual component of educational material, which includes interrelated facts, patterns, theories, generalizations, terms, which is the basis of basic knowledge of pedagogy, including special pedagogy [7-9]. Thus, a structured totality of basic concepts of special education; theory, concept, patterns, principles, methods of pedagogical activity, technologies, ethical norms, values and professional competence are structural components of the basic knowledge of a special education teacher.

We define specialized knowledge within the context of our research as systematized scientific and practical knowledge and skills that are not publicly available, well-known and not widespread, i. e. it is the knowledge that expands and deepens basic knowledge, emphasizing the principle of a comprehensive approach to overcoming the problem. The ratio of specialized and basic knowledge is variable in nature, which is determined by the level of development of society and the integration of scientific knowledge in the process of organizing correctional work with older preschool children with severe speech disorders.

The relevance of this range of problems is supplemented by the fact that the awareness of the importance of specialized knowledge in correctional work [10], as a unique organizational resource set the task of developing effective ways of their interaction, in particular the organic combination of psychological, pedagogical and medical methods should assist clear differential diagnosis and delineation of effective ways to overcome speech disorders in older preschool children. This will allow timely attention and

taking the necessary measures to organize a comprehensive rehabilitation by means of close interconnection of integrative components.

The integrative medical, psychological and pedagogical aspect as the basis of specialized knowledge in the study of motor alalia involves the study of the relationship of all body systems as a single whole and an obvious indicator of any disorders. Numerous studies confirm the dependence of different disorders on each other in conditions of this state. Therefore, in our opinion, the provision of logopedic treatment to children with motor alalia should be within an integrative approach that takes into account the preserved capabilities of the child's body to the maximum possible extent.

THE AIM

The aim is to investigate the effectiveness of comprehensive approach in correctional work with older preschool children with speech disorders.

MATERIALS AND METHODS

During 2018-2021, we conducted a retrospective analysis of outpatient cards of children with speech disorders of various aetiology. A total of 250 children participated in the research. Two groups were identified. The experimental group consisted of 150 older preschool children with motor alalia aged 5.5-7 years, the average age was 5.99 ± 0.75 years, including 57 girls and 93 boys. The control group of children without speech disorders consisted of 100 persons (48 girls and 52 boys), aged 5.5-7 years, the average age was 6.18 ± 0.63 years. All children underwent repeated outpatient neurological (including instrumental) and logopedic examinations.

Since the implementation of such a research requires appropriate medical qualification or a combination of comprehensive studies, we identified a group of children in this category, who according to anamnestic data were on outpatient observation of a pediatric neurologist and required re-examination to clarify the diagnosis by instrumental examinations, including electroencephalography (EEG). Considering the fact that one of the indications for EEG is delayed speech and psychomotor development of children, this type of examination was chosen as the safest method of additional diagnosis for the child, which is important to consider when re-used assessing the effectiveness of medical, psychological and pedagogical impact. Therefore, a comprehensive medical as well as psychological and pedagogical examination of children with developmental dysphasia, who were under the outpatient observation of a pediatric neurologist was carried out in the same conditions for all children. A request to the parents of the children to appear in their stable emotional state for the examination not being tired and hungry was the necessary preliminary preparation for the examination. This condition is important for more accurate EEG results.

The diagnostic methods of the research were based on traditional methodological principles of comprehensive examination of speech of children with motor alalia in the process of psychological and pedagogical testing, logopedic examination, determining the development level of components of communicative and speech activity, namely: impressive and expressive speech with their nonverbal manifestations and communicative skills in various forms (dialogue, monologue) of interactive interaction, which gives a broader picture and idea of the state of formation of communicative competence and personality of the older preschool child in general. The author's methodology was developed in accordance with the requirements of educational programs of preschool education institutions and the Basic component of preschool education for language and speech development. In contrast to the existing ones, the author's methodology had a comprehensive approach to the differential diagnosis of motor alalia in children. Namely, the involvement of specialists in the field of medicine contributed to the objective differential diagnosis of children with severe speech disorders, allowed to distinguish speech disorders by a certain nosological category at the initial stage.

We ranked the state of communicative competence formedness in older preschool children according to four levels such as high, sufficient, medium, low depending on the method of accomplishment and assessment of the tasks in compliance with specified criteria and indicators. Along with this, the medical component of the comprehensive diagnostic methodology was to study the features of neuropsychological development, psychophysiological readiness for correctional work, by studying the bioelectrical activity of the brain on the EEG, which reflects the process of its morphological maturation in ontogenesis.

Three levels were identified for each criterion of bioelectrical activity of the brain (slowing of the main rhythm in the frontal, temporal, fronto-temporal-parietal lobes with interhemispheric asymmetry and rhythm disorganization) such as mild, moderate, severe.

We used the coefficient of rank correlation according to the bilateral Student's t-test (for independent, unrelated samples) to compare the results of the research. The results were considered reliable at $p < 0.05$.

The research was performed according to the requirements of the Regulations on Academic Honesty of Poltava V. G. Korolenko National Pedagogical University, which were developed on the basis of Ukrainian and world experience of ethical rulemaking. The consent to participate in the research was obtained from all subjects.

RESULTS

We selected a group of older preschool children with motor alalia consisting of 150 people (57 girls and 93 boys) diagnosed at the age of about three from the total number of examined children with speech developmental disorders of various aetiology, who were under the outpatient observation of a pediatric neurologist. Anamnestic data of these patients indicate a burdensome perinatal anamnesis. Thus,

Table I. The results of bioelectrical activity of the brain in older preschool children with motor alalia and without speech disorders

The main EEG patterns		Children with motor alalia (150 people)	%	Children without speech disorders (32 out of 100 people)	%
Slowing of the main rhythm with interhemispheric asymmetry and rhythm disorganization	in the frontal lobes	73	48.6	12	12.0
	in the temporal lobes	32	21.3	12	12.0
	in the fronto-temporal-parietal lobes	45	30.1	8	8.0

according to etiological factors, the group of mothers of the examined children was distributed as follows: gestational toxicosis of the first half of pregnancy was inherent in 118 women (78.6 %), signs of placental dysfunction was peculiar for 98 women (65.4 %), rapid or prolonged childbirth was characteristic of 67 females (44.5 %), signs of mild in 50 cases (33.3 %) and moderate in 81 cases (54.1 %) of asphyxia at birth, the threat of abortion was recorded in 41 women, which makes 27.3 %.

The analysis of the results of EEG examination revealed that all studied children with motor alalia (150 people) showed diffuse changes in the bioelectrical activity of the brain. The study of EEG patterns of the examined children revealed clear local changes in biopotentials in the frontal, temporal and fronto-temporal-parietal lobes of the dominant hemisphere in the form of regional slowing of the rhythm with interhemispheric asymmetry and rhythm disorganization, indicating the organic brain lesions.

To estimate the number of oscillations of one or another rhythm, the analysis of the results of the research was used, which allowed to record the slowing down of the alpha rhythm, while in children without speech disorders the age features of the alpha rhythm were noted. It should be emphasized that synchronous rhythms in both hemispheres, absence of acute peaks of electrical activity, stable brain activity, even in the presence of short-term reactions to light or other stimuli are inherent in children without speech disorders on the EEG results. It should be noted that not all children with normative speech development have changes in the EEG. In particular, out of 100 children without speech disorders, only 32 had slight changes in EEG patterns, which were manifested mainly at the mild level. At the same time, the EEG in children with motor alalia shows the following trend: the presence of a motor component in the structure of the studied speech disorder is evidenced by EEG-signs of severe disorders of brain electrogenesis in the form of dysrhythmia and neurophysiological signs of immaturity of cortical structures, changes in zonal differences, interhemispheric asymmetry. These phenomena and their combinations were registered in our research in more than half of the examined older preschool children (102 children), which accounted for 68 % of the total number of children covered by the research. The combination of regional slowing of the rhythm with interhemispheric asymmetry and rhythm disorganization turned out to be prognostically unfavourable in the context of the rates of speech function formation.

Therefore, the comparison of the results of EEG examination of older preschool children with motor alalia was carried out in comparison with the conclusions of this method of instrumental diagnosis of children without speech disorders and are presented in Table I.

The analysis of clinical data allowed to allocate groups of children according to characteristic EEG signs. The obtained data indicate that among older preschool children with motor alalia the most common are slowing of the main rhythm with interhemispheric asymmetry and rhythm disorganization in the frontal lobes (48.6 %), slowing of the main rhythm with interhemispheric asymmetry and rhythm disorganization in the temporal lobes (21.3 %), slowing of the main rhythm with interhemispheric asymmetry and rhythm disorganization in the fronto-temporal-parietal lobes (30.0 %).

To compare the results of the research, we used the Student's t-test rank correlation coefficient (for independent, unrelated samples), which showed that the difference between the indicators was caused by the difference between the two groups states and not by random data error due to their sample assessment. Sampling indicators became different by all criteria (null hypothesis was rejected and an alternative one with a significance level of $\alpha = 0.05$ and $\alpha = 0.01$ was accepted), which indicates a significant difference in brain activity in older preschool children with motor alalia and without speech disorder and confirms the need for comprehensive correctional work.

Analysing the level indicators for each criterion, it was found that changes in biopotentials in the frontal, temporal and fronto-temporal-parietal lobes of the dominant hemisphere in the form of regional slowing of rhythm with interhemispheric asymmetry and rhythm disorganization were unevenly distributed. Higher indicators of moderate and severe levels were observed in children with motor alalia (Figure 1), while in children with normative speech development there was a predominantly mild level of EEG manifestations (Figure 2).

Therefore, the results of quantitative electroencephalography examination, taking into account the conclusion of a pediatric neurologist, were used by us to compare the results of logopedic examination.

Thus, comparative data of the results of psychological and pedagogical diagnostic methods indicate significant differences between the performance of tasks in the levels of development of impressive and expressive speech with their nonverbal manifestations and communicative skills

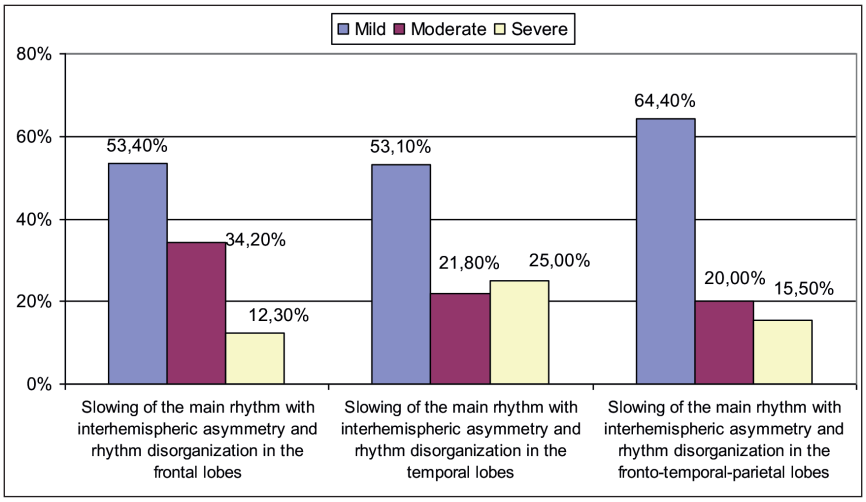

Fig. 1. Levels of EEG manifestations in children with motor alalia

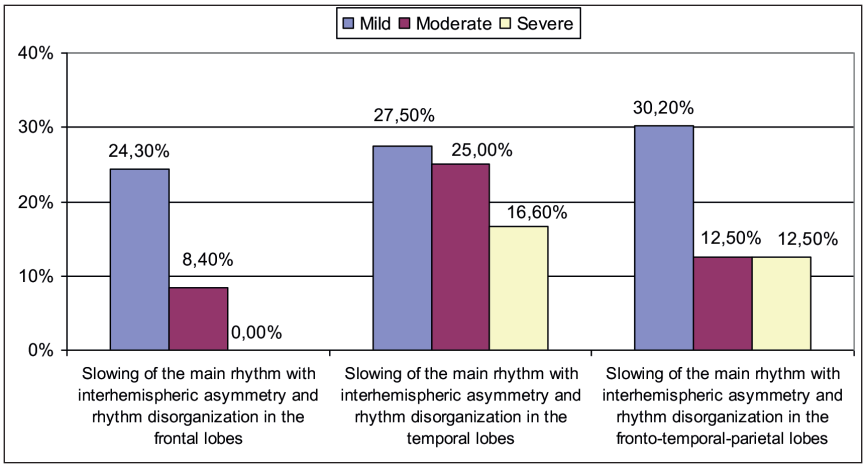

Fig. 2. Levels of EEG manifestations in children with normative speech development

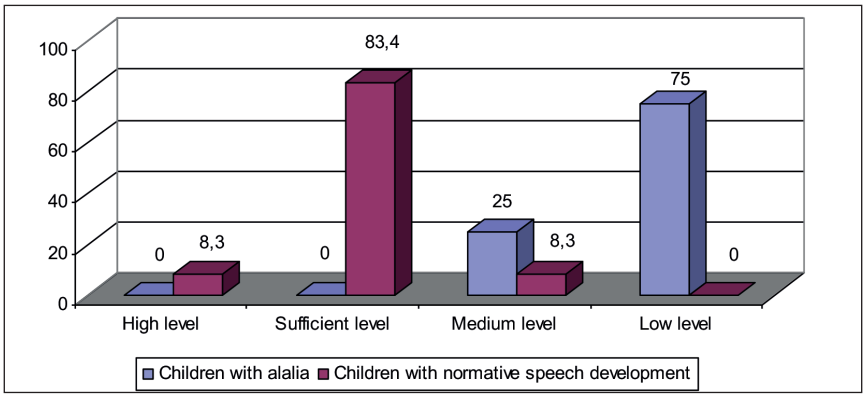

Fig. 3. Comparison of communicative competence formedness levels in older preschool children with motor alalia and children with normative speech development

in various forms (dialogue, monologue) of interactive interaction.

The levels of communicative competence formedness in older preschool children with motor alalia and without speech disorders are determined according to the formedness indicators of the components of the communicative-speech system; the results are presented in the histogram in Figure 3.

Thus, the results of the research revealed that there were no children with high and sufficient levels of communicative competence formedness among children with motor alalia, only 25 % of children with motor alalia have an average level of communicative competence formedness. A low level was inherent in 75 % of children. Children with normative speech development showed rather high indicators of the state of communicative competence formedness, a high level in 8.3 % of children, a sufficient level in 83.4 %, and a medium level in 8.3 %. No low level of communicative competence formedness was detected among these children.

DISCUSSION

Thus, the results of the research mainly confirmed and expanded the conclusions of G. Weismer, [11], W. Ziegler and H. Ackermann [12] on the creation of a scientifically

sound hypothesis of bizarre child development, assessment of its defects, finding rational ways to overcome them using an overall system of clinical, experimental and psychological, as well as pathophysiological studies. In addition, the results correlated with the studies by L. Ferri [13], H. Terband, B. Maassen and E. Maas [14], S. Diepeveen and colleagues [15] on the comprehensive diagnosis and overcoming of clinical manifestations of motor alalia in children. This conclusion can be made on the basis of a preliminary analysis of scientific research [1, 16, 17], which were based mainly on integrative approach.

The conclusions by J. R. Duffy [18] on the scientific search for new ways to overcome severe speech disorders, which are based on a comprehensive approach, were supplemented by the ideas about the medical and psychological impact on the formation of psychospeech development of children with motor alalia.

Since our research included a comprehensive approach to overcoming the problem of motor alalia, its results have expanded in the direction of scientific understanding of the impact of organic lesion of the brain not only on the clinical presentation of nonverbal symptoms, but also on psychospeech development, in particular. The influence described by us and proved by the comparative analysis of bioelectrical activity of the brain on EEG, reflects the process of its morphological maturation in ontogenesis.

The comprehensive research allows confirming the conclusion about the state of speech formedness and helps to outline clearer focal areas for the formation of communicative competence in older preschool children with motor alalia. In particular the integration of the medical component into the correctional work of a speech language therapist allows distinguishing speech disorders by a certain nosological category at the initial stage and, of course, does not reduce the importance of the psychological and pedagogical aspect in comparison with the medical one. Our opinion completely coincides with the statement by G. Weismer [11], who wrote: "correct recognition, assessment defects of child, finding rational ways of learning – all of this is impossible without an overall system of clinical, experimental and psychological, as well as pathophysiological studies."

CONCLUSIONS

It should be emphasized that a comprehensive approach to overcoming motor alalia today involves the study of the relationship of all body systems as a whole and an obvious indicator of any disorders. Numerous studies confirm the dependence of different disorders on each other in conditions of this state. Therefore, in our opinion, the provision of logopedic treatment to children with motor alalia should be within a comprehensive approach that takes into account the preserved capabilities of the child's body to the maximum possible extent. Modern methods of differential diagnosis and overcoming of various pathological states of children allow to pay attention in time and to take necessary measures for the organization of the complex collection help by means of close interrelation of integrative components.

We see the prospect of further research in the development of methods for the formation of communicative competence in older preschool children with motor alalia.

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ORCID and conrtibutionship:
Inna V. Baranets: 0000-0002-4972-6510[B,D]
Nataliya G. Pakhomova: 0000-0002-8332-8188[A,B]
Ivan M. Okhrimenko: 0000-0002-8813-5107[E,F]
Olha H. Hubar: 0000-0003-3640-1490[A,C]
Valentyna S. Padun: 0000-0001-8055-123X[D,F]
Larysa V. Drozd: 0000-0001-9722-7444[C]
Iryna A. Holovanova: 0000-0002-8114-8319[E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Ivan M. Okhrimenko
National Academy of Internal Affairs
1 Solomenskaya Square, 03035 Kyiv, Ukraine
tel: +380679903905
e-mail: ivango-07@ukr.net

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ORIGINAL ARTICLE

NEUROMETABOLIC STRATEGY OF PHARMACOTHERAPY FOR PATIENTS WITH SERONEGATIVE ARTHRITIS

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Liliia V. Burya, Nataliia V. Moisieieva, Anna A. Kapustianska, Andrii V. Vakhnenko, Iryna M. Zviagolska, Mariia O. Rumiantseva
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: The search for optimization of the strategy of neurometabolic pharmacotherapy in patients with seronegative arthritis is relevant: ankylosing spondylitis and psoriatic arthritis, taking into account the nature of the psychological response to the disease.

Materials and methods: The study included (1st observation group) 36 patients with AS (17 men and 19 women) aged 25 to 65 years, average duration of AS - 10.9 ± 0.63 years. Degree of pathological process activity was determined taking into account the Bath AS disease activity index (BASDAI) - in accordance with EULAR criteria. The second group included 32 patients with a diagnosis of PSA (19 men and 13 women) aged 25 to 65 years according to the CASPAR 2006 criteria, the average duration of psoriasis is 13.9 ± 1.9 years, PSA - 10.6 ± 0.58 years. To study the psycho-emotional state, the Spielberger anxiety self-assessment scale was used. To identify the symptoms of depression was used Hamilton Depression Scale (HDS).

Results: In the study groups noted a high frequency of inadequate socio-psychological response to the disease. In groups of patients with seronegative arthritis, multidirectional maladaptive reactions were noted: in ankylosing spondylitis, a hypochondriac type of response is characteristic, and in psoriatic arthritis, anxiety disorders with different response options. At the end of the observation period in both groups there was an improvement in almost all studied indicators of clinical and laboratory activity.

Conclusions: There was a significant improvement in the psycho-emotional status of patients, which makes it possible to improve the quality of life of patients and contribute to the optimization of treatment and rehabilitation measures.

KEY WORDS: Ankylosing spondylitis, psoriatic arthritis, adjuvant therapy, eglonil

Wiad Lek. 2022;75(6):1477-1480

INTRODUCTION

Today, the results of numerous clinical and epidemiological studies suggest that there is a close link between psycho-emotional disorders and chronic pain, which is an integral part of rheumatic pathology, including inflammatory seronegative arthritis [1-3]. The most common psycho-emotional manifestations of chronic pain are clinically pronounced disorders: anxiety, depression, apathy, fatigue and asthenia, irritability, insomnia [4,5]. Quite often, these factors, which require additional correction, conduce to the intensification of pain, including patients with rheumatic profile [6-8]. Pain itself can also cause the development of psycho-emotional disorders. Therefore, the assessment of patient psychological state is a necessary component of the diagnostic complex in the examination of patients with chronic pain [1,9].

Medico-social significance and relevance of ankylosing spondylitis (AS) and psoriatic arthritis (PSA) is caused by constant progression of the disease with vertebrae and joints ankylosis, long-term disability, morbidity at a young age, early disability and unsatisfactory effectiveness of used therapy. Uncertainty of etiopathogenesis, clinical polymorphism, frequent inconsistency of clinical manifestations of the disease and acute laboratory parameters, lack of effective etiopathogenetic drugs significantly complicate the fight against these diseases.

The severity of the disease, rapid decrease of patient's functional abilities and need for constant medication leads patients with AS to loss of the ability to perform important activities and significant complications in performing simple motor skills, loss of professional independence, significant deterioration in life quality. The patient's personality changes due to the direct impact of disease symptoms and as a result of psychological experience, which is reflected in reduced self-esteem and confidence, dissatisfaction with their lifestyle, anxiety, hostility, anger and depression.

Different personal response to the disease allows to identify patients with maladaptive types of disease response. Harmonious, ergopathic and anosognostic type of attitude to the disease does not significantly impair mental and social adaptation. Patients with intrapsychic orientation of personal response to the disease (anxious, hypochondriac, neurasthenic, melancholic, apathic types of relationships) have impaired social adaptation, as well as when the interpsychic orientation of personal response is characteristic. These are patients with sensitive, egocentric, dysphoric and paranoid type of attitude, which is characterized by impaired social adaptation [1,10,11].

That is why in the complex treatment of patients with seronegative arthritis AS and PSA it is advisable to use adjuvant drugs (anxiolytics, antidepressants, vegetative correctors, muscle relaxants), which do not have a direct analgesic effect, however, except the reduction of the anxiety severity, conduce the intensity of pain perception [12,13]. The main component in treatment of psychosomatic disorders is drug therapy, which, despite almost half a century of experience in its use, remains not always effective enough. Eglonil is widely used to eliminate various disorders, and it was found that its effectiveness is higher in those somatic disorders, which origin or pathogenesis is caused by the influence of mental factors.

Eglonil differs from most other neuroleptics by a relatively low incidence of side effects, as well as the fact that it activates antidepressant effects: increases psychomotor activity, causes a state of vitality, lifts mood and promotes more motivated patient behavior [1,4]. Therefore, Eglonil is one of the first representatives of atypical neuroleptics. Its antidepressant and anxiolytic effects can be compared with the effects of classical antidepressants (amitriptyline) and tranquilizers (benzodiazepines) in the course treatment (3-4 weeks) [8,12]. The clinic proved the feasibility of using Eglonil in cardiology (anxiety and hypochondriac disorders in coronary heart disease - especially when used concomitantly with coronary heart disease), pulmonology (anxiety and depression on the background of asthma attacks), dermatology (psoriasis, neurodermatitis) neurology (dizziness, algic myofascial pain, migraine, etc.). However, in low doses Eglonil is most widely used in gastroenterological practice as part of a comprehensive therapy of stomach and duodenum peptic ulcer, nonspecific ulcerative colitis, irritable bowel syndrome. In such cases, in addition to the psychotropic effects of Eglonil, its somatotropic action also plays an important role. Eglonil has a pronounced antiemetic effect, stimulates the motility of the digestive tract and has an antidyspeptic effect. Eglonil reduces gastric secretion, reduces the content of pepsin and hydrochloric acid in gastric juice [2,3]. The main characteristics of Eglonil, which determines its safety and good tolerability, include: lack of habituation with prolonged use, no depressant effect on activity and performance during the day, no asthenic effect on patients. In addition, Eglonil has no toxic effect on the liver and kidneys, does not change the ECG, and clinically significant interactions with other somatotropic drugs are not indicated.

Adverse reactions when taking Eglonil, commonly, develop rather seldom. They are weakly or moderately expressed and disappear after dose reduction or drug withdrawal. Thus, high efficiency, acceptable efficiency/safety ratio, absence or low incidence of serious adverse reactions, good tolerability - all this leads to widespread use of Eglonil in the pharmacotherapy of various psychosomatic disorders.

THE AIM

Optimization of neurometabolic pharmacotherapy strategy in patients with seronegative arthritis: ankylosing spondylitis (AS) and psoriatic arthritis (PSA), taking into account the nature of the psychological response to the disease.

MATERIALS AND METHODS

The study included (1st observation group) 36 patients with AS (17 men and 19 women) aged 25 to 65 years (49.1 ± 1.2 y. o.), average duration of AS - 10.9 ± 0.63 years. Degree of pathological process activity was determined taking into account the Bath AS disease activity index (BASDAI) - in accordance with EULAR criteria. The minimal degree of inflammatory process activity was established in 10 (27.8%) cases, moderate - in 21 (58.3%), maximum - in 5 (13.9%). Functional insufficiency of joints (FNS) of the II degree prevailed.

The second group included 32 patients with a diagnosis of PSA (19 men and 13 women) aged 25 to 65 years (41, 8 ± 1.8 years) according to the CASPAR 2006 criteria [13], the average duration of psoriasis is 13.9 ± 1.9 years, PSA - 10.6 ± 0.58 years. The prevalence of lesions was dominated by polyarthritis - 92.3%. I degree of inflammatory process activity is established in 9 (28,1%) cases, II - in 17 (53,1%), III - in 6 (18,8%).

To facilitate the assessment: pain syndrome, joints and spine stiffness, fatigue were assessed on a 100-mm visual analog scale by patients themselves, as well as the patient's own health indicator (PHI). Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) levels were also assessed.

To study the psycho-emotional state, the Spielberger anxiety self-assessment scale was used [11], according to which the level of anxiety < 30 points was assessed as low, 30- 45 - moderate, >45 - high. To identify the symptoms of depression was used Hamilton Depression Scale (HDS), according to which the summation of the scores of 16- 18 in young and 18- 20 in the elderly age indicates the presence of non-psychotic depression, and >18-20 points - on the possible psychotic depression [6].

Patients of both groups with identified maladaptive response types were differentially prescribed adjuvant therapy (sulpiride), the effectiveness of which was evaluated after the end of the observation period (1.5 months). Statistical analysis of the data was performed using the computer software package Statistica (StatSoft Inc., USA, version 6.0).

RESULTS

At the time of the study, all patients in both groups received continuous baseline therapy - methotrexate at a dose of 12.5- 15 mg/week or sulfasalazine 2 g/day in 2 doses for 8 months to 7.8 years, as well as nonsteroidal anti-inflammatory drugs (dose and the choice of drug was determined according to the activity of inflammatory processes and individual tolerability of the patient).

Inadequate behavioral responses diagnosed in 27 (75%) cases predominated in the diagnostic search in patients with AC. Among them, patients with an intrapsychic response to the disease predominated, mostly people with a hypochondriac type of response, which is characterized by anxiety and increased distrust of patients about the unfavorable course and prognosis of the disease and as a

result - depressed mood and mental activity. 9 patients were diagnosed with an adequate response to the disease - 4 harmonic cases and ergopathic - 5 cases, in which mental and social adaptation is not significantly impaired. Inadequate response to the disease was also found in patients with PSA in 28 (87.5%) cases. Of these, patients with intrapsychic response to the disease - 22 cases. Mixed types of response (14 cases) of anxiety-neurasthenic and anxiety-hypochondriac types dominated; among other patients, the anxiety type - 4 cases, melancholic and neurasthenic - 2 cases. Interpsychic response option - 4 patients with sensitive type and 2 with egocentric, which are characterized by maladaptive behavior with heteroaggressive tendencies towards others, impaired social functioning. 4 patients with adequate response type: 1 - harmonious, 2 - ergopathic and 1 - anosognostic (euphoric).

When testing the level of anxiety according to the method of Spielberger in patients of the 1st group, the indicators of situational (SA) 38.8 ± 1.0 and personal anxiety (PA) 43.4 ± 1.4 points were increased compared to normal. Testing with HDS in patients of the 1st group reveled data that exceed the average normative indicators - 19.3 ± 1.1 points. In patients of the 2nd group the indicators of SA and PA were also significantly increased (44.8 ± 1.4; 51.2 ± 1.3 points). When evaluating the results of testing for HDS, the average values in sick dogs significantly exceeded the norm - 18.6 ± 1.2 points.

The results of psychosomatic status study led to the appointment of adjuvant therapy. All patients in both groups who showed inadequate response to the disease (to balance psycho-emotional state), in addition to the amount of their basic and anti-inflammatory therapy was prescribed a drug with anxiolytic, antiasthenic, antidepressant, anti-hypochondriac effects. The choice of drug was made taking into account the characteristics of the types of psycho-emotional disorders identified in the groups.

DISCUSSION

Thus, 27 patients (1st group) and 28 patients (2nd group) were prescribed sulpiride, manufactured by Sanofi-Sintelabo under the trade name Eglonil. The dose was 50 mg (1 tablet) 2 times a day. Therapy was given to patients of each group during the whole observation period, 1.5 months long. The effectiveness of complex therapy was evaluated by the dynamics of clinical and laboratory activity, the level of SA and PA, HDS data. Before treatment, the 1st and 2nd group showed severe back, stiffness in the spine and joints, fatigue, high PHI, ESR and CRP level.

At the end of the observation period in both groups conclusions were made up and there was apositive change in almost every established indicator of clinical and laboratory activity. Decreased fatigue level, backpain, spine and joint stiffness and stabilisation of psycho-emotional status were observed in each group and compared using the strict data [8,11].

Thus, in the 1st group significantly decreased fatigue and the rate of PHI, decreased the severity of pain in the spine and stiffness in the spine, as well as stiffness in the joints. Patients with AS also noted a decrease in the activity of inflammatory process, this was confirmed by a significant decrease in ESR and CRP.

In the 2nd group there was also a positive trend in the reduction of back pain, spinal stiffness and stiffness in the joints. Patients with PSA noted a regression of cutaneous manifestations of disease, which probably contributed to the achievement of a significant positive dynamics of PHI and fatigue in patient on the background of a decrease in the inflammatory process activity, which was confirmed by a significant decrease in ESR and CRP.

Should be noted a statistically significant improvement in the psycho-emotional status of patients. Thus, a significant decrease in SA, PA and HDS in the 1st and in the 2nd group.

The world litterature focuses on the treatment of pain syndrome initially, but our data indicate the effectiveness of stabilizing, firstly, the patient's psycho-emotional state in order to obtain a positive response to treatment [1,2,12].

CONCLUSIONS

In both study groups, a high frequency of inadequate socio-psychological response to the disease was noted, which amounted up to 75.0% of patients with AS, and 87.5% in the group with PSA. In both groups of patients with seronegative arthritis there were multidirectional maladaptive reactions: for people with AS more hypochondriac type of response, increased suspiciousness, depressed mood and mental activity; and patients with PSA were more likely to have anxiety disorders with different response options. At the end of the observation period in both groups there was an improvement in almost all studied indicators of clinical and laboratory activity. Special mention should be made of the statistically significant improvement in the psycho-emotional status of patients, which makes it possible to improve the quality of patients life and contribute to the treatment optimization and rehabilitation measures.

In conclusion, we note that the neurometabolic strategy for the treatment of patients with seronegative arthritis is largely a new direction for domestic clinical practice. That is why the widest possible approbation of Eglonil in general medical practice will reveal its real benefits and assess its place in the clinic.

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ORCID and contributionship:
Liliia V. Burya: 0000-0003-3137-6783 [A, D, F]
Nataliia V. Moisieieva: 0000-0001-8901-3710 [B, D]
Anna A. Kapustianska: 0000-0001-9150-8472 [D, F]
Andrii V. Vakhnenko: 0000-0003-1040-7042 [C]
Iryna M. Zviagolska: 0000-0001-7531-3966 [C]
Mariia O. Rumiantseva: 0000-0001-7247-9792 [E]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Liliia V. Burya
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
e-mail: burya.lilia@gmail.com

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ORIGINAL ARTICLE

PREDICTION OF ASTHMA CONTROL STATUS IN SCHOOL-AGE CHILDREN SENSITIZED TO CAT ALLERGENS

DOI: 10.36740/WLek202206110

Mariia V. Kryvopustova
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To develop a model for predicting asthma control status in school-age children sensitized to cat allergens.

Materials and methods: The study included 302 children aged 6-17 years who were sensitized to cat allergens. The ALEX^2 test (Macro Array Diagnostics GmbH, Austria) was used to analyze the sensitization profile in these children. After 12 months of treatment, control of clinical asthma symptoms was achieved in 185 (61.26%) children. Single-factor logistic regression models were constructed to analyze the probability of achieving asthma control in school-age children with sensitization to cat allergens.

Results: It was found that asthma control status depended on the FeNO dynamics after 3 months of treatment, the number of cat allergens to which sensitization was detected, and the duration of exposure to a domestic cat after sensitization tests, which were conducted to verify the allergic capacity to cat allergens. The investigation resulted in the creation of a mathematical model for predicting the probability of asthma control, sensitivity 94.6 (95% CI 90.3 - 97.4) %, specificity - 81.2 (95% CI 72.9 - 87.8) %, PPV = 88.8 (95% CI 84.5 - 92.1) %, NPV = 90.5 (95% CI 83.8 - 94.6) %.

Conclusions: A model for predicting the probability of asthma control was created. The formula is used to calculate the patient's P. P > 0.44 allows predicting the achievement of asthma control after 12 months of treatment.

KEY WORDS: cat allergens, asthma, children, sensitization

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INTRODUCTION

Asthma is the most common chronic disease in children, imposing a consistent burden on the health system [1]. Asthma has a significant social as well as a medical impact as its prevalence among children is increasing with every passing year [2,3]. Thus, in Ukraine, the prevalence rate has increased by 69.3% over the past 25 years [4]. There is evidence that indoor allergens produced, in particular, by cats, are triggers of asthma in children, especially in the sensitized ones [5]. Domestic cats are considered the third most common cause of respiratory allergies, after pollen and house dust mites. Thus, the prevalence of sensitization to cat allergens is approximately 5-20%, and in patients with respiratory allergies - 20-30% and even more [6 - 10]. The Global Asthma Treatment and Prevention Strategy (GINA) 2021 provides clinicians with up-to-date evidence-based guidelines for the management of children with asthma [2, 3]. An important goal of asthma treatment is good control of its symptoms [11]. Today, prediction of asthma control status in children is mainly based on commitment to pharmacological treatment, including effective doctor-patient interaction, as well as personalized management of factors that provoke exacerbation of asthma [3]. This issue is extremely relevant, in particular, for school-age children [12, 13]. Consequently, more research is needed on the prediction of asthma control status in school-age children sensitized to cat allergens.

THE AIM

The aim of the study is to develop a model for predicting asthma control status in school-age children sensitized to cat allergens.

MATERIALS AND METHODS

The retrospective study included 302 patients who met the following inclusion criteria: diagnosed with bronchial asthma; children of both sexes; age 6-17 years; sensitization to at least one of the following cat allergens Fel d 1, Fel d 2, Fel d 4, Fel d 7. Among them there were 187 boys (61.92%) and 115 girls (38.08%). Careful history taking, spirometry, skin-prick test with Fel d 1 standardized extract (5,000 BAU / mL), total IgE, fractional exhaled nitric oxide (FeNO) before and after 3 months of treatment. The sensitization profile was analyzed using the ALEX^2 test (Macro Array Diagnostics GmbH, Austria), a multiplex allergy test for molecular research. Statistical analysis was performed using IBM SPSS Statistics Base (version 22). A value of $p < 0.05$ was considered statistically significant. Quantitative data are expressed as mean and with 95% confidence interval (CI).

Asthma was controlled in 185 (61.26%) children. Intermittent asthma was diagnosed in 84 (27.81%) children, mild persistent - in 134 (44.37%) patients, moderate persistent - in 65 (21.52%) patients, severe - in 19 (6.29%)

patients. 226 (74.83%) children were constantly exposed to a domestic cat before the molecular allergy testing. According to the results of skin prick test with Fel d 1 standardized extract, papules of 3-7 mm were observed in 96 (31.79%) patients, 8-12 mm in 128 (42.38%) patients, and ≥ 13 mm in 78 (25.83%) patients.

The molecular multiplex test results revealed sensitization to the major cat allergen Fel d 1 in 291 (96.36%) children, to Fel d 2 in 18 (5.96%) children, to Fel d 4 in 59 (19.54%) children, and to Fel d 7 - in 75 (24.83%) children. The combination of different cat allergens in one patient was also analyzed. Thus, combined sensitization to Fel d 1 and Fel d 7 was observed in 32 (10.60%) patients, to Fel d 1 and Fel d 4 - in 22 (7.28%) patients, to Fel d 1, Fel d 4, Fel d 7 - in 22 (7.28%) patients, and to Fel d 1, Fel d 2, Fel d 4, Fel d 7 - in 12 (3.97%) patients.

Spearman's rank correlation coefficient was used to assess the correlation between controlled asthma and sensitization to cat allergens, as this distribution differs from normal. A correlation was found between the presence of asthma control and the number of cat allergens to which the child is sensitized ($r = -0.382$; $p < 0.001$), which emphasizes the importance of multiple sensitizations. Regarding the structure of sensitization, a correlation was found between the presence of asthma control and sensitization to Fel d 4 ($r = -0.321$; $p < 0.001$) and Fel d 7 ($r = -0.384$; $p < 0.001$). In terms of sensitization to a combination of allergens, there was noted a correlation between asthma control and the combination of Fel d 1, Fel d 4, Fel d 7 in one patient ($r = -0.326$; $p < 0.001$). A correlation was established between the presence of asthma control and fractional exhaled nitric oxide dynamics after 3 months of treatment ($r = 0.677$; $p < 0.001$), and the time the cat stays at home (expressed in months) before it is kept out of the child's room ($r = -0.344$; $p < 0.001$).

Single-factor logistic regression models were constructed to analyze the probability of achieving asthma control in school-age children with sensitization to cat allergens. The design of this study was approved by the Commission on bioethical expertise and ethics of scientific research at Bogomolets National Medical University, Kyiv, Ukraine.

RESULTS

21 variables were analyzed: sex, age, body weight, height, food allergy, food allergy to cow's milk protein, family history of allergy, living in the city or in the village, active or passive smoking, recent diagnosis of atopic dermatitis or its presence in the anamnesis, diagnosis of allergic rhinitis, skin prick test, total IgE level, initial FeNO level, fractional exhaled nitric oxide dynamics after 3 months of treatment, initial level of forced expiratory volume in the first second (FEV1), the number of cat allergens to which children have sensitization, severe asthma, basic therapy, the duration of exposure to a domestic cat after the molecular allergy testing.

The conclusion can be made about the presence of a link ($p < 0.05$) between asthma control and the initial FeNO level, fractional exhaled nitric oxide dynamics after 3 months of treatment, the initial FEV1, the number of cat allergens to which sensitization is detected, the duration of exposure to domestic cats after molecular allergy testing, the presence of severe asthma, the presence of atopic dermatitis, smoking, and basic asthma therapy.

The primary endpoint included a prediction of the probability of achieving asthma control in school-age children with sensitization to cat allergens after 12 months of treatment, $Y = 0$ in case of failure to achieve asthma control and $Y = 1$ in case of achieving asthma control. After 12 months of treatment, control of clinical asthma symptoms was achieved in 185 (61.3%) children, and it was not achieved in 117 (38.7%) patients. The model, which included 21 factor traits, showed the dependence of asthma control status on the factor traits, the area under the ROC curve AUC = 0.95 (95% CI 0.92 - 0.97), statistically significantly ($p < 0.0001$) exceeding 0.5, which indicates excellent quality and adequacy of the constructed model (Figure 1).

The Stepwise variable on / off method was used to select the minimum set of factors associated with asthma control status. There were defined 3 factors associated with the probability of achieving asthma control: "The FeNO dynamics after 3 months of treatment", "The number of cat allergens to which sensitization was detected" and "The duration of exposure to a domestic cat after the molecular allergy testing" (Table I). A three-factor logistic regression model was built based on the selected factor characteristics, AUC = 0.93 (95% CI 0.90-0.97), statistically significantly ($p < 0.0001$) exceeding 0.5, which indicates excellent quality and adequacy of the constructed model (Figure 2). No deterioration was found in the predictive value of the three-factor model and the model based on all the 21 variables ($p = 0.0961$).

Among the significant factor features of the three-factor model, the most important was the FeNO dynamics, AUC = 0.90 (95% CI 0.86-0.93), statistically significantly ($p < 0.0001$) exceeding 0.5, which indicates excellent quality and adequacy of the constructed model. A comparative analysis of the three-factor and single -factor models showed that the three-factor model was statistically significantly better ($p = 0.007$) at predicting the probability of achieving asthma control based on the FeNO dynamics after 3 months of treatment. For two other significant factors, namely "The number of cat allergens to which sensitization was detected" and "The duration of exposure to a domestic cat after the molecular allergy testing", its predictive value was worse.

Thus, it was found that asthma control status is associated ($p < 0.05$) with "The FeNO dynamics after 3 months of treatment", "The number of cat allergens to which sensitization was detected", "The duration of exposure to a domestic cat after the molecular allergy testing". It was noted that with an increase in the value of FeNO dynamics after 3 months of treatment by 1% the probability of asthma control increases by 1.3 times (OR = 1.26 (95% CI 1.19-1.34) ($p < 0.0001$)). It was also found that with an increase in the number of cat allergens to which the child is sensitized by 1 allergen, the probability of achieving asthma control decreases by 3.4

Table I. Analysis of multifactor logistic regression models for the prediction of asthma control status in school-age children with sensitization to cat allergens after 12 months of treatment

Factor	Value of the coefficient of the model, $b \pm m_b$	Level of significance of difference between OR and 0, p	Odds Ratio, OR (95% CI)
FeNO dynamics after 3 months of treatment, %	0,23±0,03	<0,0001	1,26 (1,19–1,34)
Number of cat allergens, to which sensitization was detected, pcs.	-1,24±0,33	0,0002	0,29 (0,15–0,56)
Duration of exposure to a domestic cat after the molecular allergy testing, months	-0,20±0,06	0,0013	0,82 (0,73–0,93)

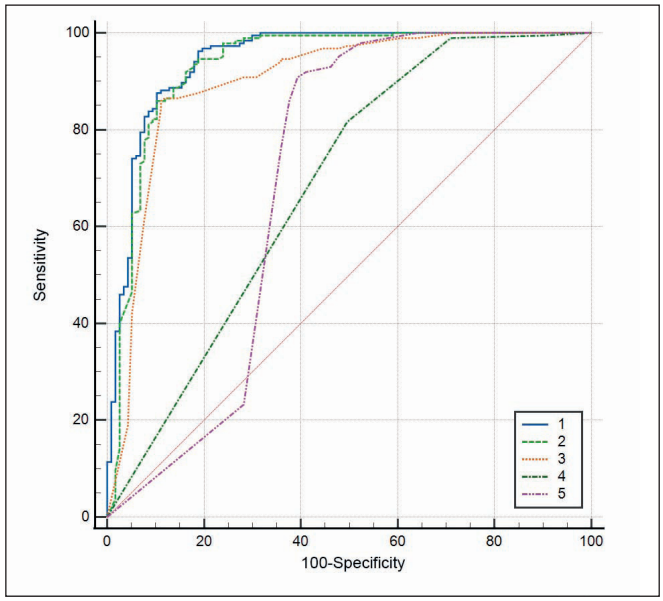

Fig. 1. Receiver Operating Characteristic (ROC) curves for asthma control prediction after 12 months of treatment for the following variables: 1 - model that included 21 factor traits, 2 - model with a minimum number of factor traits (3 traits), 3 – the FeNO dynamics after 3 months of treatment, %, 4 - number of cat allergens to which sensitization was detected, pcs., 5 - duration of exposure to a domestic cat after the molecular allergy testing, months.

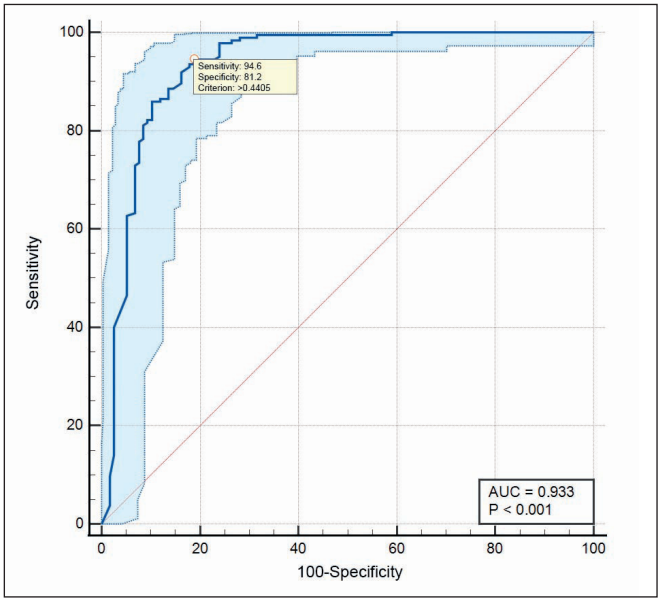

Fig. 2. Receiver Operating Characteristic (ROC) curve with 95% confidence interval for a three-factor model for predicting the probability of achieving asthma control after 12 months of treatment.

times (OR = 0.29 (95% CI 0.15-0.56) (p = 0,0002)). It was established that with the increased duration of exposure to a domestic cat by 1 month after the molecular allergy testing, the probability of achieving asthma control reduces by 1.2 times (OR = 0.82 (95% CI 0.73-0.93) (p = 0.0013)).

The obtained mathematical model for predicting the probability of asthma control can be expressed by the formula:

$$\ln\left(\frac{P}{1-P}\right) = -0{,}4 + 0{,}23 \times X1 + (-1{,}24 \times X2) + (-0{,}2 \times X3)$$

whereas

X1 – The FeNO dynamics after 3 months of treatment, %,

X2 – The number of cat allergens to which sensitization is detected, pcs.

X3 – The duration of exposure to a domestic cat after the molecular allergy testing, months.

Youden Index test optimization was used to select the optimal threshold for asthma control prediction test after 12 months of treatment. Thus, the optimal limit value for the test is determined by the level of P > 0.44: for P (patient) > 0.44, the risk of "accident" is predicted, i.e., the achievement of asthma control, for P (patient) ≤ 0.44, "not a case" is predicted, i.e., a failure to control asthma.

The test threshold is optimal when its sensitivity is 94.6 (95% CI 90.3 - 97.4) %, specificity - 81.2 (95% CI 72.9 - 87.8) %, predictability of a positive test result PPV = 88.8 (95% CI 84.5 - 92.1) %, the prognosis of a negative test result NPV = 90.5 (95% CI 83.8 - 94.6) %. Thus, if P (patient) > 0.44, it allows predicting the achievement of asthma control after 12 months of treatment and, in 88.8% of cases, this control will actually be achieved after 12 months of treatment.

DISCUSSION

Today, Pediatric Allergology is concerned with such important issues as prediction of the clinical course of asthma and asthma control. Over the years, numerous studies have aimed to develop a method for predicting asthma control

status. For this purpose, the level of vascular endothelial growth factor in sputum supernatant was studied [14].

The current study included an analysis of the fractional exhaled nitric oxide (FeNO) dynamics after 3 months of treatment, the number of cat allergens to which sensitization was detected and the duration of exposure to a domestic cat after the molecular allergy testing. It is crucial that not only the initial value of fractional exhaled nitric oxide (FeNO) was determined, but also the dynamics of eosinophilic inflammation in the airways, which is associated with the response to basic anti-inflammatory therapy.

Regarding the restriction of cats from the child's room, i.e., the elimination of further exposure to the causative factor, it is a well-known fact that keeping pets out of home reduces airway sensitivity in patients with allergic asthma and allows decreasing the dose of inhaled corticosteroids [15]. Homes with domestic cats have a level of Fel d 1 usually 80-300 times higher than homes without cats [7, 16]. However, this cannot be considered the only factor that radically solves the problem, other measures should also be taken. Thus, although keeping cats out of home can dramatically reduce the concentration of Fel d 1 [15], it may take 4-6 months or even more to reach the level observed in homes without cats [17]. In addition, there is an increased level of these allergens in the rooms where these animals do not live at all [18]. However, we have shown the importance of avoiding further constant exposure to a domestic cat, as well as the correlation between the time the cat stays at home and asthma control status.

In addition, we noted the role of the number of cat allergens to which the child is sensitized. According to the Consensus document on dog and cat allergy, sensitization to two or more allergens is associated with more severe respiratory symptoms and is a marker of severe asthma [9].

In the study, we developed and substantiated a mathematical model for predicting the probability of asthma control based on the FeNO dynamics after 3 months of treatment, the number of cat allergens to which sensitization is detected and the duration of exposure to a domestic cat after the molecular allergy testing.

CONCLUSIONS

Prediction of asthma control status in school-age children with sensitization to cat allergens should be based on the analysis of the dynamics of fractional exhaled nitric oxide (FeNO) after 3 months of treatment, the number of cat allergens to which sensitization is detected and the duration of exposure to a domestic cat after the molecular allergy testing. In this study, a model for predicting asthma control status was created. The formula is used to calculate the patient's P. $P > 0.44$ allows predicting the achievement of asthma control after 12 months of treatment.

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ORCID and contributionship:
Mariia V. Kryvopustova: 0000-0001-7200-4703 [A-F]

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The Author declare no conflict of interest.

CORRESPONDING AUTHOR
Mariia V. Kryvopustova
Bogomolets National Medical University
13 Taras Shevchenko Boulevard, 01601 Kyiv, Ukraine
tel: +38(099) 4337384
e-mail: kryvopustova@gmail.com

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ORIGINAL ARTICLE

EFFICIENT COMPREHENSIVE TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION AND POSTCOVIDAL SYNDROME IN ELDERLY PATIENTS

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Maksym M. Potyazhenko, Tetiana V. Nastroga, Nina L. Sokolyuk, Oksana Ye. Kitura, Nelya M. Motorna, Angelina S. Korpan
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: The purpose of the study is to increase the efficacy of comprehensive treatment in elderly patients with COPD , who have suffered of coronavirus disease-COVID-19 in the last 3-6 months, by using nebulizer therapy with N-acetylcysteine and 3% hypertonic sodium chloride solution (Flu-Acyl broncho) and the drug glycine, to correct psychosomatic disorders.

Materials and methods: Under our supervision there were 60 elderly patients with COPD gr D, who underwent Covid 19 in the last 3-6 months, were under observation. The average age was 66.3±2.1 years. Patients of the main and control groups were prescribed complex basic therapy. However, mucolytic therapy was administered to patients in the main group using combined drug - N-acetylcysteine and 3% hypertonic sodium chloride solution through a 5.0 №10 nebulizer. For the treatment of astheno-neurotic disorders of postcovidal syndrome was prescribed glycine 100 mg 2 times a day for 10 days. Subsequently, Flu-Acyl broncho through a nebulizer at 5.0 No.10, and glycised was used in courses once a day for 10 days per month. Patients in the control group were prescribed acetylcysteine 200 mg 3 times a day N10.

Results: The results of observation for 6 months showed that in patients of the main group, recurrence of the disease was not observed. whereas in patients of the control group in 6 patients (20%).

Conclusions: Comprehensive treatment of elderly patients with comorbid pathology - COPD group D and postcovidal syndrome, with the additional use of nebulizer delivery of the combined drug - N-acetylcysteine and 3% hypertonic sodium chloride solution in combination with the sedative drug glycine, promotes improving the quality of life in patients, reducing the duration of treatment, prevents recurrence and progression of COPD.

KEY WORDS: COPD, frail age, post-covid syndrome, N-acetylcysteine and 3% sodium chloride, glycine, nebulizer therapy

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INTRODUCTION

Population aging has become a leading demographic feature of Ukraine. According to the World Health Organization, the number of elderly and senile people will increase to almost 40% in the coming decades [1]. It is known that with age the number of comorbid conditions increases significantly, which is characterized by the presence of additional clinical picture, new mechanisms of disease development, complications and course that are not specific to the underlying disease, which significantly affect quality of life and expectancy. In this regard, the problem of personalizing a patient with comorbid pathology also acquires special attention [2].

Currently, one of the most important medical and social problems in Ukraine and in the world is chronic obstructive pulmonary disease (COPD) [3], which is complicated by the epidemiological situation associated with the spread of COVID-19. Thus, according to the WHO, today 0.8 % of the world's population suffers from COPD) [4-8]. At the same time, a very serious problem in connection with the pandemic in the world is the coronavirus disease - COVID-19. It is known that the causative agent of coronavirus infection is COVID-19, which, as a rule, severely affects elderly patients over 60 years. There is also an indisputable fact of increasing the severity of functional and morphological disorders that existed before COVID-19, so patients after the acute phase show signs of chronic diseases exacerbation [9]. The urgency of the problem lies in the large-scale spread of this pathology, reduced quality of life in patients, lack of knowledge about the frequency, features and causes of long-term consequences of postcovidal syndrome, uncertain ideas about approaches to diagnosis and therapy [10]. It is known that the rehabilitation needs of patients with COVID-19 are possible in both acute, post-acute and long-term periods [11]. Postcovcidal syndrome is a set of symptoms that develop during or after COVID-19, last ≥12 weeks, and cannot be explained by an alternative diagnosis. Postcovidal syndrome is characterized by complaints of constant fatigue, anxiety, and inactivity. Most frequently postcovidal syndrome manifests itself in the form of lung damage, mental disorders, asthenia [10,11]). Asthenia, or a state of neuropsychological and physical

weakness, is manifested by increased fatigue, weakening or loss of ability to prolonged physical or mental stress, but its specific symptoms may vary depending on the form and / or stage of the pathological process, reactive state, age and others [12]. In psychosomatic disorders, according to scientists, a rapid therapeutic effect of glycised is established. Glycine (aminoacetic acid) has the properties of a metabolism regulator and is a substitute amino acid (natural metabolite), is a neurotransmitter of the inhibitory type of action and a regulator of metabolic processes in the central nervous system. Glicised has antistress, sedative, nootropic and antitoxic effects [13], which justifies the use of glycised in the treatment of postcovidal syndrome in elderly patients.

Elderly patients with COPD are characterized by age-related changes in lung function that worsen the course of the disease. In this category of patients a significant place in the formation of respiratory diseases is given to the violation of the transport of tracheobronchial secretions. Therefore, one of the main tasks of therapy is to thin the sputum, reduce its adhesiveness and improve the drainage properties of the respiratory tract. It is known that in the treatment of COPD, preference is given to the inhalation route of drugs administration.

Today, the modern means of drug delivery to the respiratory tract is nebulizer therapy, the efficacy and safety of which is scientifically and practically justified, including in people with severe somatic pathology, the elderly and children [14]. Although COPD is a progressive disease, personalized and adequately selected and timely pathogenetic therapy with subsequent rehabilitation can significantly slow the progression of bronchial obstruction, reduce the frequency and severity of exacerbations, prevent complications with systemic consequences, and, above all, improve the quality of life in patients. Among the drugs with the possibility of inhalation, mucolytics occupy an important place. One of the means of mucolytic action is a combined drug Flu-Acyl Broncho in nebulizer solution. It consists of N-acetylcysteine, which has a mucolytic effect in direct contact with mucus, and 3% hypertonic sodium chloride solution, which increases the proportion of water in the bronchial secretion, dilutes it and facilitates its removal. [15].

THE AIM

The purpose of the study is to increase the efficacy of treatment in elderly patients with moderate-grade COPD with exacerbation of moderate severity, who have suffered of coronavirus disease-COVID-19 in the last 3-6 months, by using nebulizer therapy in the complex treatment with Flu-Acyl Broncho and with glycised to correct psychosomatic disorders.

MATERIALS AND METHODS

Under our supervision there were 60 elderly patients with COPD in group D, with exacerbations of moderate severity, who suffered from COVID-19 for the latest 3-6 months. The mean age of patients was 66.3±2.1 years. The observation period was 6 months. The diagnosis was verified on the basis of complaints, anamnesis data (number of exacerbations per year, COVID-19 coronavirus disease transferred for the latest 3-6 months), physical examination, general clinical and laboratory-instrumental methods (general blood test, sputum analysis, chest radiography, spirography, tests with a bronchodilator, CRP, coagulograms). All patients underwent a preliminary screening test for SARS-CoV-2 antigen using rapid tests for SARS-CoV-2 antigen, a negative result was obtained, which ruled out recurrence of COVID-19. Pulse oximetry was used to determine blood oxygen saturation and assess the need for additional oxygen therapy [16]. Assessment of exercise tolerance was performed using a 6-minute exercise test (6 minute walking test - 6MWT) according to a standard protocol [3]. The diagnosis of COPD was made according to the adapted clinical guideline "Chronic obstructive pulmonary disease" in 2020 [3]. Patients' quality of life was assessed using the COPD Symptom Assessment (TOC) test, and the severity of dyspnea was assessed using the Medical Research Council's modified mMDR questionnaire – modified scale of Medical Research Council'. The psychological state of elderly patients with COPD included in the study was assessed using a questionnaire of Ch.D. Spielberger - Yu.L. Hanin [17]. The applied methods are approved by the ethics commission.

The probability of the obtained results was determined using the reliability t-test by Student. Differences were considered probable in the generally accepted in biobiological studies, the probability of error $p<0.05$. Patients were divided into groups - basic (n=30) and control (n=30). The groups of patients were comparable in age and gender, as well as the degree of respiratory failure. Patients in the main and control groups were prescribed antibacterial, anti-inflammatory, anticoagulant therapy, combination bronchodilator therapy. However, mucolytic therapy was administered to patients in the main group using Flu-Acyl broncho through a 5.0 №10 nebulizer. For the treatment of astheno-neurotic disorders of postcovidal syndrome was prescribed glycised 100 mg 2 times a day for 10 days. Subsequently, Flu-Acyl broncho through a nebulizer at 5.0 No.10, and glycised was used in courses once a day for 10 days per month.

Patients in the control group, were prescribed acetylcysteine (ACC) as mucolytic therapy: 200 mg 3 times a day №10. Subsequently, acetylcysteine was recommended in courses of 200 mg 2 times a day for 10 days per month. However, patients did not adhere to compliance.

RESULTS

All elderly patients with COPD in group D, included in the study, noted cough with purulent sputum discharge - 60 patients (100%), increased shortness of breath when walking -25 (41.6) patients, shortness of breath at rest in 35 - (58.4%), poor sleep - 59 (98.3%), general weakness

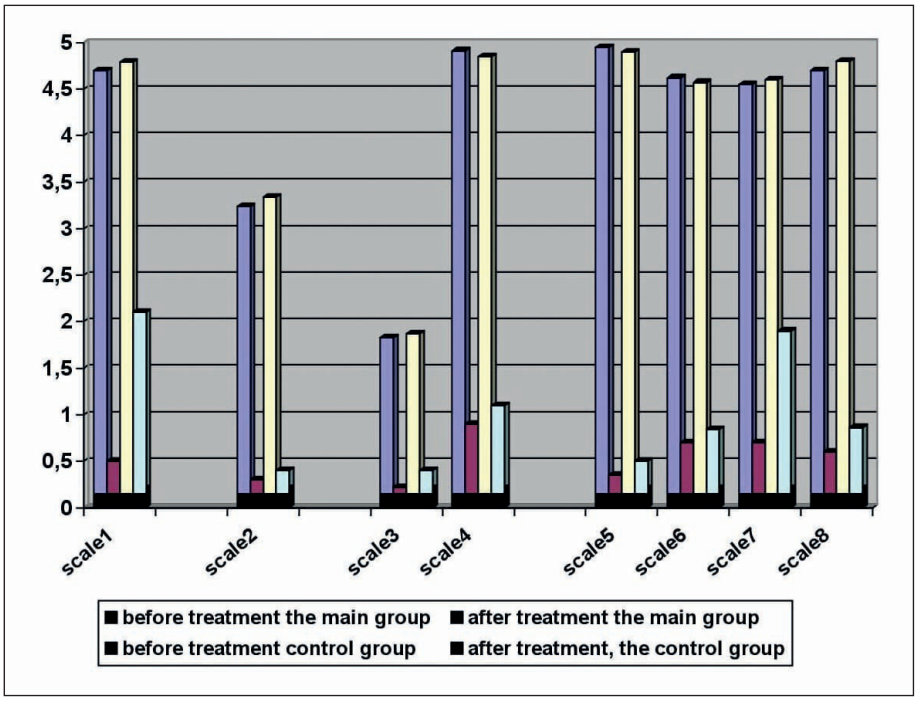

Fig. 1. Evalution of COPD symptoms in elderly patients with postcovidal syndrome according to the results of the test for the COPD (TOC) assessment by scales

Table I. Biochemical parameters and SpO2 in elderly COPD patients during treatment

Index	Main group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
Fibrinogen, g/l	5.3±0.23*	4.1±0.16	5.1±0.21*	3.8 ±0.3
APTT	24.7±0.81*	31.3±1.14	25.1±1.3*	30.7±0.79
SpO2%	92.08±0.3*	93.2±0.12	92.42±0.24	92.9±0.33

* - ($p < 0.05$) differences significant between patients before treatment and after treatment

– 60 (100%), increase in body temperature to subfebrile figures in 49 (82%). According to the results of general clinical and biochemical analysis of blood, leukocytosis was noted - 9.8±0.8l×10^9, and an increase in ESR - 32±3.6 mm/h, which indicated an exacerbation of COPD.

The study of the coagulograms in the patients included to the study showed an increase in fibrinogen and a decrease in APTT. Thus, the average values of fibrinogen were 5.2±0.8 g/l, the level of APTT - 19.8±1.4, which indicated a tendency to hypercoagulation in this category of patients and the activity of the inflammatory process [18]. The results of chest radiography revealed changes that indicated pulmonary emphysema in 60 patients (100 %), and a characteristic radiological picture of pneumosclerosis, pneumofibrosis in 24 patients (40 %), increased pulmonary pattern in 58 (96.6 %) patients.

The analysis of external function indices convincingly showed severe ventilation disorders of the mixed type (VC - 33.2±0.8; FEV1 - 30.1±1.35%, FEV1/FVC - 42.3±1.1%). The mean SaO2 saturation was 92.8%, indicating the presence of respiratory failure in the patients included in the study.

In the analysis of the patients' psychological state with the help of a questionnaire - Ch.D. Spielberger - Yu.L. Hanin, the mean level of RT was 58.8±3.1 points, which indicates a high level. Clinically, this was manifested by anxiety, worry, nervousness, poor sleep. The mean level of PT was 47.8±2.4 points, which also indicated a high level. PT is a characteristic feature of a personality and is determined by the type of higher nervous activity, temperament [1].

When interviewing patients by the MMDR scale, it was found that the mean total score before treatment in patients was 3.3±0.6 points, indicating severe shortness of breath in patients at the time of examination.

In determining the effect of infectious exacerbation of COPD in group D in elderly patients who underwent COVID-19 for quality of life for the latest 3-6 months using the TOX questionnaire, the mean index was 25.9±1.4, indicating a significant effect of disease symptoms on the quality of patients' life.

After the therapy, positive clinical dynamics were observed in patients of both groups, but significant differences were observed in terms of regression of the main symptoms of the disease - cough, shortness of breath. Thus, the mean time of cough fadeaway in patients of the main group was 7.6±0.52 days, while in patients of the control group 9.4±0.7 days ($p<0.05$). The mean time of shortness of breath fadeaway in patients of the main group was 6.8±0.6, while in patients of the control group it was 8.3±0.41 ($p<0.05$).

Analysis of external respiratory function shows that 10 days

after therapy in patients of the main group receiving comprehensive treatment there was a significant improvement in bronchial patency compared to patients in the control group ($p<0.05$), as evidenced by FEV_1. Thus, FEV_1 in patients of the main group increased by 24.8%, amounted to 29.8±1.3 % before treatment, after therapy - 37.2±1.17% ($p<0.05$). In patients of the control group, the corresponding indices increased by 12.2 % (were 30.4±1.05 %, and 34.1±1.23 %) ($p<0.05$).

When interviewing patients by the MMDR scale, it was found that the mean total score before treatment in patients of the main group was 3.34±0.6 points, after treatment - 1.2±0.32 points, i.e. decreased by 65 % ($p<0.05$), which indicated a significant reduction in the impact of disease symptoms on the quality of patients' ($p>0.05$). Whereas in patients of the control group after treatment the indices did not improve significantly, decreased by 48 % (before treatment - 3.26±0.73 points, after treatment 1.7±0.57 points) ($p>0.05$).

In determining the effect of infectious exacerbation of COPD group D in patients who have undergone COVID-19 during the latest 3-6 months, the quality of life with the help of TOC questionnaire (test of COPD asessment) showed a significant improvement in the efficacy of therapy in patients of both groups, but between patients in the main and control groups there were significant differences after treatment ($p<0.05$). Thus, in patients of the main group, the total TOC index improved by 75.6%. (before treatment was 26.2±1.3 after treatment - 6.4±0.7 points)($p<0.05$). While in patients of the control group, the total TOC improved after treatment by 63.7% (before treatment was 25.6±1.5 points, after treatment - 9.3±0.92 points) ($p<0.05$).

1. I cough constantly
2. My chest is completely filled with sputum (mucus)
3. I have a lot of pressure in my chest
4. When I go down a mountain or climb a flight of stairs, I feel very short of breath
5. I do housework with great restrictions
6. Leaving home, I feel insecure because of lung disease
7. I sleep poorly due to lung disease
8. I have no energy at all

Results of the test indicate significant differences ($p<0.05$) after treatment between patients in the main and control groups by scale of point 1- (I cough constantly), 7- (I sleep poorly due to lung disease). The mean score by scale of point 1 - (I cough) before treatment in patients of the main group - 4.7 ±0.6 points; after treatment in patients of the main group - 0.5±0.32; before treatment in patients of the control group - 4.78±0.42 points, after treatment of the control group - 2.1±0.54 ($p<0.05$). By scale of point 7- (I sleep poorly due to lung disease) before treatment in patients of the main group - 4.62±0.47 points, after treatment in patients of the main group - 0.45±0.21; before treatment in patients of the control group – 4,57±0,42, after treatment - 1.9±0.38 points ($p<0.05$).

When assessing the 6-minute test, significant differences were noted between patients in the main and the control groups ($p<0.05$). Thus, the mean distance traveled by patients of the main group was 312.4±7.2 m, while in patients of the control group, the distance traveled was 278.2±9.1 m, which is by 10.9 % less ($p<0.05$).

When studying the psychological state of elderly patients with COPD with the help of a questionnaire, by Ch.D. Spielberger –Yu.L. Khanin, the results obtained shows that in patients of the main group after treatment, the level of RA decreased significantly by 24.7% (before treatment was 57.2±2.33 points, after treatment - 43.1±1.62) ($p<0.05$). Whereas in patients of the control group the level of RA after treatment decreased by 18.5% (before treatment 58.4±3.1 points and 47.5±2.1 points) ($p<0.05$). The level of PA in patients of the main group (n=30) after treatment decreased significantly by 13.1% (before treatment was 47.5±2.31 points, after treatment - 41.1±2.12 points) ($p<0.05$). Whereas in patients of the control group (n=30) the level of PA decreased not significantly, by 12%. before treatment was 48.34±2.5 points, after treatment - 42.6±2.2 points ($p>0.05$). In addition, normalization of sleep was noted in 24 patients of the main group (80%), whereas among patients of the control group, sleep improvement was noted in 7 patients (23.3%) ($p<0.05$).

After a course of therapy, after 10 days there was a significant decrease in fibrinogen, an increase in APTT, which indicated a decrease in coagulation potential and improved rheological properties of blood .

The obtained results are presented in the table I.

In the analysis of blood oxygen saturation, there was a significant increase in the level of SpO2% after treatment in patients of the main group ($p<0.05$). Thus, in patients of the main group SpO2% before treatment was 92.08±0.3%, after treatment - 93.2±0.12% ($p<0.05$), i.e. improved by 1.2%. Whereas in patients of the control group the level of oxygen saturation improved not significantly, by 0.51% (was before treatment 92.42±0.24%, after treatment - 92.9±0.33) ($p>0.05$).

DISCUSSION

The results obtained show that the complex treatment of elderly patients with comorbid pathology - COPD group D, who underwent COVID-19 during the latest 3-6 months with the use of nebulizer therapy with the combination drug - Flu-Acyl Broncho and the sedative drug - glycised, promotes faster regression of the main COPD symptoms and manifestations of postcovidal syndrome - cough, shortness of breath, improved bronchial patency (as evidenced by increased FEV_1); reducing anxiety, normalizing sleep, improving the quality of life in patients, increasing tolerance to exercise. Thus, in addition to the etiological and pathogenetic factors affecting the quality of life (LQ) of the patients with COPD, the presence of a concomitant clinically significant syndrome the RA increases the negative effect on all components of LQ of these patients, which coincides with the authors' opinion [1,6,19]

Observations for 6 months showed that in patients of the main group who received complex therapy with nebulizer therapy and glycised, no recurrence of the disease was observed. While in patients of the control group, recurrences

of the disease were observed in 6 patients (20%). The results show that the use of nebulizer therapy with a solution of Flu-Acyl Broncho and the drug glycised, in the complex treatment of elderly patients with COPD group D, who underwent COVID-19 during the latest 3-6 months, promotes longer remission of COPD, prevention of relapses.

CONCLUSIONS

Comprehensive treatment of elderly patients with comorbid pathology - COPD group D and postcovidal syndrome, with the additional use of nebulizer delivery of the combined drug - N-acetylcysteine and 3% hypertonic sodium chloride solution in combination with the sedative drug glycine, promotes improving the quality of life in patients, reducing the duration of treatment, prevents recurrence and progression of COPD.

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ORCID and contributionship:
Maksym M. Potyazhenko: 0000-0001-9398-1378 [F]
Tetiana V. Nastroga: 0000-0001-5347-6094 [D]
Nina L. Sokolyuk: 0000-0002-7436-9965 [B]
Oksana Ye. Kitura: 0000-0001-5319-5831 [A]
Nelya M. Motorna: 0000-0002-7162-4940 [E]
Angelina S. Korpan: 0000-0002-2879-3087 [C]

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CORRESPONDING AUTHOR
Tetyana V. Nastroga
Poltava State Medical University
24 Shevchenka st., 36024 Poltava, Ukraine
tel: + 38 066 425 72 11
e-mail: tatjananastroga66@gmail.com

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ORIGINAL ARTICLE

PECULIARITIES OF MORPHOETIOPATHOGENESIS OF ACUTE APPENDICITIS AND CONSEQUENCES AFTER APPENDECTOMY

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Volodymyr H. Hryn, Vitaliy S. Drabovskiy, Dmytro A. Sytnik, Roman M. Ryabuschko, Mykola M. Riabuschko, Serhii M. Bilash, Bohdan I. Gonzhak
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To study the features of morphoethiopathogenesis of acute appendicitis and the consequences after appendectomy.

Materials and methods: 10 preparations of human appendix were studied, from which 5 appendixes were normal in people who died in adulthood and old age and 5 processes were taken intraoperatively during appendectomy. Morphometric characteristics of the tissue structures of the preparations were compared with the systematic review data, the literature search by the following keywords: morphoethiopathy", "vermiform process", "lymphoepithelial formations", "digestive system", "lymphoid nodule", "Peyer's patches", "mucous membrane".

Results: Pathogenesis of acute appendicitis – it is a consistent, staged process that is completely subject to the laws of exudative inflammation in response to microbial aggression. Removal of the appendicular process should be approached carefully and based on possible immunological consequences. Removal of the appendix as an immunocompetent organ Unreasonable removal of pathohistological unchanged appendix has medical consequences (can lead to consequences such as colon cancer) and not only.

Conclusions: Our results suggest that the vermiform appendix retains its active function throughout human life. The study provides an overview with current knowledge about the etiology, pathogenesis and possible consequences of appendectomy as the main method of treatment of acute appendicitis. The search for ways to prevent appendicitis can be successful only by finding out the causes and factors that in some individuals cause the inability of the appendix to resist bacterial invasion. Appendix is necessary to fully support the immune responses of the digestive tract, but it belongs to the category of those organs, the loss of which during forced surgery does not cause significant damage to the body.

KEY WORDS: Appendicitis, acute surgical pathology, lymphoepithelial formations

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INTRODUCTION

Currently, special importance in revealing the nature of the vast majority of diseases of the digestive system is given to the immune system, the relevant aspects of which are widely presented and discussed in many scientific journals. [1]. Although many publications on some issues are contradictory and incompletely studied, in recent years there has been a general concept of the mechanism of interaction between different parts of the immune system of the gastrointestinal mucosa, represented by the association of numerous lymphoid structures with mucosa due to migration and recirculation of immunocompetent cells between them provides the possibility of simultaneous activation of the immune response in all parts of the digestive tract, regardless of the focus of antigenic stimulus [2].

A special place in this system is occupied by the appendix, which, unlike other lymphoepithelial structures, is a relatively separate organ-type formation containing densely concentrated in the mucous membrane group of lymphoid nodules, known as Peyer's patches. [3]. The close anatomical connection between the appendix and the cecum is due to the fact that the latter breaks down food residues (mostly fiber) by putrefactive bacteria, which may include pathogenic microorganisms. It is possible that in some circumstances they are the cause of appendicitis.

Given the well-known theoretical position that any system in the body has mechanisms of adaptation and compensatory reserves, it can be argued that the immune system of the mucous membranes of the digestive tract in this regard is not an exception. Given this, not only theoretical but also practical interest is the question of why and in what form is the local immune defense compensation for the loss of the appendix after appendectomy.

THE AIM

The aim was to study the features of morphoethiopathogenesis of acute appendicitis and the consequences after appendectomy.

MATERIALS AND METHODS

10 preparations of human appendix were studied, from which 5 appendixes were normal in people who died in adulthood and old age and 5 processes were taken intraoperatively during appendectomy. After fixation in 10%

neutral formalin solution, the preparations were embedded in epon-812. Microscopic examination of the appendix tissues was carried out by obtaining sections of different thicknesses in their transverse and longitudinal directions. After thorough polishing of the end surfaces, they were stained with a 1% solution of methylene blue in a 1% solution of borax and studied using an MBS-9 and a Konus light microscope equipped with a Sigeta DCM-900 9.0MP digital microphotographic attachment with the Biorex 3 program adapted for these studies (serial number 5604). Morphometric characteristics of the tissue structures of the corresponding preparations were obtained using a system for visual analysis of histological preparations.

This bibliographic analysis is based on published articles, books, textbooks, monographs, and abstracts of dissertations. For the purposes of this systematic review, the literature search (concerning the study of morphoethiopathogenesis of acute appendicitis and consequences after appendectomy) was carried out on the Internet, domestic literature sources, scientific and electronic libraries of Poltava State Medical University by the following keywords: morphoethiopathy", "vermiform process", "lymphoepithelial formations", "digestive system", "lymphoid nodule", "Peyer's patches", "mucous membrane". The search period covered the period from 2011 to 2021, but the review includes some data from earlier publications, as these literature sources are of great scientific value.

The following inclusion and exclusion criteria were used: inclusion criteria: original articles published in journals and conference proceedings, books, textbooks, monographs, dissertation abstracts, peer-reviewed, language of publication: Ukrainian, Russian, English; Exclusion criteria: reviews, case studies, editorials, letters, etc. that are not peer-reviewed, language of publication: others.

RESULTS

With age, starting from mature (40 years) and ending with extreme old age (90 years), the appendix retains its typical structural principle in an active state. From a constructive point of view, its wall mainly consists of two (except for the serous coating) coaxial membranes - muscular and mucosal, separated from each other by a well-defined layer of loose fibrous connective tissue with an admixture of fatty tissue (Fig. 1).

A special place in the immune system is occupied by the appendix, which, unlike other lymphoepithelial structures, is a relatively isolated organ-type formation containing densely concentrated in the mucosa group lymphoid nodules known as Peyer's patches (Fig. 2).

The close anatomical connection of the appendix with the cecum is explained by the fact that in the latter there is a breakdown of food residues (mostly fiber) by putrefactive bacteria, which may include pathogenic microorganisms. Apparently, in some circumstances they are the cause of appendicitis.

Acute appendicitis is a local infectious non-specific inflammatory disease of the appendix, which develops due to changes in the biological relationship between the human body and microorganisms under the influence of various factors that require immediate surgical treatment.

A significant number of etiological theories of acute appendicitis are known. In any case, the occurrence of non-specific acute inflammation in the appendix is impossible without the participation of pathogenic microflora, which is normally present in every person. Inflammation requires certain conditions: damage to the barrier function of the mucous membrane of the appendix, increased virulence of the microflora, violation of the body's defenses.

According to the analysis of literature sources, the microflora can get into the mucous membrane in two ways: enterogenic and hematogenous. Enterogenic penetration implies the presence of damage to the mucous membrane or increase the virulence of the microflora while maintaining the normal function of the mucous membrane. Damage to the barrier function of the mucosa can be caused by trauma (foreign body, worm infestation, fecal stone, etc.) and disruption of its blood supply (arterial thrombosis, reflex spasm, etc.). If there is no damage to the mucous membrane and its barrier function is preserved, the microorganisms can penetrate the mucous membrane only with increasing virulence and activity. This can be observed in sensitization of the body, the processes of putrefaction and fermentation in the colon, constipation, and decreased acidity of gastric juice. In the case of hematogenous penetration of the microflora, inflammation is possible only in violation of the body's defenses, i.e. in any condition in which the human body develops immunodeficiency [4].

Specific inflammation of the appendix is caused by disease or factors that are not present in a normally functioning body. In this case, the diagnosis is based on the underlying disease, and inflammation of the appendix is stated as its complication (N.: ascariasis, acute phlegmonous appendicitis, worm infestations).

All theories have a right to exist, but today the most accepted theory of Aschoff's primary effect. According to her, the action of certain factors leads to functional disorders in the intestine (bauginospasm). As a result of bauginospasm there is a spasm of the vessels of the appendix, ischemia of the wall of the appendix develops (primary effect). As a result, the intestinal autoflora easily penetrates into the wall and causes acute inflammation of the appendix.

Pathogenesis of acute appendicitis – it is a consistent, staged process that is completely subject to the laws of exudative inflammation in response to microbial aggression. This process begins acutely with serous inflammation and is localized in the serous and mucous membranes.

Morphological changes observed in inflammation of the appendix are very diverse and depend mainly on the stage of the inflammatory process. There are two clinical and anatomical forms of appendicitis: acute and chronic. Each of them has a certain morphological characteristic.

We studied intraoperatively 2 catarrhal, 2 phlegmonous and 1 gangrenous forms of appendicitis.

The initial form of inflammation of the 2 appendices is defined as acute catarrhal appendicitis. Pathologists

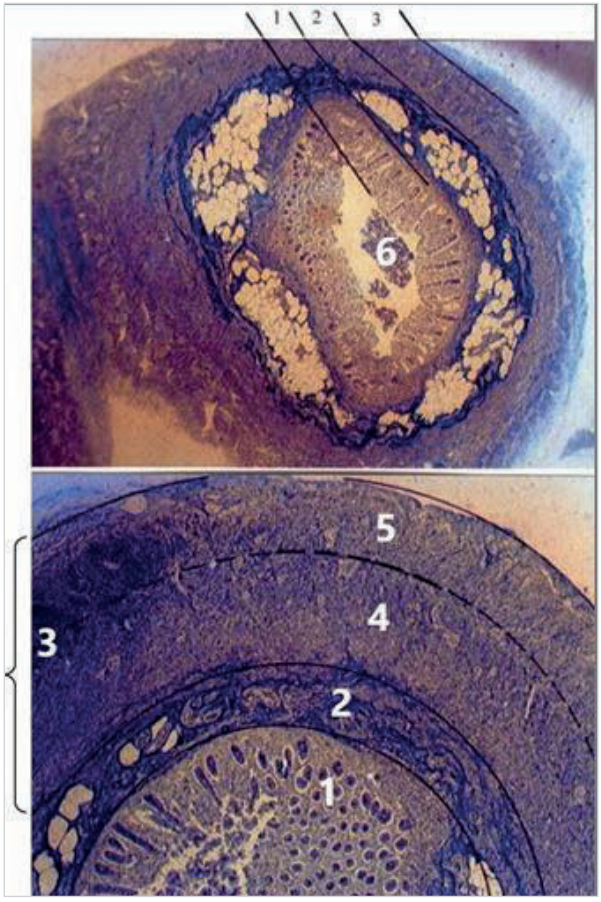

Fig. 1. Cross section of the base and middle part of the appendix. Epoxy sections; methylene blue color; 7x lens.
1 - mucous membrane; 2 - submucosal connective tissue base; 3 - muscular membrane; 4 and 5 - its inner and outer layers; 6 - internal lumen of the appendix

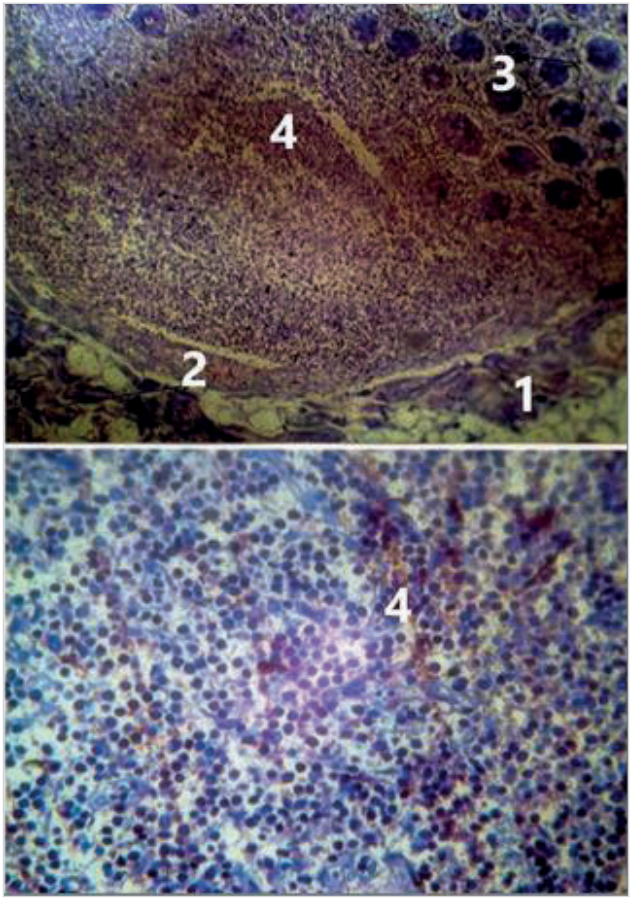

Fig. 2. Lymphoid nodule of the mucous membrane of the appendix. Epoxy sections; methylene blue staining; 10x and 40x lens.
1 - submucosa; 2 - base of the node; 3 - crypts; 4 - lymphocytes of the nodule

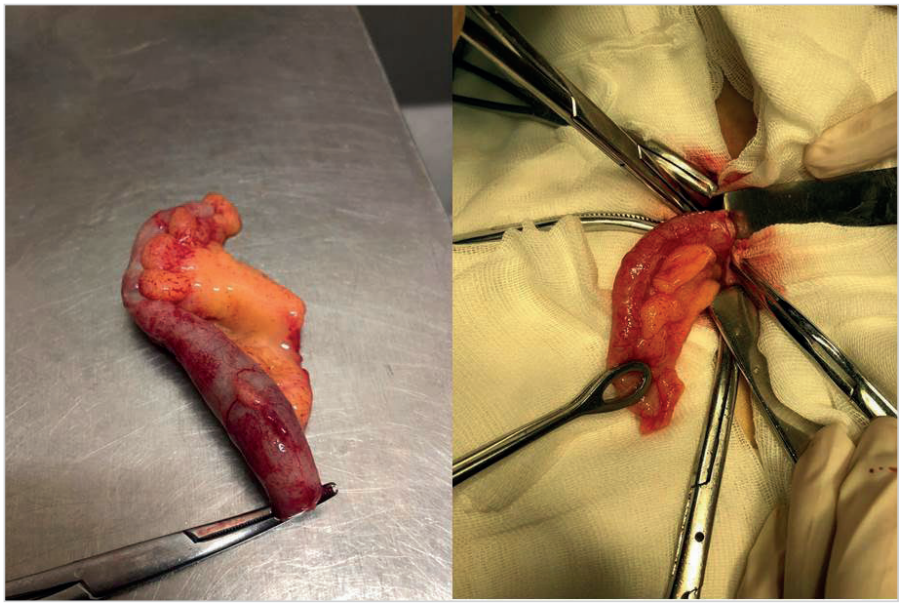

Fig. 3. Macroscopic picture of phlegmonously altered appendicular process

distinguish this form as "simple appendicitis" or "superficial appendicitis", which is more correct in terms of the essence of the inflammatory process. Macroscopically, the appendix looks a bit thickened, its serous membrane is dull, there are many small vessels filled with blood under it, which gives the impression of bright redness. In section, the mucous membrane of the appendix is swollen, gray-red, in the submucosal layer sometimes there are spots of hemorrhage. The lumen of the appendix often contains fluid of the genitalia. Microscopically, it is possible to de-

tect small defects of the mucous membrane covered with fibrin and leukocytes. Sometimes from a small defect the lesion spreads to tissues located deeper, having the shape of a wedge, the base of which is directed towards the serous membrane, this is a typical primary Aschoff's effect. There is a moderate leukocyte infiltration of the submucosal layer. The muscle membrane is not altered or slightly altered. The serous membrane contains a large number of dilated vessels, which can also be observed in the mesentery of the appendix. Occasionally there is a clear sterile reactive effusion in the abdominal cavity.

The inflammatory process is acute phlegmonous appendicitis (2 macropreparations). Macroscopically, the appendix looks significantly thickened; his serous and mesentery decreased, brightly hyperemic. The appendix is covered with a layer of fibrin, which in phlegmonous form is always more or less. Due to the fact that the process of transition to the peritoneum, you can see fibrinous layers on the dome of the cecum, parietal peritoneum, adjacent loops of the small intestine. Abdominal disease is often always exuded due to a large admixture of leukocytes. The effusion can be infected. The lumen of the appendix usually contains liquid, gray or green pus. The mucous base of the appendix is reduced, easily vulnerable and often you can see multiple and fresh ulcers, which gives pathologists the opportunity to distinguish the so-called phlegmonous-ulcerative form of acute appendicitis (Fig. 3.).

Microscopically in all layers of the appendix there is a massive leukocyte infiltration, covering the epithelial area and often exfoliated, sometimes there are multiple primary Aschoff's affects. In the mesentery of the appendix, in addition , there are leukocyte infiltrates.

A type of phlegmonous inflammation is an empyema of the appendix, in which a closed space filled with pus is formed in the lumen of the appendix due to obstruction by fecal stones or a connective process. The morphological feature of this form of appendicitis is that the process rarely passes to the peritoneum. The vermiform appendix in empyema is bulbous swollen and sharply tense, there is a clear fluctuation. Along with this, the serous membrane of the appendix looks like a catarrhal form of acute appendicitis: it is dull, hyperemic, but without layers of fibrin. Serous sterile effusion may be observed in the abdominal cavity. At the opening of the appendix, a large amount of smelly pus is poured out. Microscopically, there is a significant leukocyte infiltration in the mucous membrane and submucosal layer, which decreases to the periphery of the appendix. Typical primary effects are rare.

Gangrenous appendicitis develops (1 macropreparation), characterized by necrotic changes in the appendix. At the same time its total necrosis happens rather seldom, in the vast majority of cases the necrosis zone covers only a small part of a shoot. Contribute to the necrosis of the wall located in the lumen of the process fecal stones and foreign bodies. Macroscopically necrotic area is dirty green, loose and easily torn, the rest of the appendix looks the same as in the phlegmonous form of acute appendicitis. There are fibrinous layers on the organs and tissues surrounding the inflammatory appendix. The abdominal cavity often contains purulent effusion with fecal odor. Sowing this effusion gives the growth of typical colon flora. Microscopically in the area of destruction of the wall layers of the appendix can not be differentiated, they have the appearance of typical necrotic tissue, in other parts of the process there is a picture of phlegmonous inflammation.

If gangrenous appendicitis is not operated on in time, then perforation occurs and the process proceeds to the next stage - the so-called perforative appendicitis. The contents of the appendix are poured into the abdominal cavity. As a result, purulent peritonitis occurs. Macroscopically perforated appendix differs little from the gangrenous form of acute appendicitis. Areas of necrosis are also dirty green with signs of perforation, from which flows a smelly, often and chorous pus. The surrounding peritoneum is covered with massive fibrinous layers. The abdominal cavity contains abundant purulent effusions, sometimes fecal stones that have fallen out of the appendix.

DISCUSSION

According to modern literature, various etiological theories of the origin of this disease are known, which we will dwell in more detail [5].

L. Ashoff's infectious theory. According to this theory, the pathogen penetrates the mucous membrane of the appendix from the lumen, in the mucosa there is a "primary affect" - the area of violation of the epithelium of the mucous membrane, but the inflammatory process develops only when the virulence of microorganisms increases.

Cortico-visceral theory. According to this theory, pathological impulses from the gastrointestinal tract, entering the nerve plexuses and the CNS, after some time lead to dysfunction of the neuro-regulatory apparatus of the appendix. This is manifested by reflex spasm of blood vessels and muscles of the appendix, which leads to circulatory disorders (vascular stasis, edema). Trophic disorders end in necrosis of certain areas of the mucous membrane. The microflora joins the secondary. Kalitievsky PF, Saveliev VE and Savchuk VD believe that the dysfunction of intramural vegetative formations of the appendix causes contraction of the muscles of the appendix, which in turn leads to segmental disruption of blood supply to its wall.

Neurogenic theory. It is based on the fact that in the appendix under the influence of various factors there are pathological impulses that enter the CNS. Here the center of the "inert process of disturbance" is formed. When this focus is formed, any new irritation that comes from the body itself or from the outside, getting into the hearth, causes a clinic of acute appendicitis. This explains the discrepancy between the clinic and morphological changes in the process. Primary pathological impulses are associated with reversible functional and irreversible changes in the intramural nervous system of the appendix. Millller NA proposed to identify the reversible stage of acute appendicitis and call it "neurogenic appendicitis" [6].

The theory of stagnation of fecal masses. Proposed in 1892 by Talamone K. According to this theory, stagnation

of fecal masses leads to the formation of fecal stones in the lumen of the appendix, which damages the mucous membrane. The accession of pathogenic microflora is secondary [7].

The theory of constipation and "lazy gut". According to statistics, for those patients who later developed acute appendicitis, characterized by chronic, perennial constipation; defecation is less common in them than in those who did not suffer from acute appendicitis. Thus, at the turn of the 80's and 90's of the twentieth century in world literature was dominated by the idea that coprolites of the appendix occur due to delayed fecal content in the right parts of the colon during its prolonged passage. Limited epidemiological studies have found that cancer, diverticulosis, and glandular polyps of the colon are less common in populations that do not suffer from appendicitis. There is a well-known assumption (so far there is no strong evidence) that acute appendicitis may be an early precursor to the development of colon and rectal cancer, one of the main factors in the development of which is chronic constipation.

The theory of "closed cavities". If the outflow of contents from the lumen of the appendix is difficult or impossible, the secretion that has accumulated in it will cause overstretching and trauma to the mucous membrane. In addition, stagnant secretion serves as a nutrient medium for the growth and reproduction of pathogenic microorganisms, the attachment of which to the inflammatory process is secondary. The reasons for the formation of a "closed cavity" can be different: sclerosis with obliteration of the lumen of the appendix; obstruction of the lumen by a foreign body, helminth or fecal stone; inflammation with the development of edema of the mucous membrane; torsion of the appendix due to adhesions and scars caused by inflammation or injury of adjacent tissues, etc.

Hematogenous theory. Imagining that microbes enter the appendix mucosa hematogenously, we compared the pathological processes in the appendix and pharyngeal tonsils, based on the fact that often acute appendicitis occurs during or immediately after sore throat. This theory has been partially confirmed, because in sore throats, acute respiratory diseases, influenza, pharyngitis, pneumonia, often in the walls of removed worm-like processes were found the same microorganisms that were sown from the oropharynx of patients [8].

Alimentary theory. It has been noted that inflammation of the appendix is much more common in people who eat a lot of meat. According to the authors of the theory, protein foods enhance the processes of putrefaction in the colon, thereby increasing the virulence of the microflora of the cecum and appendix. In favor of this theory is the fact of a sharp reduction in the incidence of acute appendicitis during the starvation.

The theory of congenital bends. According to this theory , congenital anomalies can cause inflections, compression or fixation with impaired trophic process or obstruction of its lumen. Joining the microflora is secondary.

The theory of bauginospasm. Increased nervous excitability leads to the fact that any irritant etiology and strength causes spasm of the Bauginian valve, which causes pain and reflex stagnation of the contents in the lumen of the appendix, reflex vasospasm [9].

Allergic theory. Protein food, constantly sensitizing the human body, in some conditions causes an allergic reaction such as the Arthus phenomenon from the appendix [10].

The theory of immunodeficiency. Acute appendicitis was considered an autoinfection of a sensitized organism due to a "breakthrough of immunity". Many studies have found that acute appendicitis reduces the functional activity of T and B lymphocytes [11].

Viral theory. Predicts that the trigger for acute appendicitis is a virus. In the experiment, this assumption was not confirmed [12].

Theory of arterial thrombosis. According to this theory, thrombosis of the appendicular artery leads to destruction in the wall of the process up to perforation. Joining the microflora is secondary [13, 14].

Meteorological theory. The literature also notes the dependence of the incidence of acute appendicitis on meteorological conditions - increasing its frequency with fluctuations in air temperature, increasing relative humidity, fluctuations in solar activity and the state of the Earth's biosphere [15].

According to the literature described acute appendicitis caused by the presence of helminths in the lumen of the appendix. Helminths (pinworms, roundworms, spiral trichinae, hookworms, echinococci) were found in approximately 2% of worm-like appendages removed due to acute appendicitis. These parasites do not give a specific clinical picture, but the clinic of acute appendicitis may occur against the background of an erased clinical picture of this disease. As a rule, an accurate diagnosis is possible only after microscopic examination of the removed appendix. Defeat of a mucous membrane at worm invasion is twofold: direct mechanical damage by a parasite and chemical damage by those toxic substances which are allocated by parasites in the course of the vital activity. It should be emphasized that the roundworm can perforate the wall of the appendix [16].

According to the literature, amoeba was found in 7% of removed appendages, balantidial in 7%, trichomoniasis (Devian's intestinal form) in 12.5%, and in very rare cases - Plasmodium falciparum malaria. Surprisingly, no specific clinical picture of acute appendicitis caused by protozoa is observed, and the diagnosis is established only after microscopic examination of the removed appendix.

Many works are devoted to the defeat of the appendix by fungi. Actinomycosis and histoplasmosis are most often found, and in actinomycosis - only destructive forms of inflammation [17].

Changes in the appendix in typhus have been described. Changes in the appendix in typhoid fever and paratyphoid fever were divided into two groups: vulgar appendicitis (swelling of the lymphoid apparatus) and typhoid appendicitis with specific changes (ulcers) that can lead to perforation of the appendix wall. According to the literature, perforation of the appendix is 10% of all perforations of the intestine in typhoid fever [18].

Appendicular form, which usually affects children, occurs in approximately 3% of cases of clinical dysentery [19].

Lesions of the appendix by tuberculosis are very rare and, according to various authors, account for 0.016% of all removed appendages. The specific clinical picture of appendicitis in the defeat of mycobacteria of tuberculosis is not described [20].

Serous inflammation under the influence of the body's defenses can have a favorable outcome. Inflammation can progress, progressing sequentially from serous inflammation to the stage of fibrinous and purulent inflammation up to gangrene. This sequence of stages is always preserved and does not depend on etiological factors. Only the duration of one or another stage of inflammation depends on them. The development of inflammation in the appendix is due to the specificity of the pathogen (pathogenicity and virulence), the state of immunological reactivity and allergic reorganization of the patient's body. The predominance of microbial aggression factors over protective factors leads to a relatively rapid development of the disease, in which the initial stage is short. At the initial relative balance of forces of aggression and protection the inflammatory process can be long and end with regression or progress of inflammation [21].

Another point of view is that all forms of appendicitis develop in the first 24 hours after the disease and are independent, not transitional stages of a single inflammatory process in the appendix.

There is another point of view - destructive forms of appendicitis can have a stage of development, and simple forms are independent forms of inflammation that do not turn into destructive. According to Kalitievsky PF simple and destructive forms develop at once depending on degree of ischemia to which initial disturbances of blood supply of a worm-shaped shoot lead. A simple form of acute appendicitis is considered the most morphologically complex. The author concluded that the boundary between the initial signs of inflammation and different variants of tissue leukocytosis is almost impossible to draw.

Some scientists have noted that catarrhal appendicitis has nothing to do with classical appendicitis and is neither the initial form nor the stage of appendicitis. In this regard, the theory of appendicopathies was put forward, according to which acute appendicitis and appendicopathy are distinguished as different nosological units. Appendicopathy, according to the authors, is a set of clinical symptoms of acute appendicitis without an anatomical picture of inflammation of the appendix (ie, vasomotor, functional changes in the appendix or in the ileocecal intestine). In addition, the authors introduced the term "pseudo-appendicitis", which referred to a complex of subjective sensations (suffering), similar in some clinical symptoms to acute appendicitis or appendicopathy, but which are the result of adjacent or distant diseases [22].

Many scientists have proposed various schemes for the development of inflammation in appendicitis. Some scientists distinguish three stages: the stage that corresponds to the "primary affect" - lasts up to 12 hours from the onset of the disease; stage of development of phlegmonous inflammation - lasts from 12 to 24 hours from the onset of the disease; stage of gangrenous and perforated appendicitis - develops after 24 hours of illness [23].

Another scheme has 4 stages: the stage of functional disorders (appendicular colic); stage of formation of "intraapendicular abscess", or "stage of illusions"; stage of spread of peritoneal inflammation; stage of diffuse peritonitis. The term "stage of illusions" is applied more to the clinical course of the disease, rather than to the morphological stages of the inflammatory process. The destruction of the wall of the appendix continues, but the patient feels a clear improvement - the pain subsides. This is due, on the one hand, to the death of the intramural nerve endings of the appendix, and on the other - before the peritoneal irritation has occurred. In domestic literature, this period is known as the "stage of imaginary well-being".

Morphologists distinguish the following forms of acute appendicitis: simple (catarrhal); superficial; destructive: phlegmonous, apostematous, phlegmonous-ulcerative, gangrenous [24].

According to statistics, appendectomy is one of the most common surgeries in surgical practice. Acute appendicitis is a surgical disease for which the largest number of urgent operations is performed. As a result, acute appendicitis sometimes becomes a source of diagnostic errors. The risk of complications of acute appendicitis, a common rule among surgeons - "you can not rule out acute appendicitis - operate!" leads to the fact that the decision to operate on the patient is made quickly and often it is unwise. Studies show that most patients are operated on by surgeons either immediately after hospitalization or after short-term monitoring of their condition and changes in laboratory parameters. Morphological changes in the appendix may increase to perforation, which causes peritonitis and sometimes death of the patient. Therefore, when the diagnosis is problematic, surgeons are traditionally more likely to have surgery than to wait until they are confident in the diagnosis. Among other factors, active tactics have reduced mortality from acute appendicitis. At the same time, this tactic leads to the removal of the unaltered appendix, according to various authors, in 15-40% of patients [25].

Thus, the problem of acute appendicitis has two opposite aspects: on the one hand - delayed surgery can cause serious complications and even death, on the other - the cause of unjustified, erroneous surgery. Such a "simple", at first glance, intervention as appendectomy for chronic, subacute or catarrhal appendicitis is associated with complications and even fatalities [26].

CONCLUSIONS

Our results suggest that the vermiform appendix retains its active function throughout human life. The study provides an overview with current knowledge about the etiology, pathogenesis and possible consequences of appendectomy as the main method of treatment of acute appendicitis.

Currently, the search for ways to prevent appendicitis can be successful only by finding out the causes and factors that

in some individuals cause the inability of the appendix to resist bacterial invasion.

Obviously, the appendix is necessary to fully support the immune responses of the digestive tract, but it belongs to the category of those organs, the loss of which during forced surgery does not cause significant damage to the body. Apparently, this is due to the large reserve capacity of other lymphoepithelial formations of the mucous membrane of the digestive tract, which can compensate for its loss during appendectomy.

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ORCID and contributionship:

Volodymyr H. Hryn: 000-0001-5894-4416 [A, B, D, F]
Vitaliy S. Drabovskiy: 0000-0003-4111-7179 [A, B, E, F]
Dmytro A. Sytnik: 0000-0002-4885-334X [B, C, E]

Mykola M. Riabushko: 0000-0002-3617-4542 [C, E, F]
Roman M. Riabushko: 0000-0002-5073-9095 [B, D, E]
Serhii M. Bilash: 0000-0002-8385-6090 [B, E, F]
Bohdan I. Gonghak: 0000-0002-6726-6618 [B, C, D]

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CORRESPONDING AUTHOR
Vitaliy S. Drabovskiy
Poltava state medical university
23 Shevchenko st., 36011 Poltava, Ukraine
tel: +380668968998
e-mail: drabovskiy1987@gmail.com

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ORIGINAL ARTICLE

CADETS' PHYSICAL HEALTH AND PSYCHO-EMOTIONAL STATE DURING COMBAT SPORT TRAINING

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Ivan M. Okhrimenko[1], Victoria A. Shtykh[2], Hanna L. Boiko[3], Yurii V. Novytskyi[3], Olha M. Pasko[4], Liudmyla M. Prudka[4], Tetyana V. Matiienko[4]

[1]NATIONAL ACADEMY OF INTERNAL AFFAIRS, KYIV, UKRAINE
[2]KHARKIV STATE ACADEMY OF PHYSICAL CULTURE, KHARKIV, UKRAINE
[3]NATIONAL TECHNICAL UNIVERSITY OF UKRAINE "IGOR SIKORSKY KYIV POLYTECHNIC INSTITUTE", KYIV, UKRAINE
[4]ODESA STATE UNIVERSITY OF INTERNAL AFFAIRS, ODESA, UKRAINE

ABSTRACT

The aim: To study the influence of sambo training on the dynamics of indicators of physical health and psycho-emotional state of cadets in the process of their education.

Materials and methods: The research was conducted at the National Academy of Internal Affairs in 2018-2021. The research involved 17-23 years old male cadets. Two groups of cadets were formed: the experimental group (EG, n = 30), the cadets of which were engaged in sambo during their physical training sessions, and the control group (CG, n = 30), the cadets of which were engaged in the traditional methods of physical training sessions. The level of cadets' physical health was examined according to the method of the professor G. L. Apanasenko.

Results: The positive effect of sambo training on the cadets' physical health and psycho-emotional state was revealed. The EG cadets showed significantly ($p < 0.05$-0.001) better indicators among the studied ones than the CG cadets.

Conclusions: The results of the research allows coming to the conclusion that the high level of physical health and psycho-emotional state of the cadets who were engaged in sambo training will improve the effectiveness of their service tasks performance in the future.

KEY WORDS: health, psycho-emotional state, sambo, cadets

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INTRODUCTION

The future service activities of cadets studying in educational institutions of the National Police of Ukraine involve significant physical and psychological stress. Their systematic influence on the body worsens the health of the police officer and can lead to such negative consequences as fatigue, overexertion, injury, illness, professional burnout, etc. [1]. Thus, for example, according to many scientists [2], the professional activities of a modern patrol police officer have its own specifics: round-the-clock patrolling of the service area in order to ensure proper protection of public order; maintaining public safety and monitoring compliance with traffic rules, ensuring road-traffic safety; first response to a report of an offense; self-detection and cessation of offenses during patrols; detention of offenders and escorting them to police stations; protection of the scene of the event; etc. Characteristic features of police service, according to scientists [3], are: social and state significance; significant physical, intellectual and psychological tension, high rate and dynamics of the service; stricter, compared to other professions, regulatory activity and legal regulation of relations between its members; the need to perform duties in different climatic, weather conditions, time intervals, etc.; high degree of cooperation in the process of activities; orderliness of relations vertically and horizontally; frequent change of some types of actions to others, due to different operational environment, etc.. At the same time, police officers are in constant contact with persons under the influence of drugs and alcohol; aggressive individuals; mentally ill and other categories, which increases the requirements for the development of psychological qualities of police officers [4].

The scientists [5, 6] argue that a modern police officer should have not only knowledge of the legislature, but also developed physical and psychological qualities, a high level of physical health and developed skills and abilities to apply coercive measures. At the same time, special physical training, as an academic subject in higher educational institutions where future police officers are trained, does not fully ensure the solution of the tasks set to improve the efficiency of police work and strengthen their health. This necessitates the search for such means of special physical training that would contribute to the development of physical and psychological qualities of future police officers, strengthen their health, and improve their performance in general. Effective means of special physical training of

Table I. The dynamics of the indicators of physical health of EG (n=30) and CG (n=30) cadets in the process of training (Mean±SD)

The indicators investigated	Groups	Years of training				Level of significance (p_{1-4})
		1st	2nd	3rd	4th	
Body mass index, kg / m²	EG	23.4±0.26	23.1±0.24	22.8±0.23	22.3±0.21	<0.01
	CG	23.3±0.23	23.2±0.22	23.3±0.21	23.4±0.22	>0.05
	p_{EG-CG}	>0.05	>0.05	>0.05	<0.01	
Vital index, ml / kg	EG	56.5±1.31	57.8±1.29	59.6±1.28	62.2±1.26	<0.01
	CG	56.7±1.29	56.9±1.28	57.2±1.29	57.5±1.27	>0.05
	p_{EG-CG}	>0.05	>0.05	>0.05	<0.05	
Strength index, %	EG	58.2±0.97	62.3±0.95	67.8±0.93	72.1±0.91	<0.001
	CG	57.9±1.02	59.2±0.98	61.3±0.96	63.7±0.95	<0.001
	pEG-CG	>0.05	<0.05	<0.001	<0.001	
Robinson index, c.u.	EG	87.8±1.18	86.2±1.16	84.6±1.14	81.8±1.12	<0.01
	CG	87.9±1.20	87.3±1.19	86.4±1.17	85.5±1.16	>0.05
	p_{EG-CG}	>0.05	>0.05	>0.05	<0.05	
HRR time, s	EG	128.9±2.56	122.7±2.51	115.1±2.48	107.3±2.46	<0.001
	CG	129.1±2.61	124.4±2.56	119.8±2.53	114.6±2.50	<0.001
	p_{EG-CG}	>0.05	>0.05	>0.05	<0.05	
Physical health level, points	EG	3.71±0.41	4.29±0.40	7.84±0.38	11.64±0.35	<0.001
	CG	3.89±0.39	4.02±0.38	5.91±0.37	7.16±0.36	<0.001
	p_{EG-CG}	>0.05	>0.05	<0.01	<0.001	

Mean - arithmetical average, SD - standard deviation, p - the significance of the difference between the studied indicators

future police officers, according to many scientists [7, 8], are martial arts, the main place among which belongs to sambo.

Sambo (self-defence without weapons) is a modern sport, one of the most popular types of martial arts, which is currently widely cultivated in the international sports arena. Sambo, also called the "invisible weapon", combines physical culture and entertainment, sports and self-defence [9]. Sambo is not only a form of martial arts and a system of counteracting the enemy without the use of weapons, but also a system of education that promotes the development of moral and psychological qualities, patriotism and civic consciousness. Sambo training form a strong character, resilience of spirit, develop strength and endurance, contribute to the improvement of self-discipline and the formation of qualities necessary to achieve life goals. Sambo forms people who are able to defend themselves, their family, the Motherland [10]. Sambo includes the most effective techniques and tactics of various types of martial arts, combat sport and wrestling. Constant development, renewal, openness to all the best is at the heart of the sambo philosophy. Sambo absorbed the moral principles of the peoples who passed sambo part of their culture along with the methods of struggle. These values gave sambo the strength to go through the severe trials of time, to endure and harden in them. And today, young people practicing sambo not only learn to defend themselves, but also gain experience of decent behaviour based on the values of patriotism [11]. Thus, the analysis of a number of scientific publications on sambo problematics shows the effectiveness of this type of martial arts to improve the effectiveness of police service, but not enough research has been done in terms of the impact of sambo training on the dynamics of indicators of psychological qualities and physical health of cadets – future police officers in the process of their training in educational institutions.

THE AIM

The aim is to study the influence of sambo training on the dynamics of indicators of physical health and psycho-emotional state of cadets in the process of their education.

MATERIALS AND METHODS

MATERIALS

The research was conducted at the National Academy of Internal Affairs (Kyiv, Ukraine) in 2018-2021. The research involved 17-23 years old male cadets during the 1st – 4th years of their training at the academy. The experiment lasted for 4 years. Two groups of cadets were formed: the experimental group (EG, n = 30), the cadets of which were engaged in sambo during their physical training, and the control group (CG, n = 30), the cadets of which were engaged in the traditional methods of physical training. The EG training sessions were conducted by a professional coach-instructor in sambo, and the CG training sessions

Table II. The dynamics of the indicators of psycho-emotional state of EG (n=30) and CG (n=30) cadets in the process of training (Mean±SD)

The indicators investigated	Groups	Years of training		Level of significance (p_{1-4})
		1st	4th	
Distribution and scope of attention, points	EG	5.06±0.23	8.21±0.19	<0.001
	CG	5.09±0.22	8.04±0.18	<0.001
	p_{EG-CG}	>0.05	>0.05	
Visual operative memory, points	EG	5.17±0.25	7.75±0.22	<0.001
	CG	5.21±0.24	7.68±0.20	<0.001
	p_{EG-CG}	>0.05	>0.05	
Features of thinking, points	EG	4.87±0.27	6.89±0.25	<0.001
	CG	4.90±0.25	6.76±0.23	<0.001
	p_{EG-CG}	>0.05	>0.05	
Concentration and stability of attention, %	EG	88.07±0.74	94.26±0.68	<0.001
	CG	87.89±0.72	93.67±0.69	<0.001
	p_{EG-CG}	>0.05	>0.05	
Situational anxiety, c.u.	EG	52.94±0.94	30.91±0.85	<0.001
	CG	53.05±0.95	34.95±0.88	<0.001
	p_{EG-CG}	>0.05	<0.01	
Self-assessment of emotional state, points	EG	5.12±0.21	7.41±0.19	<0.001
	CG	5.08±0.22	6.27±0.19	<0.001
	p_{EG-CG}	>0.05	<0.001	
Well-being, points	EG	6.82±0.21	8.48±0.18	<0.001
	CG	6.77±0.20	7.92±0.16	<0.001
	p_{EG-CG}	>0.05	<0.05	
Activity, points	EG	5.91±0.25	8.13±0.22	<0.001
	CG	5.87±0.24	7.19±0.22	<0.001
	p_{EG-CG}	>0.05	<0.05	
Mood, points	EG	6.94±0.22	8.26±0.19	<0.001
	CG	6.99±0.20	7.73±0.17	<0.05
	p_{EG-CG}	>0.05	<0.05	

Mean - arithmetical average, SD - standard deviation, p - the significance of the difference between the studied indicators

were piloted by an academic instructor of the department of special physical training.

The selection of cadets into groups was carried out by the method of questionnaires at the cadets' own will to engage in sambo training. The number of hours for physical education training sessions was the same for the cadets of both groups and made 4 academic hours of training per week (2 times for 2 hours). The initial level of indicators of psychological qualities and physical health in the EG and the CG cadets did not differ significantly.

METHODS

The level of students' physical health was examined according to the method of the professor G. L. Apanasenko [12] based on the anthropometry indicators (height, weight, lungs vital capacity, wrist dynamometry) and the state of the cardiovascular system (heart rate, arterial blood pressure). The health level was evaluated in points and it included the estimation of the body mass index, vital index, strength index, Robinson's index and heart rate recovery (HRR) time after a standard exercise. The cadets' physical health surveys were conducted in the medical support department of the National Academy of Internal Affairs by medical staff four times during each year of their training.

The research of the psycho-emotional state of cadets during the process of their training was carried out according to the following methods: the test of "Finding numbers" (assessment of distribution and scope of attention), the methods of operating with numbers (visual operative memory), the method of "Complex Associations" (features of thinking), the method of Ch. D. Spielberger, Yu. L. Khanin (situational anxiety), the correction task of Bourdon-Anfimov (concentration and stability of attention), the method of A. Wessman and D. Rix (self-assessment of emotional state), the method of "WAM" (well-being, activity, mood) [13]. The choice of these methods is due to the need to study the professionally important psycho-

physiological qualities of cadets both in the process of their training activities at the academy and during their future service activities. The study of the cadets' psycho-emotional state was conducted twice during the training period (the 1st and 4th years of their training) by the specialists of the Department of Psychological Support of the National Academy of Internal Affairs.

Research methods: theoretical analysis and generalization of literature sources, medical and biological methods, psychological testing, pedagogical experiment, methods of mathematical statistics. During the researches the authenticity of difference between the indicators of cadets by means of Student's t-test was determined.

ETHICAL APPROVAL STATEMENT

The research was carried out according to the requirements of the Code of Ethics of National Academy of Internal Affairs, which was approved by the Academic Council (protocol No. 01 of 10 January 2019) and implemented by the order of the Rector of the Academy. Informed consent was received from all individuals who took part in this research.

RESULTS

The analysis of body mass index in the EG and the CG cadets showed that no significant difference was found between the indicators of the EG and the CG cadets ($p > 0.05$) during the 1st, the 2nd and the 3rd years of their training (Table I). The 4th year cadets of the EG revealed significantly better body mass index than the CG cadets by 1.1 kg / m^2 ($p < 0.01$). The research of the vital index in the cadets of the studied groups shows that the indicators in the EG cadets during the 4th year of training were better than in the CG cadets; the difference is 4.7 ml / kg and is significant ($p < 0.05$) (Table I). The analysis of the dynamics of the vital index in each group showed that the indicators in both groups improved during the period of training at the academy, but the difference between the indicators of the 1st year and the 4th year cadets is 5.7 ml / kg in the EG and is significant ($p < 0.05$), and in the CG it makes 0.8 ml / kg ($p > 0.05$). The comparative analysis of strength index indicators shows that the difference between the indicators of the EG and the CG cadets during the 2nd year of their training makes 3.1 % ($p < 0.05$), the 3rd – 6.5 % ($p < 0.001$), the 4th – 8.4 % ($p < 0.001$) (Table I). The strength index of the cadets of both groups significantly ($p < 0.001$) improved during the period of their training, but if the difference between the indicators of the 1st and the 4th year cadets of the CG is 5.8 %, then it makes 13.9 % in the EG. The analysis of the Robinson index in the EG and the CG cadets showed that no significant difference between the indicators of the EG and the CG cadets was detected ($p > 0.05$) during the 1st year of their training, as well as during the 2nd and the 3rd years of education (Table I). The EG cadets showed significantly ($p < 0.05$) better indicators during the 4th year of training, compared with the CG cadets: the difference is 3.7 c.u. The analysis of the time of recovery of heart rate to baseline shows that significant difference was found only in the 4th year of training – the indicators of the EG cadets were significantly better at 7.3 s than those of the CG cadets' (Table I). The research of the level of cadets' physical health showed that this level was significantly higher in the EG cadets than in the CG cadets during the 3rd year of their training by 1.93 points ($p < 0.01$), and by 4.48 points ($p < 0.001$) during the 4th year of their training (Table I). The difference between the indicators of the 1st and the 4th years of training is 3.27 points in the CG cadets, then this difference makes 7.93 points in the EG cadets, which indicates a positive effect of sambo training on the health of cadets.

The analysis of indicators of distribution and scope of attention in the cadets on the test of finding numbers showed that the indicators of the EG and the CG cadets did not differ significantly among themselves ($p > 0.05$) both at the beginning and at the end of the research. The indicators of distribution and scope of attention in both groups significantly ($p < 0.001$) improved in the process of training (Table II). The dynamics of the indicators of visual operative memory, studied by the method of operating with numbers, the indicators of features of thinking (by the method of "Complex Associations"), as well as concentration and stability of attention (by the correction task of Bourdon-Anfimov) is similar to the dynamics of distribution and scope of attention character i. e. significant ($p < 0.001$) improvement of the indicators in both groups of the cadets for the period of their training and the absence of a significant difference between the indicators of the groups both of the 1st and the 4th years of training ($p > 0.05$). The research of the indicators of situational anxiety in the cadets shows that the level of anxiety was assessed as "high" and did not differ significantly ($p > 0.05$) during the 1st year of cadets' training of both study groups. During the training period, the level of anxiety in the EG and the CG cadets significantly decreased ($p < 0.001$), but the comparative analysis of the indicators showed that the level of anxiety is significantly lower in the EG than in the CG at 4.04 c.u. ($p < 0.01$) (Table II). The analysis of the indicators of self-assessment of emotional state of the cadets showed that if they did not differ significantly ($p > 0.05$) in the study groups during the 1st year of training, then the level of self-assessment of emotional state was significantly better in the EG cadets during the 4th year of their training than in the CG cadets by 1.14 points ($p < 0.001$) (Table II). The level of self-assessment of emotional state of the cadets in both groups significantly ($p < 0.001$) improved during their training period, but a more pronounced difference was found in the EG cadets. The research of the dynamics of such characteristics of the emotional state of the cadets as well-being, activity and mood according to the method of "WAM" shows that they significantly improved during the training period ($p < 0.05$-0.001) in both study groups (Table 3). At the same time, all studied indicators of the emotional state of the EG cadets were significantly better than in the CG cadets ($p < 0.05$) during the 4th year.

DISCUSSION

Professional personnel training for the National Police of Ukraine requires constant improvement. This is due to a number of reasons, including: reforming the law enforcement agency, changing the concept of the National Police, applying new forms of selection of candidates for police service, optimizing the structure and content of police training, the specifics of police service [14]. The service activities of police officers of most units of the National Police of Ukraine are characterized by irregular working hours, day's duties, frequent services for the protection of public safety and order, etc. [15]. The forcible detention of offenders occupies a particularly important place in the service activities of the police. Detention of the offender is accompanied by forceful resistance and requires the performance of the fastest possible and exact actions; pursuit and overcoming obstacles overloads the musculoskeletal and cardiovascular systems. This results in constant physical and psychological overload and, over time, to chronic fatigue of police officers [16].

The modern police officer must ensure the safety of people by applying, if necessary, sufficient coercive techniques and methods; be able to distinguish situations of danger; under any circumstances to act without prejudice, guided by ethical norms. The analysis of law enforcement practice shows that the functional responsibilities of a modern police officer can be performed by a person with a high level of responsibility for the results of his own activities, who has a set of knowledge, practical skills and professionally important traits, good health, high level of physical and psychological qualities acquired during special training. It is these components that ensure the professional readiness of police officers to effectively perform complex, sometimes dangerous tasks. However, today, the training of future police officers requires further improvement, as the analysis of their service activities revealed a high level of injuries and even deaths of police officers in the line of duty.

The scientists [17, 18] consider the improvement of special physical training of cadets on the basis of modern martial arts, in particular sambo, to be a promising direction for improving the efficiency of police service activities. Our research has confirmed the findings of many scientists, which show the positive impact of sambo training on the level of physical health and psycho-emotional state of cadets.

CONCLUSIONS

The research revealed a more pronounced positive effect of sambo training, compared to the traditional method of conducting physical training sessions, to improve the physical health of cadets during their training. Thus, the 4th year cadets engaged in sambo training revealed significantly ($p < 0.05$) better indicators of body mass index, vital index, strength index, the Robinson index, heart rate recovery time and physical health than the CG cadets. The results of the comparative analysis of psycho-emotional state of the EG and the CG cadets revealed that the indicators of situational anxiety, self-assessment of emotional state, well-being, activity and mood in the EG cadets during the 4th year of their training are significantly better than in the CG cadets. The results suggest that the high level of physical health and psycho-emotional state of the cadets who were engaged in sambo training during their education will improve the effectiveness of their service tasks performance in the future.

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ORCID and contributionship:
Ivan M. Okhrimenko: 0000-0002-8813-5107[A,B]
Victoria A. Shtykh: 0000-0002-6881-7047[C]
Hanna L. Boiko: 0000-0002-4751-6923[E]
Yurii V. Novytskyi: 0000-0003-1268-3817[F]
Olha M. Pasko: 0000-0001-9555-1101[D,F]
Liudmyla M. Prudka: 0000-0001-5440-2361[D]
Tetyana V. Matiienko: 0000-0001-9695-2222[B]

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CORRESPONDING AUTHOR
Ivan M. Okhrimenko
National Academy of Internal Affairs
1 Solomianska Square, 03035 Kyiv, Ukraine
tel: +380679903905
e-mail: ivango-07@ukr.net

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ORIGINAL ARTICLE

THE OVERWEIGHT AND OBESITY ROLE IN THE OCCURRENCE OF CHEMOTHERAPY-INDUCED HEPATOTOXIC REACTIONS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA

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Igor M. Skrypnyk, Ganna S. Maslova, Tetiana V. Lymanets, Roman I. Skrypnyk
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate the frequency of development and nature of cytostatic-induced hepatotoxic reactions in patients with acute myeloid leukemia (AML) with overweight and obesity during remission induction chemotherapy (CT).

Materials and methods: We examined 25 patients with newly diagnosed acute leukemia (AL), of which 56% (14/25) were men, 44% (11/25) were women. Depending on the body mass index (BMI), patients were divided into groups: I (n=10) – patients with AML and BMI of 18.5-24.9 kg/m^2; II (n=15) – patients with AML and BMI ≥25.0 kg/m^2. The biochemical blood analysis was evaluated twice: before and on the 56th day of CT, which included alanine-, aspartate-aminotransferases, gamma-glutamyltranspeptidase (GGT), alkaline phosphatase (ALP), total protein and total bilirubin.

Results: In patients with AML and normal BMI, CT conduction increased the risk of GGT (RR=3.00; 95% CI=1.14-7.91; p<0.05) and ALP activity impairment (RR=2.67; 95% CI=0.98-7.22; p>0.05). The presence of overweight and obesity in patients with AML of group II led to significant risk of increase the GGT (RR=3.00; 95% CI=1.46-6.14; p<0.05) and ALP activity (RR=4.00; 95% CI=1.41-11.35; p<0.05) during CT. GGT and ALP activity in the blood serum of group II patients after CT exceeded the baseline data in 2.4 times (p<0.0001) and 1.6 times (p=0.0007), respectively.

Conclusions: The remission induction CT of AML is accompanied by the risk of cytostatic-induced liver injury. The presence of overweight, obesity and primary disorders of biochemical liver tests due to the oncohematological disease influence are the risk factors for hepatotoxic reactions development during CT.

KEY WORDS: acute myeloid leukemia, chemotherapy, overweight, obesity

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INTRODUCTION

Obesity is an important medical and social problem. Over the past three decades, the prevalence of obesity in the world has tripled and become an epidemic [1-4]. The pathogenetic basis of diseases associated with obesity is dyslipidemia and insulin resistance. Hyperinsulinemia with obesity-associated insulin resistance increases the risk of acute leukemia occurrence and reduces the chemotherapy (CT) effectiveness [5, 6]. Chronic systemic inflammation is also considered to be one of the important pathogenetic mechanisms of development and progression of oncological diseases in patients with obesity [7].

At the same time, overweight and obesity promote xenobiotic metabolism violation, which can lead to an increased risk of hepatotoxicity [5, 8-10]. However, data from individual studies of cytostatic-induced liver injury are conflicting. In some retrospective studies conducted in a limited number of patients, the toxicity of intensive CT was assessed in overweight and obese patients [8, 11-18], which did not show increased toxicity and deterioration of treatment outcomes in adult patients. However, the Crysandt M [4] study demonstrated that increased body mass index (BMI) is a negative prognostic factor for incidence of de novo acute myeloid leukemia (AML) and overall survival for patients younger than 65 years with the presence of cytogenetic mutations FLT3, NPM1 or CEBPA, which was characterized by a decreased long-term survival in 5-7% (3-year OS 39.9% vs. 47.3%; 10-year OS 28.7% vs. 33.8%, P=0.0002). Deterioration of the CT results in patients with acute leukemia (AL) with overweight and obesity may be associated with a decreased of the cytostatic therapeutic doses, done to prevent their toxic effects, especially in patients with body surface area greater than 2 m^2 [13].

Therefore, the incidence and nature of liver injury in patients with de novo AML and under the influence of CT need to be studied in detail, which is of particular importance for the prediction and prevention of cytostatic-induced hepatotoxic reactions.

THE AIM

To investigate the frequency of development and nature of cytostatic-induced hepatotoxic reactions in patients with acute myeloid leukemia (AML) with overweight and obesity during remission induction chemotherapy (CT).

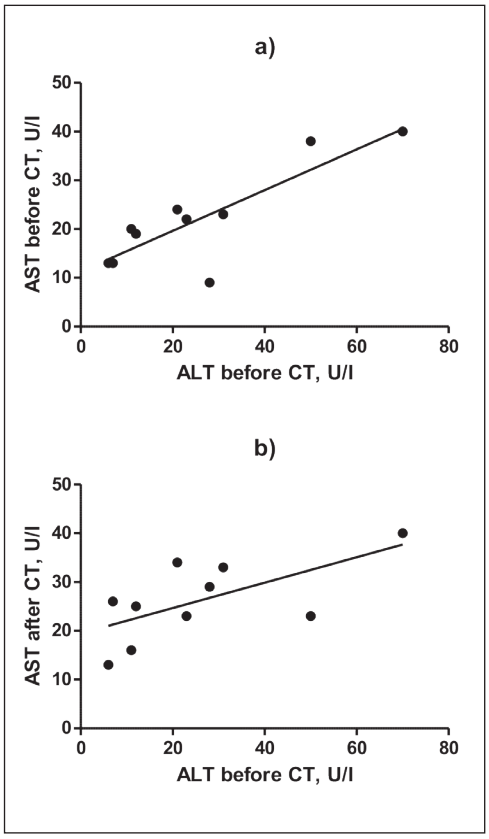

Fig.1. Direct correlation in patients of I group: a) between the ALT and AST activity before CT; b) between ALT activity before CT and AST after CT.

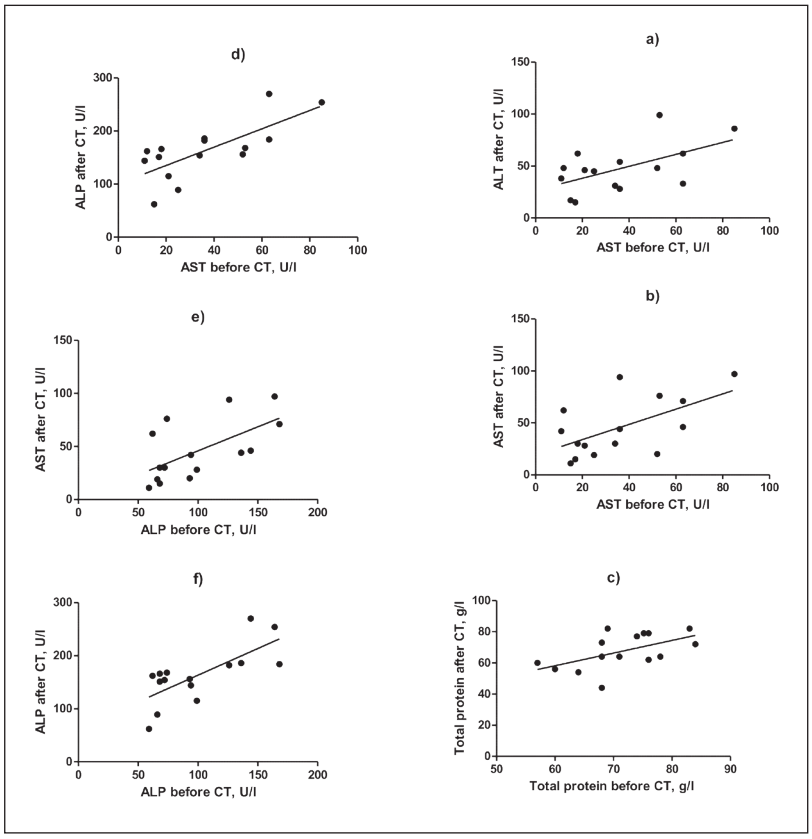

Fig. 2. Direct correlation in patients of II group: a) between the ALT activity before CT and AST after CT; b) between AST activity before and after CT; c) between the total protein content before and after CT; d) between AST activity before CT and ALP after CT e) between ALP activity before CT and AST after CT; f) between AST activity before and after CT.

MATERIALS AND METHODS

We examined 25 patients with newly diagnosed AML, who were treated in the hematology department of PE "Poltava Regional Clinical Hospital n.a. M.V. Sklifosovsky of Poltava Regional Council" since 2015 till 2019. The cohort consisted of 56% (14/25) males and 44% (11/45) females. The general patient's condition by ECOG was I-II, and according to Karnovsky performance status scale – 60-80%. The study included 25 patients with AML, classified by FAB criteria. AML variants M0, M1, M2 were determined in 40% (10/25) of patients, M3 – in 8% (2/25), M4 and M5 – in 52% (13/25) patients.) The body mass index (BMI) was calculated for all of them initially according to formula: BMI = weight (kg) / height (m^2). Adults, the patient's BMI was assessed: BMI in the range of 18.5-24.9 kg/m^2 was considered normal, and ≥25.0 kg/m^2 – overweight. Depending on the BMI, patients were further divided into groups: I (n=10) – AML patients with BMI 18.5-24.9 kg/m^2; II (n=15) – AML patients with BMI ≥25.0 kg/m^2;

All patients received CT in accordance with the Ministry of Health of Ukraine guidelines № 647 from 30 Jul 2010. Patients with AML were treated with "7+3" or "5+2", which included cytarabine and anthracycline antibiotic (doxorubicin, idarubicin, mitoxantrone), promyelocytic (M3) AML variant – "7+3" or "5+2 " with transretinoic acid, myelomono- (M4) and monoblastic (M5) – "7+3" or " 5+2" with etoposide [19].

The biochemical blood analysis parameters of all patients were evaluated twice: before CT and on the 56th day: alanine (ALT), aspartate (AST) aminotransferases, gamma-glutamyltranspeptidase (GGT), alkaline phosphatase (ALP), total serum protein and total bilirubin. The severity of cytostatic-induced hepatotoxic reactions was assessed by Common Terminology Criteria for Adverse Events (CTCAE).

The control group consisted of 20 healthy individuals (9 (45%) women and 11 (55%) men, age 22-26 years.

Statistical data analysis was performed on a Pentium 4 personal computer using Excel spreadsheets Microsoft Office – 2000 (USA). The Shapiro-Wilk test was used to verify the data distribution normality. The study results were processed by the Student-Fisher variation statistics method. Under normal distribution conditions, tables of Student's critical distribution points according to criteria (t) and (p) were used. The average value for each variation series (M) and its error (m) were calculated. Nonparametric study results were calculated by Wilcoxon (W). The relationship between the studied parameters was evaluated using Pearson correlation analysis (r). Relative risk analysis was performed by calculating the risk ratio (RR) and its 95% confidence interval (CI). Used the formula: RR=A (C+D) / C(A+B), where A, B, C, D is the number of observations in the coupling table.

Table I. The biochemical blood analysis parameters in AML patients during CT

Parameters	Almost healthy	I (n=10)		II (n=15)	
		Before CT	After CT	Before CT	After CT
ALT, U/l	14.65±1.03 95% CI 12.50-16.80	25.90±6.46 95% CI 11.28-40.52	39.80±6.98 95% CI 24.01-55.59	33.93±4.40 95% CI 24.49-43.37	47.47±5.99 95% CI 34.61-60.32
p		p_1>0.05 p_2>0.05	p_3=0.01	p_1=0.03 p_2=0.003	p_3=0,0003
AST, U/l	18.75±0.83 95% CI 17.01-20.49	22.10±3.21 95% CI 14.83-29.37	26.20±2.59 95% CI 20.33-32.07	36.07±5.81 95% CI 23.61-48.52	45.67±7.28 95% CI 30.05-61.28
p		p_1>0.05 p_2>0.05	p_3=0.03	p_1>0.05 p_2=0.02	p_3=0.004
Total protein, g/l	14.65±1.03 95% CI 12.50-16.80	69.08±2.84 95% CI 62.65-75.51	69.37±1.37 95% CI 66.28-72.46	71.41±1.99 CI95% 67.14-75.69	67.47±2.94 CI95% 61.16-73.77
p		p_1>0.05 p_2>0.05	p_3>0.05	p_1>0.05 p_2>0.05	p_3>0.05
GGT, U/l	21.10±0.47 95% CI 20.11-22.09	41.90±4.01 95% CI 32.82-50.98	71.40±14.50 95% CI 38.60-104.2	44.27±3.87 95% CI 35.96-52.57	107.5±25.79 95% CI 52.23-162.8
p		p_1=0.007 p_2=0.005	p_3=0.005	p_1<0.0001 p_2=0.0007	p_3=0.0007
ALP, U/l	61.35±4.31 95% CI 52.34-70.36	109.7±17.19 95% CI 70.82-148.6	211.4±25.17 95% CI 154.5-268.3	99.53±9.88 95% CI 78.34-120.7	162.9±13.75 95% CI 133.4-192.4
p		p_1=0.009 p_2>0.05	p_3=0.002	p_1=0.0007 p_2=0.004	p_3=0.0001
Total bilirubin, µmol/l	9.80±0.63 95% CI 8.48-11.12	11.13±1.46 95% CI 7.82-14.43	15.12±1.31 95% CI 12.16-18.08	14.19±2.07 95% CI 9.74-18.64	17.21±3.17 95% CI 10.40-24.01
p		p_1=0.01 p_2>0.05	p_3=0.009	p_1>0.05 p_2>0.05	p_3>0.05

Note: p_1 – the significant difference between the pre- and post-CT values in group I and II; p_2 – the significant difference between parameters in groups I and II before CT and almost healthy; p_3 – the significant difference between parameters in groups I and II after CT and almost healthy.

Table II. The incidence and relative risk of cytostatic-induced hepatotoxic reactions in AML patients

Parameters	I (n=10)		II (n=15)	
	Before CT (number of patients, %)	After CT (number of patients, %)	Before CT (number of patients, %)	After CT (number of patients, %)
ALT, U/l	2 (20%)	4 (40%)	7 (46.7%)	9 (60%)
RR (95% CI)	RR=2.00; 95% CI=0.46-8.56; p>0.05		RR=1.28; 95% CI=0.65-2.54; p>0.05	
AST, U/l	0	0	5 (33.3%)	8 (53.3%)
RR (95% CI)	-		RR=1.60; 95% CI=0.67-3.77; p>0.05	
Total protein, g/l	2 (20%)	1 (10%)	2 (13.3%)	8 (53.3%)
RR (95% CI)	RR=0.5; CI=0,05-4.67; p>0.05		RR=4.00; 95% CI=1.01-15.81; p<0.05	
GGT, U/l	3 (30%)	9 (90%)	5 (33.3%)	15 (100%)
RR (95% CI)	RR=3.00; 95% CI=1.14-7.91; p<0.05		RR=3.00; 95% CI=1.46-6.14; p<0.05	
ALP, U/l	3 (30%)	8 (80%)	3 (20%)	12 (80%)
RR (95% CI)	RR=2.67; 95% CI=0.98-7.22; p>0.05		RR=4.00; 95% CI=1.41-11.35; p<0.05	
Total bilirubin, µmol/l	0	1 (10%)	3 (20%)	5 (33.3%)
RR (95% CI)	-		RR=1.67; 95% CI=0.48-5.76; p>0.05	

Note: p – relative risk significant difference

RESULTS

The liver injury was detected in 60% (6/10) of patients of group I with AML and normal BMI during the initial examination (Table II), of whom 1 patient had mixed syndrome, 1 patient – cytolytic and 3 – cholestatic syndromes, isolated decrease in the total protein content in the blood serum was observed in 2 patients.

The presence of overweight and obesity in patients with AML of group II contributed to an increase frequency of hepatotoxic reactions. At baseline the liver injury was detected in 73.3% (11/15) of group I patients (Table II), of whom cytolytic syndrome was recorded in 27.3% (3/11) of patients, cholestatic – in 18.2% (2/11), mixed syndrome – in 45.5% (5/11), isolated serum total protein decrease – in 9.1% (1/11) of patients. The biochemical blood analysis parameters before CT in all patients with AML were increased within the limits of grade I by CTCAE. Thus, the development of liver injury was observed against the

AML background, regardless of BMI, which is due to the oncohematological disease influence.

The ALT, AST, ALP activity, total protein and total bilirubin content in the blood serum in patients with AML and normal BMI did not significantly differ from almost healthy individuals at baseline (p>0.05) (Table I). However, the GGT activity in patients of group I was 2 times higher than normal (p=0.005) (Table I).

In the presence of overweight and obesity in patients of group II before CT, the ALT activity in the blood serum was 2.3-fold higher (p=0.003), AST – 1.9-fold (p=0.02), GGT – 2.1-fold (p=0.0007), ALP – 1.6-fold higher (p=0.004) compared with almost healthy individuals (Table I).

The frequency and severity of liver injury in patients of groups I and II increased after two courses of CT and achieving clinical and hematological remission. Thus, on the 56th day, the biochemical liver tests violation was recorded in 90% (9/10) of patients with AML of group I (Table II), of which 4 patients had a mixed syndrome, 5 – cholestatic syndrome. The mixed syndrome detection in 1 patient was accompanied by an increased total bilirubin level and decreased serum total protein. The violations of biochemical liver tests in patients with AML and normal weight after CT did not exceed grade 1 according to CTCAE. There was a general tendency to increase the risk of hepatotoxic reactions development in patients with AML and normal BMI under the cytostatic drugs influence (RR=1.28; CI=0.81-2.02; p>0.05) (Table II).

On the 56th day of observation in patients of group I, the ALT and AST activity of in the blood serum exceeded the normal range in 2.7 (p=0.01) and 1.4 times (p=0.03) respectively (Table I).

Two courses of CT, which contained a combination of cytarabine and anthracycline antibiotic, increased the risk of GGT activity impair (RR=3.00; 95% CI=1.14-7.91; p<0.05) and ALP impair (RR=2.67; 95% CI=0.98-7.22; p>0.05) in the blood serum of patients with AML and normal BMI (Table II). Thus, the GGT and ALP activity in the blood serum of group I patients after remission induction CT exceeded the baseline parameters by 1.7 times (p=0.007) and 1.9 times (p=0.009) respectively (Table I).

The total bilirubin level in AML patients of group I after CT was 1.3-fold higher (p=0.01) compared with the baseline and 1.5-fold higher (p=0.01) compared with normal (Table I).

It is important that the use of cytarabine and anthracycline antibiotic combination in patients of group I with AML and normal BMI did not lead to the hypoproteinemia (Table II).

The biochemical liver parameters during the initial examination were of particular importance to predict the growth of hepatotoxic reactions during CT. A direct correlation was recorded between ALT and AST activity at baseline (r=+0.65; p=0.04 by Pearson) (Fig. 1, a) and ALT activity during the initial examination and AST activity after CT (r=+0.84; p=0.002 by Pearson) (Fig. 1, b). From our point of view, the AML progression affects the primary liver injury, and also creates the preconditions for the development of cytostatic-induced hepatotoxic reactions in patients with normal BMI.

The overweight and obesity were among the risk factors for the cytostatic-induced hepatotoxic reactions development in patients with AML. After two courses of remission induction CT, the biochemical liver tests violations were recorded in 100% (15/15) of group II patients with overweight and obesity (Table II), of which cholestatic syndrome was detected in 20% (3/15) of patients and mixed syndrome – in 80% (12/15) of patients. The GGT activity increased to grade 2 according to CTCAE in 1 patient after CT, other indicators of liver tests during the second examination were within the CTCAE grade I toxicity. Therefore, patients with AML of group II with overweight and obesity showed a significant increase in the risk of hepatotoxic reactions during CT (RR=1.36; 95% CI=1.00-1.85; p<0.05) (Table II). The increased risk of the mixed liver injury development was detected in this category of patients under the influence of cytostatic drugs, namely cytarabine and anthracycline antibiotics (RR=2.4; 95% CI=1.12-5.13; p<0.05).

The ALT activity in the blood serum of overweight patients with AML of group II after CT exceeded the baseline parameter in 1.4 times (p=0.03) and almost healthy individuals in 3.2 times (p=0.003), AST activity increased in 2.4 times (p=0.004) compared with norm (Table I).

CT led to a significant risk of increased GGT activity (RR=3.00; 95% CI=1.46-6.14; p<0.05) and ALP activity (RR=4.00; 95% CI=1.41-11.35, p<0.05) in the blood serum in patients of group II (Table II). The GGT activity in the blood serum in patients of group II after CT exceeded the baseline in 2.4 times (p<0.0001) and almost healthy individuals – 5.1 times (p=0.0007) (Table I). The ALP activity in the blood serum of overweight and obese patients after CT increased in 1.6 times (p=0.0007) compared with the parameter before CT and in 2.6 times (p=0.0001) compared with norm (Table I).

The remission induction CT, which contained cytarabine and anthracycline antibiotic, led to a significant increase in the risk of hypoproteinemia development in patients with AML of group II (RR=4.00; 95% CI=1.01-15.81; p<0.05) (Table II). However, the average values of the total protein level in the blood serum in patients of group II after CT did not differ from those before CT and almost healthy individuals (p>0.05 according to t and W criteria). At the same time in patients of group II the total bilirubin content in the blood serum did not significantly increase after CT (p>0.05) (Table I).

The importance of biochemical liver tests primary violation in the prediction of cytostatic-induced liver injury was confirmed in overweight and obese patients with AML. This opinion was confirmed by a direct correlation between the AST activity before CT and ALT after (r=+0.56; p=0.03 by Pearson) (Fig. 2; a), AST (r=+0.59; p=0.02 by Pearson) (Fig. 2; b) and ALP after two CT courses (r=+0.73; p=0.002 by Pearson) (Fig. 2; d), as well as between the ALP activity before CT and AST activity after CT (r=+0.61; p=0.02 by Pearson) (Fig. 2; e). At the same time, the direct correlation

was observed between the total protein content before and after CT (r=+0.55; p=0.03 by Pearson) (Fig. 2; c). Increased ALP activity during the initial examination of overweight and obese AML patients poses a significant risk of cytostatic-induced hepatotoxic reactions development. This opinion was confirmed by a strong direct correlation between ALP activity before and after CT in patients of group II (r=+ 0.72; p=0.002 by Pearson) (Fig. 2; f).

DISCUSSION

During the initial examination of AML patients, we found that the manifestation of oncohematological disease leads to biochemical liver tests violation. Should be noted, that in patients with overweight and obesity, primary liver injury is more common than in patients with a normal body mass index. It can be concluded that the presence of severe intoxication syndrome, liver tissue infiltration by tumor cells are the main pathogenetic mechanisms of liver injury in the onset of AL. However, the presence of overweight and obesity potentiates the development of liver injury with the AL progression, which was confirmed by the higher frequency and severity of biochemical liver tests violations in this category of patients compared with patients with normal BMI patients.

Remission induction in patients with AML is accompanied by a general tendency to biochemical liver tests changes, regardless of the presence of additional risk factors. It should be noted that in patients with normal BMI on the background of induction chemotherapy there was a high risk of following changes development: increased GGT activity and total serum bilirubin level. And in the presence of overweight and obesity – increased GGT, ALP activity and decreased serum total protein level.

In addition, AML patients with overweight and obesity during CT developed hepatotoxic reactions of mixed type, the probability of which depended on the presence of primary liver injury before the start of specific treatment, which coincides with other studies [6, 14]. Therefore, patients with oncohematological profile who have abnormal liver biochemical tests at the initial examination are at increased risk of developing cytostatic-induced hepatotoxic reactions. This fact must be taken into account for supportive care therapy.

An additional risk factor for chemotherapy-induced hepatotoxicity is overweight and obesity. Given that reducing the dose of cytostatic drugs will reduce the CT effectiveness, patients with overweight and obesity need to undergo specific treatment with strict adherence to doses and regimens of drugs administration [5, 8, 13, 14]. Patients of this category need to be carefully monitored for biochemical blood test changes during CT. The individual approach for supportive treatment should be developed.

CONCLUSIONS

Primary biochemical liver tests changes in patients with AML, regardless of BMI, are associated, first of all, with the influence of oncohematological disease, which may be based on several pathogenetic factors from intoxication to tumor liver tissue infiltration.

There is an increased risk of cytostatic-induced hepatotoxic reactions in patients with AML during remission induction CT. The overweight and obesity presence is a risk factor for liver injury development in the dynamics of acute leukemia treatment.

In patients with AML, regardless of BMI, induction CT was associated with a risk of increased GGT and ALP activity. However, in patients with normal BMI, GGT and ALP activity increase was associated with hyperbilirubinemia, and in overweight and obese patients – with hypoproteinemia development. Moreover, the increased ALT activity after CT compared with the baseline data was observed in AML patients with high BMI.

It should be noted that the level of biochemical blood analysis parameters after CT was primarily influenced by their baseline level, which can be used to predict the cytostatic-induced hepatotoxic reactions and determine the category of patients in need of cytostatic-induced liver injury drug prevention.

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ORCID and contributionship:
Igor M. Skrypnyk: 0000-0002-3426-3429 [A, E, F]
Ganna S. Maslova: 0000-0002-4729-1736 [A, B, D, E]
Tetiana V. Lymanets: 0000-0001-6021-7066 [B, C]
Roman I. Skrypnyk: 0000-0003-1828-3371 [B, D]

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CORRESPONDING AUTHOR
Igor M. Skrypnyk
Poltava State Medical University
23 Shevchenko St., 36011 Poltava, Ukraine
tel: +380505974908
e-mail: inskrypnyk@gmail.com

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ORIGINAL ARTICLE

PROJECTING OF COMPLEX HEALTH TRAINING FOR MATURE MEN WITH METABOLIC SYNDROME

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Oksana K. Kornosenko[1], Iryna V. Taranenko[1], Yevheniia Yu. Shostak[1], Yuliia V.Zaitseva[1], Oleksandr V. Petryshyn[2]
[1]POLTAVA V.G. KOROLENKO NATIONAL PEDAGOGICAL UNIVERSITY, POLTAVA, UKRAINE
[2]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To identify risk factors for metabolic syndrome; to model, justify and experimentally test the effectiveness of a program of complex health training for mature men with MS.

Materials and methods: Theoretical – analysis, generalization, pedagogical observation, modelling; empirical – methods of implementation of the results in practice (pedagogical experiment involving 50 mature menwho had no contraindications to training), methods of monitoring and measuring of physical evolvement, body systems functional status (samples: Rufier, Stange), general performance level (Harvard step test), medical indicators (blood glucose level, arterial tension).

Results: A complex organized health training program (graduated, systematic, all-round motor activity managed by an instructor) showed better results (24,5 %) compared an independent health training system(15,2 %). Both types of activity contributed to weight loss(CG2 – 10,1 %; EG2 – 15,5 %) and reduction of body parts overall size; functional improvement of cardiovascular and respiratory systems of the male body, in particular in the indicators of the Stange test (CG2 – 29,8 %,EG2 – 33,9 %), Ruffier index (CG2 – 5,8 %, EG2 – 23,0 %) and step test (CG2 – 15,8 %, EG2 – 26,9 %); positive changes in blood glucose levels (CG2 – 20,7 %, EG2 – 31,5 %) andarterial tension (CG2 – 6,2 %, EG2 – 9,8 %); development of different muscle groupsstrength endurance.

Conclusions: Positive changes according to the studied indicators show the decrease in risk factors for mature men metabolic syndrome and thereby preventingcomplications.

KEY WORDS: health training, mature men, metabolic syndrome

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INTRODUCTION

Health research shows that health is a system of social, mental, genetic and somatic well-being of a person in particular, and of society in general. State of health, its preservation and improvement is a medical and social problem that requires an immediate solution. The current state of health of the population of the Ukraine is accompanied by high early mortality (compared to other European countries the average lifespan of Ukrainians is lower by 10-15 years), significant rates of disablement and morbidity. The biggest problem is diseases of the circulatory system, the mortality of which exceeds the European average twice. Obesity is one of the global problems nowadays. According to the World Health Organization, 58,4 % of Ukrainians of working age in 2016 were overweight and 25 % of Ukrainians were obese. In its turn, the obesity causes the development of lymphostasis in lower limbs, passive congestion, and hence an increased risk of thrombosis. Another obesity complication is the development and progression of respiratory failure. The accumulation of excess visceral fat in the abdomen results in migration of its organs towards the diaphragm which significantly reduces the excursion of the diaphragm and lungs (especially their lower parts), development of passive pulmonary congestion and increase of pulmonary susceptibility to infection, etc.

In recent years, there has been a growing interest in health-improving physical culture that considers human health in close connection with physical activity, genetic preconditions, energy potential and lifestyle. Negative physiological changes in the human body due to hypodynamia and unhealthy diet have been studied in the works of medical researchers. In particular, C. G. D. de Silva and others scientists [1] draw social attention to the problem of the relationship between cardiorespiratory fitness and obesity. In the study, the authors warn that obesity is a chronic disease, a risk factor for other lifelong health conditions and early mortality. S. W. Farrell and other scientists [2] point to the correlation of cardiorespiratory fitness with obesity indicators and risk of death from cardiovascular disease among women. They concluded that high levels of cardiorespiratory fitness lead to lower risk of death from cardiovascular disease among women with healthy weight than the ones with obesity.

T. Hornstrup and others scientists [3] studied the effects of handball training on the cardiovascular system and metabolic health of overweight women and found a significant increase in VO2max (7 +/– 4 %) and intermittent endurance (26 +/– 14 %), as well as a decrease of total body fat weight (4 +/– 6 %), total body fat rate (4 +/– 5 %) and android fat weight (7 +/– 12 %). The results show positive changes in the metabolic health of women during aerobic continuous group training.

The positive effect of physical exercising is proven in the works of a number of researchers. In particular,F. Morales-Palomo and other scientists [4] studied the efficiency of continuous and interval aerobic dancing programs on the improvementof health of people with metabolic syndrome. Scientists concluded that any 16-weekaerobic training program with training frequency three times a week is effective enough to improve health statusof people with metabolic syndrome and low level of physical activity. On the other hand, more intensive, but shorter aerobic dancing program is proved to be less effective, that is why it is not recommended by the scientists for health improvement forpeople with metabolic syndrome and low level of physical activity.

A thorough analysis of special studies showed that obesity is a risk factor for metabolic syndrome; the problem of defining the concept of metabolic syndrome is not solved; the body response to graduated physical exercising of mature men with metabolic syndrome needs further investigation because the indicated age group is at greatest risk.

THE AIM

The aim was to identify risk factors for metabolic syndrome; to model, justify and experimentally test the effectiveness of a program of complex health training for mature men with metabolic syndrome.

Formulating the hypothesis of the study, we proceeded from the assumption that the experimental health training program for men of the middle period of adulthood with metabolic syndrome which requires a systematic comprehensive training process and provides graduated instructor-led physical exercise regimens (moderate, moderate training, training) will be more effective compared to the system of independent training, and therefore will aid weight reduction, reducing body parts circumference, improving cardiovascular system functioning, formation of strength endurance, and general performance increase.

MATERIALS AND METHODS

Experimental work to test the effectiveness of complex health training program for mature men with metabolic syndrome required the use of theoretical and empirical research methods. Among the theoretical methods we used analysis, generalization, systematization, pedagogical observation, direct questioning, and modeling; among the empirical ones we used methods of implementing research results into practice (pedagogical experiment), methods of control and measurement, data processing methods. In order to develop a systematic approach to the study of the problem, methods of analysis, generalization and systematization of literary sources were used at the following stages: analysis of domestic scientific works on somatic health criteria, motor activity control, physiological negative changes caused by hypodynamia and positive changes as a result of motor activity optimization; works related to research in the field of health and fitness. Pedagogical observation was conducted in order to identify means and methods used by the instructors in conducting health training; control over the implementation of the experimental program by men. The modeling method was used to model a complex organized system of fitness training for men of the middle period of adulthood with metabolic syndrome, optimal for meeting their biological needs in physical activity, improving the functional body status and weight loss. Pedagogical experiment is a specially organized study conducted to test the effectiveness of the experimental program and the system of independent recreational training for men, and to determine their somatic health status before and after the experiment. The experiment involved 50 men aged 40-60 years with metabolic syndrome, who had no contraindications to active training, significant motor experience (without training experience) and were divided into two homogeneous groups (the control and the experimental groups) of 25 people in each group. The experimental group performed the tasks of the experimental program at fitness clubs, and the control group trained according to the system of independent recreational and health-improving training in the home area.

ORGANIZATION OF THE EXPERIMENT

On the first stage, literary sources were analyzed, the basic concept of the subject of the research and the organization of the experimental work were substantiated; object, subject, purpose and objectives of the study were established; men polling was conducted (training motivation, needs and health problems were found out); preliminary test on three indicators – physical development, functional status, general performance level (strength endurance) – was conducted; based on the data obtained, the control (25 people) and the experimental (25 people) groups were formed; the experimental training program for the experimental group was set up; instructional guidelines for the control group were elaborated. The second stage of the research involved practical application of a system of fitness training and monitoring the fulfilment of conditions. On the third stage, a control check of the men's health status was carried out according to certain indicators.

In order to obtain reliable data on the health status of men during the experiment we used an integrated assessment and monitoring upon the following indications:

1. Physical development (height, weight, body parts circumference: chest, waist, hips) and physical performance level (strength endurance (arm bending and extension in plank position; squats; lifting the torso to the buttocks from a supine position). To get the data, a set of tools was used – a measuring tape, the scales, and a stopwatch.
2. The functional status of body systems (cardiovascular and respiratory systems). The cardiovascular system status was assessed using the Ruffier index, and the respiratory system status was characterized by Stange test and Harvard step test. To get data we used a stopwatch.
3. Medical parameters – detection of capillary blood glucose level (taken from the finger) and arterial tension.

Table I. General characterization of the metabolic syndrome

Metabolic syndrome (MS) is a set of four pathologic processes: overweight (obesity), high blood glucose (hyperglycemia), disorders in the qualitative and quantitative composition of various types of cholesterol (dyslipidemia), high arterial tension (hypertension). The greatest danger for people with MS is a high risk of death, mainly from cardiovascular disease.
Characterization of MS risk factors
Obesity is an excess body weight, mostly due to the accumulation of visceral fat in the abdomen. Dangerous signal is men's waist circumference > 94 cm.
Hyperglycemia is a significant(40 %) decrease in tissue sensitivity to insulin, which gradually stops lowering blood glucose levels. Blood glucose concentration > 5,8 mol/l is dangerous.
Dyslipidemia is a violation of the proportions of the lipid profile – an increase in triglycerides and low-density lipoprotein (LDL-cholesterine), while reducing the content of high-density lipoprotein (HDL-cholesterine), that carries a risk of cardiovascular disease. Triglycerides > 1,7 mol/landLDL-cholesterine< 1,03 mol/l are dangerous for men.
Hypertension is an increase in the volume of circulating blood and peripheral vascular resistance that gradually leads to a stable increase in blood pressure and atherosclerosis development. The danger is blood pressure increase to 130/85 mm Hg.
The most dangerous complications of MS: stroke, heart attack, type II diabetes.
Treatment of MS is aimed at elimination of excess body weight through the use of, inter alia, drug-free modalities: rationalization and reduction of caloric intake, systematic physical activity.

Table II. Health training program for mature men with metabolic syndrome

Session №	Exercise №	Session №	Exercise №	Session №	Exercise №
1-2	1, 17, 3, 6, 10	7-8	18, 10, 5, 14,8	13-14	8, 13, 6, 1, 10
3-4	2, 8, 19, 11, 12	9-10	4, 15, 13, 19, 8	15-16	11, 15, 8, 2, 19
5-6	3, 16, 8, 5, 9	11-12	7, 13, 20, 14, 6	17-18	5, 9, 3, 14, 13

Table III. Comparative analysis of somatic health status of men of the middle period of adulthoodwith metabolic syndrome, in the control (n=25) and the experimental (n=25) groups before and after the experiment

Indicators, tests, measurement units	CG1 -> CG2 M± m				EG1 -> EG2 M± m				CG2 -> EG2 M± m
	CG1	CG2	Growth	D	EG1	EG2	Growth	D	Change
Age (yrs)	54,8	54,8			53,8	53,8			
Body weight (kg)	121,6±2,1	109,3±2,1	10,1%	>0,05	122,7±2,15	103,7±1,8	15,5%	>0,05	5,4%
Chest circumference (cm)	111,1±3,8	107,1±3,5	3,6%	>0,05	112,9±4,15	102,8±3,9	9%	>0,05	5,4%
Waist circumference (cm)	122,3±2,7	114,9±2,6	6,0%	>0,05	124,5±2,95	110,1±2,5	11,5%	>0,05	5,5%
Hips circumference (cm)	103,8±3,2	97,7±3,1	5,9%	>0,05	105,9±4,2	96,8±4,3	8,6%	>0,05	2,7%
Push-ups	5,2±1,34	6,4±1,86	23,1%	>0,05	6,1±0,98	8,3±1,95	26,5%	>0,05	3,4%
Squats	16,2±2,34	21±2,34	29,6%	>0,05	16,3±1,33	25,4±2,5	55,8%	>0,05	26,2%
Sit-ups	13,2±1,7	16,7±2,32	26,5%	>0,05	14,0±2,1	19,8±1,83	41,4%	>0,05	14,9%
Ruffier index (c.u.)	12,0±0,9	11,3±0,71	5,8%	>0,05	11,3±0,8	8,7±0,63	23,0%	>0,05	17,2%
Stange test (sec)	32,2±1,9	41,8±3,06	29,8%	>0,05	35,4±1,7	47,4±3,1	33,9%	>0,05	4,1%
Harvard step test (c.u.)	74,6±1,46	86,4±1,67	15,8%	>0,05	77,2±1,7	98±1,7	26,9%	>0,05	11,1%
Blood glucose levels	8,7±0,9	6,9±1,7	20,7%	>0,05	8,9±1,3	6,1±1,6	31,5%	>0,05	10,8%
Arterial tension	145/94±1,6	136/87±2,3	6,2%	>0,05	148/97±1,9	132/85±2,1	10,8%	>0,05	4,6%

Statistical processing of empirical data was performed by the calculating the value of the Student's t-test, the difference between the sample averages was taken with a probability of 95 % ($p < 0,05$).

RESULTS

Metabolic syndrome is a pathogenetically interrelated metabolic disorder in health status of a patient. The definition of metabolic syndrome has changed several times in recent years. There is currently no well-established definition of the syndrome, so there is no common valid ICD-10 code for documentation. The current classification is based either on insulin resistance (insulin resistance syndrome, WHO classification, 1999), or clinical manifestations (NCEP-ATP-III). Thus, for proper documentation of the syndrome, codes for obesity, high blood pressure,

hyperglyceridemia and impaired glucose tolerance are established. This is understandable, because the metabolic syndrome is not considered to be an independent disease, but a group of risk factors for the cardiovascular system (table I).

The study found that physical exercising in MS is used at all rehabilitation stages. The therapeutic effect of physical exercising is showed in the trophic effect on the body, improving redox processes that occur due to increased blood and lymph circulation, supply of oxygen and nutrients to cells for more efficient assimilation, intensification of removal of metabolic products. Metabolic syndrome is treated comprehensively, including increasing amount of training load and limiting the energy value of food, mainly due to carbohydrates and fats. If necessary, hormonal drugs and medications that reduce appetite or are aimed at treating comorbidities are prescribed.

The main tasks that will contribute to weight normalization are: increasing energy assumption, redox and metabolic processes; gradual increase in physical activity, the use of physical exercises for medium and large muscle groups in alternation with respiratory ones that causes increased energy expenditure and oxygen uptake, promotes to consumption of large amounts of carbohydrates, as well as leaving that depot and lipolytic digestion. Contraindications are exacerbation of comorbidities; hypertensive and diencephalic crises.

The course of exercises is divided into two periods. In the first training period physical exercises are used to restore person's movement skills and adapt to physical activity. In the second training period that includes moderate training and training movement regimens, the intensity of physical load gradually increases. Considerable attention should be paid to exercises that strengthen core muscles, corrective and breathing exercises. The training density should reach 60-70 %,and the duration of physical exercising should reach 45-60 min.The training program is recommended for people with alimentary and endogenous forms of obesity, in which there are no significant changes in the organs and systems that limit the amount of exercise. However, with the endocrine-cerebral form of obesity the overall physical training load is reduced; there are more exercises for the middle muscle groups and breathing exercises, the pace of performance is slow to medium, and the training duration is shorter. Exercise dosage is controlled by subjective and objective indicators: well-being, blood and urine glucose levels, body weight.

The analysis of special literary sources the specifics of the disease and the peculiarities of the organization of training sessions and rehabilitation of people with metabolic syndrome prompted us to develop the experimental health training program for men of the middle period of adulthood with metabolic syndrome. The physical exercises of the program are divided into three difficulty levels (moderate, moderate training, training) according to fitness levels and health status of the men.

Exercise 1. *Moderate regimen.* From thepreparatory position(hereafter –p.p.) – narrow leg rack cut to perform a half-squat, then straighten up and raise on toes. Put your hands together in front of your chest. *Moderate training regimen.*Same exercise, but when bending the legs, lower the arms down, and when stretching the legs, raise the arms up. *Training regimen.*When performing a squat, keep your hands on your hips, and straighten up to jump up. Exhale when stretching the legs. This exercise strengthens the quadriceps muscle of thigh and Achilles tendons, anterior and posterior femoral ligaments, sciatic and calf muscles.

Exercise 2. *Moderate regimen.*P.p. – sitting on the edge of a high bench so that your feet don't touch the floor. Weights (dumbbell or bag with stones) should be attached to the right of left foot. The leg with the weight must be straightened and then bent. The exercise strengthens the quadriceps muscle of thigh and knee ligaments. Exhale when stretching the leg. *Moderate training regimen.*Same exercise, but more weight.*Training regimen.* Extending the legs with an exercise machine. The exercise strengthens the thigh extensor muscles.

Exercise 3. *Training regimen.* P.p. – right leg sitting support, left leg back. The angle in the knee joint is straight, the knee does not go beyond the foot "projection"; body weight should be evenly distributed between the hands and feet. From this position, jump up and swap legs. Exhale when changing the position of the legs. This exercise strengthens sciatic muscles, quadriceps muscles of thigh, ligaments and thigh extensor muscles.

Exercise 4. *Moderate regimen.*P.p. – lying on the right side, bend the right leg, straighten the left leg, straighten the right arm up, put your head on the arm. From this position lift the left leg up, then return to p.p. Perform the same exercise with the right leg. *Moderate training regimen.* Same exercise, butattach 1-3 kg ankle weightsto the legs. Exhale while lifting. The exercise strengthens the muscles of inner and outer thighs.

Exercise 5.*Moderate regimen.*P.p. – wide rack legs apart, hands behind head. Bow to the right and to the left. The hips when bowing should not deviate from the main center of gravity. *Moderate training regimen.*Same exercise, but hold 3-5 kg dumbbells in your hands. *Training regimen.* Same exercise, buthands with dumbbells at the top are connected; the weight of the dumbbells is 1-2 kg. Exhale when straighten the body. This exercise strengthens and tones the oblique and transverse abdominal muscles.

Exercise 6. *Moderate regimen.*P.p. – lying on the back, legs bent, arms behind the hand. Round the back, slightly lift your body up, stretch your chin forward without pitching the thyroid gland, then return to p.p. *Moderate training regimen.*P.p. – the same, buthold one 1,5-2 kg dumbbell in your hands, hands up (alongside the body).Sit up, press your body against the floor, hold your arms with a dumbbell forward, then return to p.p. *Training regimen.* Same exercise, but more weights. The exercise strengthens abdominal muscles.

Exercise 7. *Moderate regimen.*P.p. – stand legs apart, hold a barbell weighting up to 10 kg on the shoulders. Lean forward to the right angle, bend at the back, lift the chin, then return to p.p. *Moderate training regimen.*Same exercise, but

the weight of the barbell is more. Exhale when stretching the body. The exercise strengthens biceps muscle of thigh, sciatic and back extensor muscles.

Exercise 8. *Moderate regimen.*P.p. – lying on your back on the bench, legs bent on the floor, arms holding 2-3 kg dumbbells forward. Spread your arms out to the sides so that your shoulders are horizontal to the floor (don't allow overextension in the shoulder joint), then return to p.p. *Moderate training regimen.*Same exercise, but more weights. The exercise strengthens greater pectoral muscles.

Exercise 9. *Moderate regimen.* P.p. – stand legs apart, arms holding 3-5 kg dumbbells down. Raise your shoulders up, then return to p.p. *Moderate training regimen.*Same exercise, but more weights. Exhale when lifting the shoulders. This exercise strengthens trapezius muscle.

Exercise 10. *Moderate training regimen.* P.p. – standing on the bench in front of the crossbar at chin level, hands on a pole shoulder-width apart, grip from above, chin lightly above the crossbar. Holding on to the pole, slowly descend from the bench to the height of the crossbar. Going down you need to control the body so that it doesn't fall down, then step up on the bench. Exhalewhen stretching the arms. *Training regimen.*Pull-ups (hanging lying down) on the crossbar. The exercise strengthens shoulder muscles.

Exercise 11. *Moderate training regimen.*P.p. – stand in the kneeling position, hands narrowly on the floor or bench, lower hips. Bend your arms while touching the bench, then unbend your arms. *Training regimen.* Same exercise, butknees don't touch the floor. Exhale when stretching the arms. The exercise strengthens shoulder muscles, triceps and abdominal muscles.

Exercises with an athletic tubular shock absorber (possible with a medical tourniquet), the dosage is regulated by the amount of repetition and the amplitude of movement.

Exercise 12. P.p. – stand feet apart, the ATSA forward. Spread your arms out to the sides, stretch the ATSA and exhale, then return to p.p.andinhale. Rhomboid and deltoid muscles are active.

Exercise 13. P.p. – lunge right forward, clamp the ATSA with right foot, hold the ends of the ATSA in right hand, palms out, the left hand on the waist. The right arm-pumping. Exhale when bending the arm. Perform the same exercise with left arm. Focus on the biceps muscle of arm.

Exercise 14. P.p. – lunge left leg forward, press the ATSA in the center with the right foot, arms bent up, the ATSA behind the back, grip at both ends (perform the exercise with a long ATSA or a medical tourniquet). Extend your arms up and exhale, then bend and inhale. The triceps muscle of the shoulder is active.

Exercise 15. P.p. – stand with both feet in the center of the ATSA,squat legs apart, and grab the ends with both hands. Pull arms backwards andexhale, then lower hands and inhale. In this exercise involves the posterior cords of deltoid muscle and trapezius muscle.

Exercise 16. P.p. – stand legs apart, standing in the center of the ATSA, arms bent to the sides, grasping both ends of the ATSA. Extend your arms up – exhale, bend – inhale. The deltoid and trapezius muscles are active.

Exercise 17. P.p. – the same. Bringing the bent arms forward – exhale, p.p. – inhale. The greater pectoral muscles are active; anterior cords of deltoid muscle work statically.

Exercise 18. P.p. – the same (ATSAis slightly stretched). Bend your legs – inhale;spread your legs, arms up – exhale;lower your arms through the sides down. The quadriceps and deltoid muscles are active.

Exercise 19. P.p. – the same, but transfer body weight to the left leg (ATSAis slightly stretched). The right leg abduction to the side – exhale, leg in p.p. – inhale. Repeat the same exercise with the left leg. The sciatic muscles are active.

Exercise 20. P.p. – lunge with the right leg, press the ATSAto the floor with the right foot, grab both ends with your hands. Bend your legs, arms to the sides – exhale. P.p. – inhale. The quadriceps muscles of thigh, sciatic muscles and middle deltoids are active.

Due to the peculiarities of men's health, we have developed and implemented a program to normalize weight and maintain results, increase muscle tone and performance capability. For the effectiveness and safety of exercising, the program is developed to focus on strengthening of the relevant muscle groups. The amount of repetition of each exercise of the set is 10-20 (duration – 30-60 sec), depending on the individual ability of the man to perform it in the maximum amount in the specified time and start performing another exercise, but training another muscle group. As men trained, we included exercises with a load that slightly exceeded the physical capabilities of the men, but didn't overload them.

The program begins with a warm-up that includes walking and running exercises,combined developing exercises for the muscles of the neck, pectoral arch, upper body and lower extremities. The main part is built up on the system of circuit training. One circle consists of 5 weight-lifting exercises that should be performed in the sequence specified in the program. A set of exercises should be performed three times, each time maintaining a certain speed of movement. The relatively fast tempo of performance of exercises and short rest breaks between the sets (stations) can increase physical load, increase oxygen uptake by the body and give the effect of a full-fledged functional aerobic training. Active rest after the exercise is a transition to the next type of movement, after one circle – rest for 30 sec. After performing the program of weight-lifting exercises for the third time, it is necessary to perform a set of cool down exercises for stretching. The exercises for stretching are performed on the principle of progressive static stretching. They should be performed slowly until you feel a slight pain from tension; this position should be hold for another 10-20 sec. It is not recommended to make abrupt movements, so as not to injure muscles and ligaments.

The program is designed for 18 sessions – three sessions per week, so the full cycle lasts 6 weeks. The results of exercising (the amount of repetitions in a set, the weights, an amplitude of movement, an exercise heart rate, general physical state, etc.) should be recorded in a diary (table II).

Therefore, the developed program was implemented by the members of the experimental group. The men of the control group took part in recreational and health-improving training that don't include regulated physical activity; they independently chose activities that meet their subjective needs and capabilities. They trained at a convenient time, without taking into account the time to perform the exercises and a third-party consultation.

Abbreviations: CG1 – the control group before the experiment; CG2 – the control group after the experiment; EG1 – the experimental group before the experiment; EG2 – the experimental group after the experiment; n – sample number; M – arithmetic mean; m – standard error of the arithmetic mean; D – validity of difference according to Student's t-tes (table III).

DISCUSSION

Obesity is a chronic disease, a risk factor for other chronic conditions and early mortality. This conclusion was reached by scientists de Silva CGD et al. [1]. Their study was based on comparing the frequency of visits of patients with obesity to the doctor. Scientists have found that annual costs among obese people are at least 30% higher than those of their peers with normal weight. When conducting our study, the economic side of the organization of training was not taken into account. When organizing the experiment, we took in to account only the idea of finding out the relationship between cardiorespiratory endurance and obesity.

Scientists Farrell SW et al. [2], whos estudies we relied on, note the correlation of cardiorespiratory fitness with rates of obesity and the risk of mortality from cardiovascular diseases in women. Studies show that higher levels of cardiorespiratory endurance are associated with lower risks of cardiovascular death in normal weight women than in obese women. Interesting for us was the choice of research methodology by scientists, which made it possible to carry out accurate measurements. In our study, we used a measurement experience including body mass index, waist circumference, body-to-skinfold ratio. However, we focused not only on objective indicators of weight loss, but also on the dynamics of the functionalstate of men. To obtain data in this cluster, we used the Rufier index, Stange index, step-test, measured blood glucose levels and blood pressure. This, in our opinion, should most accurately convey the results of a cohort study.

An important contribution to the study of the effect of aerobic training on the state of the cardiovascular system and metabolic health in women was made by scientists T. Hornstrup et al. [3]. The results obtained indicate positive changes in the health status of women during group training, which are of a continuous aerobic nature. These studies attracted attention in that scientists achieved a significant reduction in fat mass in women through a continuous loading method. Therefore, we use this method of organizing a lesson in our study. A distinctive feature of our study is the emphasis not on sports and gaming practice, but on an integrated approach to physical improvement based on exercises of a general developmental nature.

Scientists Morales-Palomo F. et al. [4]. Focus their attention on the use of continuous and interval methods to improve health during the metabolic syndrome. Their results show that for people with metabolic syndrome, any aerobic training program lasting 16 days, three times a week is effective. Scientists have proven that a shorter high-intensity workout is not effective for this group of individuals. Listening to the recommendations, we have selected physical exercises so that men with metabolic syndrome and different levels of fitness can perform them with the appropriate frequency, pace, amplitude and intensity. Accordingly, the complexes of exercises were distributed by us into sparing, sparingly training and training modes, which gave a significant healing effect.

In general, in comparison with the results of studies of other scientists on this issue, we have proved the effectiveness of differentiation of general developmental physical exercises in three modes of work (sparing, sparing-training and training), which werecarried out by a continuous method. This made it possiblein a short time (6 weeks) to switch from a sparing exercise regimen, the purpose of which was adaptation to physical exertion and weight loss, to a training regimen – body shaping, normalization and stabilization of weight, body circumference.

In particular, body weight, chest circumference, waist circumference in the experimental group decreased by an average of 5.5% compared with CG2, which contributed to the correction of the physique. Indicators of formation of strength endurance increased both in CG2 and EG2. But, we can note a significant increase in the indicators of EG2 in the test exercises: «Squats» (by 55.8%) and «Raising the torso into a sitting position from a supine position» (by 41.4%), in CG2 by 29.6% and 26.5% respectively. Positive changes occurred in the functional state of the body systems of men, including in terms of the Stange test (CG2 - 29.8%, EG2 - 33.9%), the Rufier index (CG2 - 5.8%, EG2 - 23.0%) and step test (CG2 - 15.8%, EG2 - 26.9%), indicating an improvement in the activity of the cardiovascular and respiratory systems. We also note positive changes in blood glucose levels (CG2 - 20.7%, EG2 - 31.5%) and blood pressure (CG2 - 6.2%, EG2 - 9.8%). In the course of the study, it turned out that the methodology we chose to check the health status of men turned out to be effective and efficient.

CONCLUSIONS

In the course of the study we identified risk factors for metabolic syndrome, modelled, justified and experimentally tested the effectiveness of the program of complex health training for mature men with metabolic syndrome. In general, the training program helped to reduce body weight, reduce the circumferences of body parts, improve cardiovascular and respiratory systems, increase general performance level, reduce blood glucose levels and lower arterial tension that proves the effectiveness of a systematic approach to training of the men with metabolic syndrome in this age group. It is important to note that the advan-

tages of the program under the guidance of an instructor over the independent training which is more significantly reflected in the indicators. At the same time, the positive dynamics, according to the studied indicators, shows a decrease in risk factors for metabolic syndrome for mature men, thus preventing the development of MS and related complications.

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ORCID and contributionship:
Oksana K. Kornosenko: 0000-0002-9376-176X [A, B, D, E]
Iryna V. Taranenko: 0000-0001-5009-9641 [B, C]
Yevheniia Yu. Shostak: 0000-0002-3668-0875 [D, E]
Yuliia V. Zaitseva: 0000-0001-7155-392X [B, D]
Oleksandr V. Petryshyn: 0000-0002-5722-8036 [F, E]

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CORRESPONDING AUTHOR
Oksana K. Kornosenko
Poltava V.G. Korolenko National
Pedagogical University
2 Ostrogradskogo st., 36000 Poltava, Ukraine
tel: +38(099)7226184
e-mail: kornosenko@ukr.net

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ORIGINAL ARTICLE

ANALYSIS OF STUDENTS' HEALTH INDICATORS IN THE COURSE OF PHYSICAL EDUCATION CLASSES WITH A SPORTS FOCUS

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Andrii A. Rebryna[1], Anatolii A. Rebryna[1], Natalia A. Lyakhova[2], Iryna I. Shaposhnikova[3], Svitlana M. Korsun[3], Liudmyla V. Shuba[4], Victoria V. Shuba[5]

[1]KHMELNYTSKYI NATIONAL UNIVERSITY, KHMELNYTSKYI, UKRAINE
[2]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE
[3]KHARKIV STATE ACADEMY OF PHYSICAL CULTURE, KHARKIV, UKRAINE
[4]NATIONAL UNIVERSITY "ZAPORIZHZHIA POLYTECHNIC", ZAPORIZHZHIA, UKRAINE
[5]PRYDNIPROVSK STATE ACADEMY OF PHYSICAL CULTURE AND SPORTS, DNIPRO, UKRAINE

ABSTRACT

The aim: To conduct a comparative analysis of the health indicators of students who were engaged in various types of sports during physical education classes (using the example of power sports).

Materials and methods: The research was conducted in 2019-2021 when the male students (n=96) were studying at the 1st and 2nd years in Kharkiv State Academy of Physical Culture. We examined the health indicators of 17-19-year-old students, who were engaged in various power sports: powerlifting, kettlebell lifting, armsport and CrossFit. Students' health was assessed by indicators of body weight, cardiovascular, respiratory and muscular systems.

Results: It was found that during the study period, the most pronounced changes in the activity of the cardiovascular (Robinson's index) and respiratory systems (vital index) were found among students who were engaged in CrossFit and kettlebell lifting. In the indicators that characterize the muscular system (power index), the greatest increase was found among students who were engaged in powerlifting and armsport.

Conclusions: It has been revealed that classes in any power sport positively affect the improvement of certain indicators of students' health, which, in general, will positively contribute to mastering the skills and abilities to independently use the means of physical culture and sports in everyday life to maintain high performance both during academic and future professional activities.

KEY WORDS: health indicators, physical education, power sports, students

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INTRODUCTION

The situation that has developed in the system of physical education of students in Ukraine has brought to the fore the contradiction between intellectualization and humanization of the educational level of a future specialist who should master in a higher education institution (HEI) not only the mandatory and selective components of the educational program, but also one of the basic cultures – the physical culture of the individual [1]. Despite the rich arsenal of tools, methods and forms of development of physical qualities, this was not enough to form the physical culture of the future specialist's personality and his physical readiness for future professional activity [2, 3]. Scientists [4, 5] found out that the main reasons for these problems are: inefficient organization of the process of physical education of students in HEI; low level of physical fitness and health of young people entering HEI; insufficient effectiveness of traditional physical education classes. The latter causes a low level of motivation and interest of students in physical education classes, a large percentage of absences from physical education classes, and a further decrease in the level of physical fitness and health of future specialists [6, 7].

According to a number of scientists [8, 9] a promising way for solving these problems is the introduction in the HEI of physical education classes with a sports focus, which provide for taking into account the interests of students in various sports. At the same time, scientists [10] note that it is necessary to take into account the capabilities of the sports facilities that are available at the HEI and availability of coaches in various sports in the physical education departments of the HEI. Effective means of physical education, which were always popular among students, especially males, are power sports [11, 12]. In the process of practicing strength exercises, students develop all motor qualities, and above all – strength. Strength is an integral motor quality, on which the manifestation of all other motor qualities depends to a greater or lesser extent [13]. The results of many scientists' study of students' interests in power sports show that, as a rule, the largest percentage of male students surveyed during their studies at the HEI want to go in for modern power sports, such as: powerlifting, kettlebell lifting, arms-

Table I. Level and dynamics of BMI of studied groups of students (n=96) during the study period (Mean±SD), kg/m^2

Studied groups of students		Stages of the study		Certainty of the difference, $p_{beg.}$-p_{end}
		Beginning	End	
Group P, n=26		23.38 ±0.41	24.32±0.43	>0.05
Group K, n=22		23.20 ±0.38	23.16±0.35	>0.05
Group A, n=21		23.22 ±0.39	23.96±0.41	>0.05
Group C, n=27		23.19 ±0.42	23.14±0.40	>0.05
Certainty of the difference	p_P-p_K	>0.05	>0.05	
	p_P-p_A	>0.05	>0.05	
	p_P-p_C	>0.05	>0.05	
	p_K-p_A	>0.05	>0.05	
	p_K-p_C	>0.05	>0.05	
	p_A-p_C	>0.05	>0.05	

Note: Mean - arithmetical average; SD - standard deviation; p_P-p_K (p_P-p_A, p_P-p_C …) - the significance of difference between the indicators of each group during the research due to the Student's t-test; $p_{beg.}$-p_{end} - the significance of difference between the indicators of studied groups at the beginning and the end of research due to the Student's t-test

Table II. Level and dynamics of VI of studied groups of students (n=96) during the study period (Mean±SD), ml/kg

Studied groups of students		Stages of the study		Certainty of the difference, $p_{beg.}$-p_{end}
		Beginning	End	
Group P, n=26		56.12±0.57	57.43±0.62	>0.05
Group K, n=22		56.27±0.61	60.29±0.67	<0.001
Group A, n=21		56.31±0.64	59.52±0.73	<0.01
Group C, n=27		56.24±0.53	60.87±0.69	<0.001
Certainty of the difference	p_P-p_K	>0.05	<0.01	
	p_P-p_A	>0.05	<0.05	
	p_P-p_C	>0.05	<0.01	
	p_K-p_A	>0.05	>0.05	
	p_K-p_C	>0.05	>0.05	
	p_A-p_C	>0.05	>0.05	

Note: Mean - arithmetical average; SD - standard deviation; p_P-p_K (p_P-p_A, p_P-p_C …) - the significance of difference between the indicators of each group during the research due to the Student's t-test; $p_{beg.}$-p_{end} - the significance of difference between the indicators of studied groups at the beginning and the end of research due to the Student's t-test

port, CrossFit [14-17]. Scientists are convinced that power sports can improve the physical fitness, functional state and performance of students, develop all muscle groups, effectively solve the problems of forming and correcting the body structure, form moral and volitional qualities, and improve athletic performance [18, 19]. At the same time, insufficient research has been conducted on comparing students' health indicators in the process of practicing various power sports during their studies at the HEI.

THE AIM

The aim of this study is to conduct a comparative analysis of the health indicators of students who were engaged in various types of sports during physical education classes (using the example of power sports).

MATERIALS AND METHODS

MATERIALS

The research was conducted in 2019-2021 when the male students (n=96) were studying at the 1st and 2nd years in Kharkiv State Academy of Physical Culture. 4 groups of students aged 17-19 of different faculties were formed. They were engaged in various power sports in the process of physical education: powerlifting – group P (n=26), kettlebell lifting – group K (n=22), armsport – group A (n=21), CrossFit – group C (n=27). These groups of students were formed by conducting an entrance survey of students at the first physical education class in the first semester, during which their interests in various sports in the HEI were studied. Before beginning the survey, students' health status was assessed in order to find out

Table III. Level and dynamics of PI of studied groups of students (n=96) during the study period (Mean±SD), %

Studied groups of students		Stages of the study		Certainty of the difference, $p_{beg.}$-p_{end}
		Beginning	End	
Group P, n=26		59.83±0.72	68.29±0.73	<0.001
Group K, n=22		59.67 ±0.75	67.05 ±0.77	<0.001
Group A, n=21		60.08 ±0.73	68.52 ±0.75	<0.001
Group C, n=27		58.94 ±0.68	66.35 ±0.78	<0.001
Certainty of the difference	p_P-p_K	>0.05	>0.05	
	p_P-p_A	>0.05	>0.05	
	p_P-p_C	>0.05	>0.05	
	p_K-p_A	>0.05	>0.05	
	p_K-p_C	>0.05	>0.05	
	p_A-p_C	>0.05	>0.05	

Note: Mean - arithmetical average; SD - standard deviation; p_P-p_K (p_P-p_A, p_P-p_C …) - the significance of difference between the indicators of each group during the research due to the Student's t-test; $p_{beg.}$-p_{end} - the significance of difference between the indicators of studied groups at the beginning and the end of research due to the Student's t-test

Table IV. Level and dynamics of RI of studied groups of students (n=96) during the study period (Mean±SD), c.u.

Studied groups of students		Stages of the study		Certainty of the difference, $p_{beg.}$-p_{end}
		Beginning	End	
Group P, n=26		87.18±0.78	84.11±0.80	<0.05
Group K, n=22		86.99 ±0.81	81.14 ±0.77	<0.001
Group A, n=21		87.11 ±0.75	83.54 ±0.79	<0.01
Group C, n=27		87.09 ±0.79	80.30 ±0.76	<0.001
Certainty of the difference	p_P-p_K	>0.05	<0.05	
	p_P-p_A	>0.05	>0.05	
	p_P-p_C	>0.05	<0.01	
	p_K-p_A	>0.05	<0.05	
	p_K-p_C	>0.05	>0.05	
	p_A-p_C	>0.05	<0.05	

Note: Mean - arithmetical average; SD - standard deviation; p_P-p_K (p_P-p_A, p_P-p_C …) - the significance of difference between the indicators of each group during the research due to the Student's t-test; $p_{beg.}$-p_{end} - the significance of difference between the indicators of studied groups at the beginning and the end of research due to the Student's t-test

whether there were any contraindications to practicing their chosen sports. At the beginning of the research the students of all studied groups had the same indicators of physical health (p>0.05). Physical education classes for students in all sports were held three times a week under the guidance of coaches in selected sports for 2 hours each. The total weekly workload of students in all groups was the same. The main study's limitation was the lack of control of the studied group's extra-curricular physical activities during the research period.

METHODS

Research methods: analysis and generalization of literature sources, questionnaires, pedagogical observation, medical and biological methods, methods of statistical data processing. Students' health was assessed by indicators of body weight, cardiovascular, respiratory and muscular systems. Body weight, height, vital capacity of the lungs, wrist dynamometry, heart rate at rest, arterial (systolic and diastolic) pressure at rest were studied. Based on the results of the data obtained, we calculated indexes that indicate the level of health of students: body mass index, vital index, power index and Robinson's index. Body mass index (BMI) is the ratio of body weight to body length (the norm for men of this age is 20.1-25.0). Vital index (VI) is the ratio of vital capacity to body weight (the norm is 56-60 ml/kg). Power index (PI) is the ratio of the indicators of handgrip test to body weight (the norm is 66-70%). Robinson's index (RI) is a product of heart rate and systolic blood pressure (the norm is 85-94 c.u.). The study of students' health indicators was conducted by medical personnel in the academy polyclinic three times during the study period: at the beginning of the 1st year (beginning of the experiment),

at the end of the 1st year, at the end of the 2nd year (end of the experiment).

STATISTICS

During the research the authenticity of difference between the indicators of students of studied groups by means of Student's t-test was determined. The significance for all statistical tests was set at $p<0.05$. All statistical analyses were performed with the SPSS software, version 21, adapted to medical and biological researches.

ETHICAL APPROVAL

This research has followed the tenets of the World Medical Association (WMA) Declaration of Helsinki – ethical principles for medical research involving human subjects. Informed consent has been obtained from all students included in this study.

RESULTS

Analysis of the dynamics of BMI showed that at the beginning of the study, the indicators of the studied groups did not significantly differ from each other ($p>0.05$). During the study period, certain changes occurred: students who were engaged in powerlifting and armsport showed slightly increased indicators due to an increase in muscle mass, and students who were engaged in kettlebell lifting and CrossFit – slightly decreased their indicators due to a decrease in the fat component of body weight (Table I). At the same time, the indicators for the study period did not significantly change in any of the groups, and at the end of the study, there was also no significant difference between the groups ($p>0.05$). Herewith, the BMI indicators of all groups of students are within the normal range.

Analysis of the VI indicators of students showed that during the experiment there was a significant improvement in the indicators of the respiratory system of students of all groups. in Group P by 1.31 ml/kg, in Group K by 4.02 ml/kg, in Group A by 3.21 ml/kg, in Group C by 4.36 ml/kg (Table II). However, significant changes were recorded in groups of students who were engaged in CrossFit, kettlebell lifting and armsport ($p<0.01$-0.001). Comparing the VI performance of students at the end of the study, we found that the performance of powerlifting students was significantly worse than that of the other three groups ($p<0.05$-0.01), while there was no significant difference between the performance of students in groups K, A and C ($p>0.05$). VI indicators of students in all groups, both at the beginning and at the end of the study, are within the normal range.

A comparative analysis of the PI indicators of students showed that both at the beginning and at the end of the study, there was no significant difference between the indicators of students who were engaged in various power sports ($p>0.05$) (Table III). This indicates that during the study period there was a significant increase in the strength indicators of students of all groups. The greatest increase in muscle development indicators was found among students who were engaged in powerlifting (8.46 %) and armsport (8.44 %). In Group K and C, indicators improved by 7.38% and 7.41%, respectively.

Studying the dynamics of RI, it should be noted that a decrease in the index value indicates an improvement in the activity of the cardiovascular system of students. So, during the study period, the performance of students in all four groups significantly improved ($p<0.05$-0.001), but the most pronounced changes occurred in students who were engaged in kettlebell lifting and CrossFit (Table IV). This is due to the fact that these sports are mainly aimed at developing students' endurance. A comparative analysis of students' RI indicators at the end of the study showed that the best RI scores were found among Group C students (80.30 c.u.), and the lowest – among students of Group P (84.11 c.u.).

DISCUSSION

The scientists [20, 21] indicate that by the age of 17-18, a comprehensive improvement of motor function is completed, and the alignment of the topography ratio of the strength of various muscle groups, which is typical for adults, ends. An increase in the maximum indicators of strength and speed indicates that the developing motor system becomes active in various functional parameters. Scientists [22, 23] considered student age to be the period of completion of the formation of the young person's body, which is characterized by a fairly high plasticity, adaptation to physical exertion. Therefore, according to the authors, student age is the most favorable, optimal time for practicing power sports.

Studying students' interest in systematic power sports, the scientists [24] established leading incentives, including: improvement of performance in training and future professional activities; rest (switching) during training activities; slim strong figure; improvement of their own sports results; friendship (communication), tension, empathy, drama during competitions; trials and success; determination and confidence.

Each of the power sports (powerlifting, kettlebell lifting, armsport and CrossFit) differs in the specifics of competitive activities, but combines their nature of training work, which has a strength orientation using both traditional (barbell, dumbbells, kettlebells, rubber, etc.) and non-traditional (simulators and devices with variable load) means [12, 13, 25]. Every power sport that is popular among students of the HEI is characterized by requirements for the predominant development of a particular type of strength. So, for example, in powerlifting, the leading quality is maximum (absolute) strength, in CrossFit – high-speed (explosive) strength and power endurance, in kettlebell lifting – power endurance, in armsport – high-speed (explosive) and maximum strength. This, accordingly, leaves a certain imprint on the level and dynamics of students' health indicators in the learning process [14-17].

In our study, we found out the impact of various strength sports on the health indicators of male students in the learning process. It has been revealed that all the studied strength sports have a positive effect on improving students' health indicators: body weight stabilizes and even decreases due to a decrease in the fat component; the activity of internal organs and the main life support systems of the body improves; indicators of muscle system development significantly increase, which is reflected in improving the level of physical fitness of students, improving their appearance. At the same time, indicators that characterize the activity of the cardiovascular and respiratory systems of students are more effectively developed among students who are engaged in sports aimed at developing endurance (strength, speed, general) – CrossFit and kettlebell lifting. Students who are engaged in armsport and powerlifting have more pronounced changes in the power indicators, since these sports are aimed at developing maximum strength.

CONCLUSIONS

It was found out that each power sport has its own specifics, is characterized by different requirements for the development of strength qualities and, accordingly, for the physical development of students and the functional state of their main body systems. So, among students who were engaged in CrossFit and kettlebell lifting, the most pronounced changes were found in VI and RI indicators. Among students who were engaged in powerlifting and armsport, the largest increase occurred in PI indicators. It has been revealed that classes based on any power sport positively affect the improvement of certain indicators of students' health, which, in general, will positively contribute to mastering the skills and abilities to independently use the means of physical culture and sports in everyday life to maintain high performance both during academic and future professional activity.

In the future we plan to study the impact of power sports on the state of health of female students while studying at university.

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ORCID and contributionship:
Andrii A. Rebryna: 0000-0002-5108-2793[A]
Anatolii A. Rebryna: 0000-0001-7707-5324[A,E]
Natalia A. Lyakhova: 0000-0003-0503-9935[C,E]
Iryna I. Shaposhnikova: 0000-0003-1020-6486[B,F]
Svitlana M. Korsun: 0000-0002-2272-8786[D,F]
Liudmyla V. Shuba: 0000-0002-8037-4218[C]
Victoria V. Shuba: 0000-0001-5042-3106[F]

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CORRESPONDING AUTHOR
Natalia A. Lyakhova
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
tel: +380506147638
e-mail: natanew2017@ukr.net

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ORIGINAL ARTICLE

MORPHOLOGICAL FEATURES OF THE LIVER PARENCHYMA IN THE EXPERIMENTAL SUPPLEMENTATION OF RATION WITH THE FOOD ADDITIVES

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Haliia M. Mustafina, Ivan I. Starchenko, Boris M. Fylenko, Volodymyr M. Koka, Valentyna V. Cherniak, Nataliia V. Roiko, Serhiy A. Proskurnya
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: The aim of the paper was the experimental study of the morphological features of albino rat hepatocytes after the consumption of the complex of food additives (monosodium glutamate, sodium nitrite, Ponceau 4R) supplemented into the ration and consumed for four weeks.

Materials and methods: The study was performed on 30 outbred albino rats of both genders, weighing 204±0.67 g. The ration of the experimental animals, supplemented with a combination of food additives, namely, monosodium glutamate, Ponceau 4R, sodium nitrate, was consumed for 1 and 4 weeks. The study of the structure of hepathocytes was carried out on traditional histological preparations and preparations stained with Best's carmine.

Results: Supplementation of ration with the complex of food additives for one week showed the phenomena of fatty degeneration that dominated in hepatocytes, and in a longer consumption of food additives in the ration (for four weeks), the number of liver cells with the phenomena of hydropic degeneration significantly increased, while individual hepatocytes had signs of irreversible destructive changes.

Conclusions: Consumption of the complex of food additives supplemented into the standard ration of laboratory animals for 4 weeks leads to a significant change in the dimensions of the liver cells, a decrease in their glycogen content, and a progressive increase in the number of hepatocytes with alterations.

KEY WORDS: liver, hepatocytes, food additives, monosodium glutamate, Ponceau 4R, sodium nitrate

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INTRODUCTION

The liver in the human body plays a key role in the metabolism and, in addition, performs many other vital functions [1]. The main cellular elements of the liver parenchyma are hepatocytes, which are involved in the metabolism of proteins, carbohydrates, cholesterol synthesis, detoxification and excretion of a number of endogenous substances from the body [1,2].

Destructive changes in hepatocytes underlie the pathogenesis of most liver diseases, and therefore, numerous clinical and experimental studies are devoted to the morphofunctional changes of the latter, developed under the influence of various endo- and exogenous factors [3,4]. At the same time, current publications underestimate the description of the structural and functional features of the liver cells when various food additives are supplemented into the ration. At the same time, on the basis of experimental data, it has been found that the complex of food additives (monosodium glutamate, Ponceau 4R, sodium nitrate) supplemented into the ration leads to morphological changes in some organs of the digestive system [5,6].

THE AIM

The experimental study of the morphological features of albino rat hepatocytes after the consumption of the complex of food additives (monosodium glutamate (E621), sodium nitrite (E250), Ponceau 4R (E124)) supplemented into the ration and consumed for four weeks.

MATERIALS AND METHODS

The study involved 30 outbred albino rats of both genders, weighing 204±0.67 g. All experimental studies have been carried out in accordance with the Rules for the Humane Treatment of Animals in accordance with the requirements of the Declaration of Helsinki of the World Medical Association and in accordance with the general ethical principles for working with experimental animals, which were approved by the National Congress of Bioethics [7,8].

The animals were assigned into three groups (10 animals in each). The animals of the first group (intact animals) received regular ration, the animals of the second and third (experimental) groups consumed the combination of food additives, namely, monosodium glutamate, Ponceau 4R, sodium nitrate, supplemented into the ration for 1 and 4 weeks, respectively.

After euthanasia under thiopentone anesthesia overdose (200 mg/kg of the body weight), the liver was removed, the fragments of which were fixed during the 24 hours in the 10% neutral formalin solution. The formalin-fixed mate-

rial, after dehydration, was embedded into liquid paraffin using the "Microm" station for pouring paraffin blocks according to the standard technique. Sections of 5-7 μm thick were made from the paraffin blocks on the "Leica" rotary microtome, which were stained with hematoxylin and eosin according to the conventional technique and Best's carmine to detect glycogen [9,10].

The study of micropreparations and the determination of morphometric parameters were carried out using the Olimpus BX 41 microscope, equipped with a digital microphotographic attachment and a package of attached licensed software.

RESULTS

The findings of the studies have shown that in the liver of albino rats, hepatocytes were the main cellular elements that form the parenchyma of the organ. In typical cases, hepatocytes had distinct contours, a polygonal shape, arranged in two layers, forming hepatic beams, radially diverging from the central vein and separated from each other by intralobular sinusoidal capillaries (Fig. 1). The morphometry has established that the average length of hepatocytes of intact animals was 24.79±1.67 μm; the average width was 17.42±1.11 μm. The average area of the liver cells was 432.5±40.93 μm^2, respectively. The average diameter of the nuclei was 7.61±0.25 μm, the average area of the nuclei was 45.46±3.06 μm^2. The liver cells contained one or two orbicular nuclei. The relative number of binuclear hepatocytes was (20.59±3.16) %. Insufficient number of liver cells with dystrophic changes was found (Fig. 1).

The use of stain for glycogen made it possible to identify three subpopulations of hepatocytes. The most numerous were hepatocytes with a moderate content of glycogen and they generally occupied the intermediate sections of the hepatic lobules; liver cells with a small amount of glycogen granules in the cytoplasm, which were located in the periphery of the hepatic lobules were somewhat less common. The fewest were hepatocytes with a significant content of glycogen and they were localized mainly in the central parts of the hepatic lobules.

The consumption of the complex of food additives supplemented into the ration of the animals for one week showed that the histological structure of the liver did not undergo any significant changes, and there were no noticeable changes in the metric parameters of the liver cells. The average length and width of the latter was 24.26±2.51 μm and 17.07±1.49, respectively. The area of hepatocytes also did not significantly change and accounted for 417.5±78.19 μm^2, respectively. More significant changes were observed in terms of the size parameters of the nuclei, the diameter of which was 8.5±0.28 μm, the average area was 56.6±3.38 μm^2. The relative number of binuclear hepatocytes significantly decreased, compared to the control animals, accounting for (14.53±3.20) %.

In the described experimental group, hepatocytes with dystrophic changes were detected; their total number accounted for 3.7%. At the same time, among the latter, cells with morphological signs of fatty degeneration, which had a dust-like or small-drop appearance, predominated. Changes characteristic of hydropic dystrophy were observed much less frequently in the liver cells.

In addition to the cells described above, we have found liver cells in a small amount with intensely stained, homogeneous cytoplasm, so called "dark hepatocytes". These cells, in addition to the indicated tinctorial features, were characterized by an irregular polygonal shape, variable linear dimensions, an intensely basophilic swollen homogeneous, often pycnotic nucleus. Quite often, such hepatocytes did not have distinct visual contacts with adjacent liver cells, forming hepatic beams. This morphological picture allowed us to consider these cellular elements as hepatocytes, which were at the initial stages of the development of irreversible alterations. Similar cells were found in the subcapsular and in the central portions of the liver and were located mainly on the periphery of the hepatic lobules, near the triads (Fig. 2).

In the animals of the experimental group the number of hepatocytes containing a significant amount of glycogen significantly decreased, compared to the control animals, while the number of liver cells with low glycogen content, on the contrary, increased significantly.

The consumption of the complex of food additives supplemented into the ration of the animals for four week led to significant increase in the size of liver cells, the average length of which was 24.9±1.11 μm, the average width was 19.5±0.87 μm, and the average area, was 484.8±43.08 μm^2, respectively.

The metric characteristics of the nuclei in this group, on the contrary, did not significantly differ from the control values. The average diameter of the nuclei of hepatocytes in this experimental group was 7.8±0.33 μm, the area was 47.8±4.06 μm^2. The relative number of binuclear hepatocytes (15.47±1.52) % was almost the same compared to the previous experimental group.

As previously described, along with hepatocytes with a typical structure, we occasionally detected liver cells with dystrophic changes. The total number of the latter increased significantly and accounted for 8.6% of the entire population of the liver cells. At the same time, the number of hepatocytes with the phenomena of hydropic dystrophy increased markedly, while the number of the liver cells with fatty degeneration, on the contrary, decreased. It is quite possible that a significant number of hepatocytes with the phenomena of hydropic dystrophy along with swelling of the cytoplasm, causes the previously described change in the metric characteristics of liver cells.

In this experimental group, "dark hepatocytes" were also constantly detected, the morphological features of which were described earlier. The number and nature of the localization of the latter in the hepatic parenchyma did not change significantly (Fig. 3.).

Hepatocytes containing a small amount of glycogen were located on the periphery of the lobules, near the hepatic triads, forming the group clusters. Periodically, similar hepatocytes were also found in the intermediate parts of the hepatic lobules, where they tended to be solitary. The total number of described cells slightly increased, compared to the previous group.

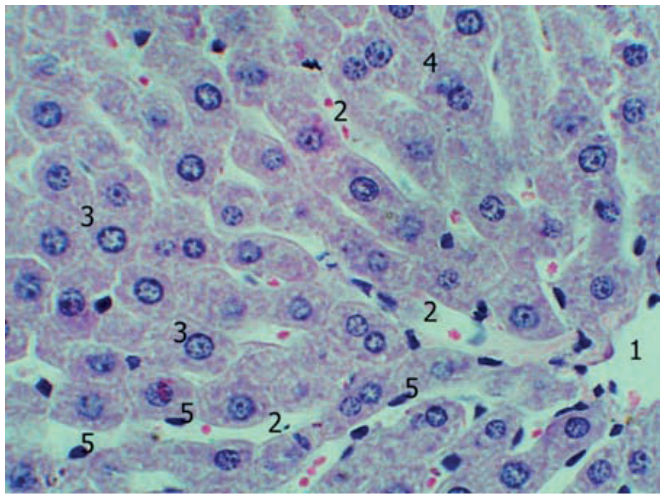

Fig. 1. The structure of the liver of intact albino rats. H&E stain. Objective lens: ×40 magnification, ocular lens: ×10 magnification.
1 – central vein; 2 – intralobular sinusoidal capillaries; 3 – mononuclear hepatocytes; 4 – binuclear hepatocytes; 5 – cells of sinusoid capillaries.

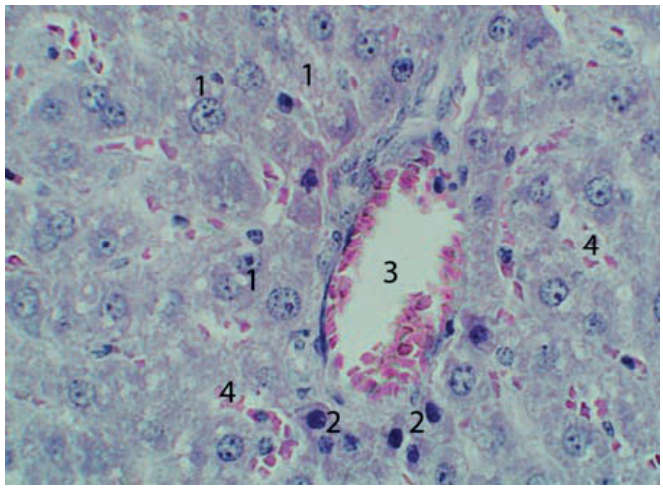

Fig. 2. The structure of the liver of albino rats (combined exposure to the food additives for 1 week). H&E stain. Objective lens: ×40 magnification, ocular lens: ×10 magnification.
1 – hepatocytes with dystrophic changes; 2 – "dark hepatocytes"; 3 – branch of the hepatic vein; 4 – hepatic sinusoids with blood cells

The liver cells containing a moderate amount of glycogen granules occupied mainly the intermediate parts of the hepatic lobules, their number did not significantly change compared to the control animals and the previous experimental group. The number of hepatocytes containing a significant amount of glycogen granules in the cytoplasm significantly decreased; similar to the previous groups they were located in the center of the hepatic lobules.

DISCUSSION

The findings of the study show that the complex of food additives (monosodium glutamate, sodium nitrite, Ponceau 4R) supplemented to standard ration of laboratory animals leads to noticeable morphological changes in the liver parenchyma.

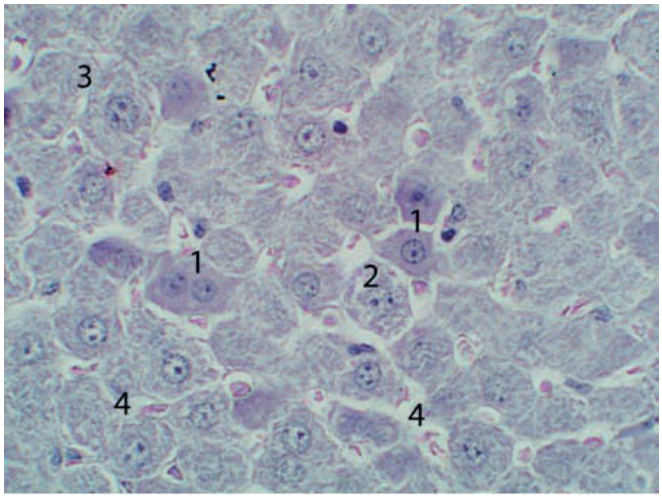

Fig. 3. The structure of the liver of albino rats (combined exposure to the food additives for 4 weeks). H&E stain. Objective lens: ×40 magnification, ocular lens: ×10 magnification.
1 – dark hepatocytes; 2 – hepatocyte with the phenomena of hydropic dystrophy; 3 – enlarged hepatocytes; 4 – hepatic sinusoids with blood cells.

The most significant changes should be considered a change in the metric characteristics of the liver cells, a decrease in their glycogen content and a progressive increase in the number of hepatocytes with alterations. At the same time, consumption of the complex of food additives supplemented into the ration for one week led to the phenomena of fatty degeneration, and a longer term of its consumption (for four weeks) showed that the number of liver cells with morphological features, that are characteristic of hydropic degeneration, noticeably increased. Such changes in the liver occur under the influence of a number of endogenous pathogenic factors, and in some cases may be reversible [11]. The occurrence of "dark hepatocytes" should be assigned to alterations of the liver cells, which, in our opinion, are cells with irreversible destructive changes.

An increase in the size of the liver cells revealed by morphometric studies can be both a consequence of dystrophic changes and a manifestation of the compensatory process associated with an increase in the functional activity of these cellular elements.

CONCLUSIONS

Consumption of the complex of food additives supplemented into the standard ration of laboratory animals for 4 weeks leads to a significant change in the dimensions of the liver cells, a decrease in their glycogen content, and a progressive increase in the number of hepatocytes with alterations.

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ORCID and contributionship:
Haliia M. Mustafina: 0000-0002-1596-2486[B-D]
Ivan I. Starchenko: 0000-0002-6666-1448[A,D]
Boris M. Fylenko: 0000-0002-8659-2267[E,F]
Volodymyr M. Koka: 0000-0003-2987-7255[A]
Valentyna V. Cherniak: 0000-0003-4594-565X[C]
Nataliia V. Roiko: 0000-0001-7478-0773[E,F]
Serhiy A. Proskurnya: 0000-0003-2675-9843[E,F]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Haliia M. Mustafina
Poltava State Medical University
23 Shevchenko street, 36011, Poltava, Ukraine
tel: +380503059214
e-mail: margocvt@gmail.com

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ORIGINAL ARTICLE

CHANGES IN IMMUNOLOGICAL INDICATORS UNDER THE INFLUENCE OF TREATMENT OF GENERALIZED PERIODONTITIS IN PATIENTS WITH MANIFESTATIONS OF PSYCHOEMOTIONAL STRESS

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Oksana V. Kononova, Tetiana O. Timokhina, Anatoliy V. Borysenko
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: The aim of investigation was to determine the effect of the proposed treatment of patients with generalized periodontitis and psychoemotional stress on changes in the immune system of patients.

Materials and methods: The clinical and laboratory investigations were conducted to revealed the effectiveness of the proposal complex of adrenoblockers in complex treatment of generalized periodontitis in 40 patients with psychoemotional stress. To assess the effectiveness of the treatment, the level of cortisol in saliva was determined. 40 patients with chronic course of generalized periodontitis I-II grade were divided into two subgroups: main and control. For the treatment of main subgroup patients used a modified enhanced complex of adrenoblockers to suppress the manifestations of psychoemotional stress.

Results: The effectiveness of usage of the proposed complex of adrenoblockers were revealed after treatment of main group patients. The complex of adrenoblockers lead to stabilization of the generalized periodontitis in patients with psychoemotional stress. Such combination of adrenoblockers oppresses main symptoms of psychoemotional stress in with generalized periodontitis as evidenced by the decrease of cortisol levels in the patients saliva.

Conclusions: As a result of researches the obtained data testify to achievement of stabilization of pathological process in a periodontium. All this together demonstrates the beneficial effect of the proposed complex of adrenoblockers on the dystrophic-inflammatory process in the periodontium. Decreased levels of cortisol in saliva indicate a decrease in the manifestations of psychoemotional stress in patients with generalized periodontitis.

KEY WORDS: generalized periodontitis, psychoemotional stress, cortisol levels in the saliva

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INTRODUCTION

Periodontitis is one of the manifestations of chronic inflammation. Many variable risk factors, such as smoking, contribute to increased systemic markers of inflammation through a variety of biological mechanisms [1-3]. The ability of psychological stress to promote the development and progression of the inflammatory response of the periodontal disease has been shown [4]. This interaction is most evident in the adaptive capacity of overload during psychological stress [5].

In the case of the development of chronic psychoemotional stress, there is an increase in circulating neutrophils and functional immunosuppression [6]. Given that chronic psychoemotional stress leads to dysregulation of the immune system with increased levels of cytokines and other pro-inflammatory mediators [7], this may be the cause or progression of periodontal disease under stress.

For the treatment of patients with generalized periodontitis in conditions of psycho-emotional stress was proposed a complex of medicines: Zoxone (0.002 g once a day), Nicergoline (0.005 g three times a day), Sibazone (0.005 g once a day) [8, 9]. Our previous experimental (biochemical and pathohistological) studies showed a positive influence of the adrenoblocker complex on the development of experimental periodontal lesions [10, 11].

THE AIM

The aim of investigation was to determine the effect of the proposed treatment of patients with generalized periodontitis and psychoemotional stress on changes in the immune system of patients.

MATERIALS AND METHODS

The clinical and laboratory investigations were conducted to revealed the effectiveness of the proposal complex of adrenoblockers in complex treatment of generalized periodontitis in 40 patients with psychoemotional stress. To assess the effectiveness of the treatment, the level of cortisol in saliva was determined. 40 patients with chronic course of generalized periodontitis I-II grade were divided into two subgroups: main and control.

In the complex treatment of patients of the main subgroup used a modified enhanced complex of adrenoblockers to suppress the manifestations of psychological stress.

For the treatment of main subgroup patients used a modified enhanced complex of adrenoblockers to suppress the manifestations of psychoemotional stress.

Patients in the control subgroup were treated similarly to patients in the main subgroup, but without the use of a modified complex of adrenoblockers. The level of psychological stress was assessed using questionnaires (DASS-21; Spielberger-Khanin) [12]. All patients underwent thorough scaling and root planning of the subgingival surfaces of the tooth roots, so-called SRP therapy. The presence of gingival inflammation was assessed using the Schiller-Pisarev test (1962) and the PMA index according to C. Parma (1961) [13]. The state of oral hygiene was assessed using the OHI-S index (1964) [14] and the O`Leary index [15], the level of gingival bleeding was assessed by the bleeding index PBI (HR Mühlemann, S. Son, 1971) [16]. In general, the condition of the periodontium was assessed using the periodontal index PI by A.L. Russel [16]. The diagnosis of periodontal disease was established according to the classification of NF Danilevsky [14].

Cortisol content was determined in the oral fluid samples. The patients were asked to abstain from taking meals and drinks to hours before taking saliva for test. The oral fluid was collected in the morning on an empty stomach in special Eppendorf tubes.

After the samples were transported to the laboratory, they were centrifuged at 3000 rotations per minute during 5 minutes. In case of necessity saliva samples could be kept at the temperature of 20 ° C. 20 mcl were taken from saliva and put into the sample's cup. Cortisol content was determined in nmol/L by means of RP Elecsys set (Roche Diagnostics, USA) in the analyzer Cobas e 411 [17, 18].

Venous blood (taken in the morning on an empty stomach) was used as the material to examine immunologic parameters. The blood was in the amount of 5 ml in Vacuum Tubes EDTA.K3 (whole blood). The blood was examined during 2 hours after it had been taken. Lymphocytes were immunophenotyped by means of immunofluorescence analysis using flow laser cytometer BD FACS Canto II (Becton Dickinson, USA).

The results obtained were statistically processed in the packet "STATISTICA 6.1" applying parametric and non-parametric methods [19].

RESULTS

In our previous investigation [20] was determine possible relations between the level of psychological stress in the organism of a patient with generalized periodontitis, and evaluate the parameters in the immune system cellular part. The study was conducted on the group of 40 patients of a young age. They were distributed into the following 4 subgroups. The first subgroup included 10 clinicallyhealthy individuals without stress signs and healthy periodontal tissues. The second subgroup included10 patients with generalized periodontitis and without stress manifestation. The third subgroup included 10 individuals with psychological stress signs without vivid lesions of the periodontal tissue. And the fourth subgroup included 10 patients suffering from generalized periodontitis and psychological stress signs [20].

The patients from the first (control) subgroup did not present stress signs, common somatic diseases, and had clinically healthy periodontal tissues. Cortisol content in the oral fluid was 14,67±2,71 nmol/L. This level was accepted as a norm in case ofcomparison with parameters of patients from other subgroups.

The second subgroup included patients suffering from I degree generalized chronic periodontitis. Thepatients from the second subgroup did not present psychoemotional stress signs either. Cortisol content in the oral fluid was 24,33±5,47 nmol/L.

The third subgroup included patients with psychoemotional stress signs and practically unnoticeable lesions of the periodontal tissues. Cortisol content in the oral fluid was 29,33±2,55 nmol/L.

The fourth subgroup included patients suffering from I degree generalized chronic periodontitis andwith psychoemotional stress signs. Cortisol content in the oral fluid was 41,67±5,67 nmol/L (Fig. 1).

The parameters of the lymphocyte subpopulation content CD3+, CD4+, CD8+ in patients from different subgroups (first and fourth) differs statistically. Detection of the parameters of the lymphocyte subpopulation content: CD3+, CD4+, CD8+ in this category of patients, demonstrated decrease of their absolute amount. For example, the ratio of CD4+/CD8+ lymphocytes in patients of the fourth subgroup was the lowest, which indicates a decrease in the immune resistance of the patient's organism.

In the complex treatment of patients of the main subgroup used a modified enhanced complex of adrenoblockers to suppress the manifestations of psychological stress. Patients in the control subgroup were treated similarly to patients in the main subgroup, but without the use of a modified complex of adrenoblockers.

After treatment, patients noted an improvement in the condition of periodontal tissues, reduction of gingival bleeding and pain in gums. The color of the gingiva was pale pink, it was dense without swelling. After the treatment there was an improvement in hygienic level in patients of both subgroups. The hygienic index OHI-S improved 3.28 times from 1.54±0.14 points to 0.47±0.06 points. In patients of the main subgroup with the first degree of generalized periodontitis, the hygiene index OHI-S decreased 3.18 times from 1.57±0.09 points to 0.44±0.05 points, in patients with the second degree of generalized periodontitis, it decreased by 3.49 times from 1.62±0.16 to 0.46±0.05 points (Table I). This indicated a good hygienic condition of the oral cavity. In patients of the control subgroup with stage I disease, the index OHI-S decreased by 2.32 times from 1.72±0.16 points to 0.78±0.08 points,

It is possible to estimate a hygienic condition of an oral cavity as a whole by means of the O`Leary index. After

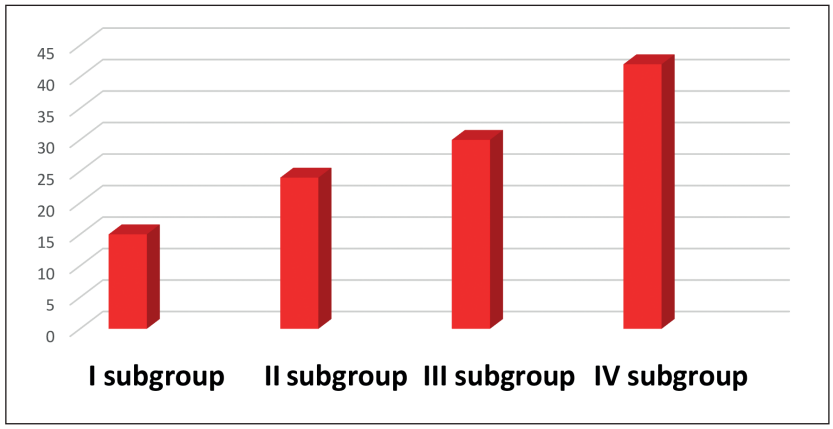

Fig. 1. Graphic representation of cortisol content in oral fluid (nmol/L)

Table I. Indicators of periodontal tissue status in patients with generalized periodontitis with manifestations of psychoemotional stress (M ± m)

Indicators	Timing of the survey	I grade		II grade	
		Study subgroups			
		Main	Control	Main	Control
OHI-S, points	Before treatment	1,57±0,09	1,72±0,16	1,62±0,16	1,82±0,17
	After treatment	0,44±0,05*	0,78±0,08	0,46±0,05*	0,78±0,08
O`Leary index (%)	Before treatment	68,5±5,4	66,4±5,3	75,4±5,8	74,8±5,7
	After treatment	10,4±0,92*	13,7±0,86	11,7±0,95*	15,7±1,2
PMA, %	Before treatment	62,5±2,5	64,1±2,3	65,2±2,5	69,3±2,8
	After treatment	8,2±0,72*	9,8±0,8	9,1±0,7*	12,3±0,9
BOP, points	Before treatment	2,58±0,18	2,51±0,19	2,75±0,18	2,76±0,18
	After treatment	0,54±0,05*	0,78±0,08	0,64±0,05*	0,89±0,08
PI, points	Before treatment	1,97±0,12	2,05±0,11	2,15±0,12	2,19±0,11
	After treatment	1,69±0,11	1,87±0,11	1,81±0,13	2,03±0,12

Note: * - the data are significantly ($p < 0.05$) different from the comparison subgroup data.

a comprehensive treatment, the value of the periodontal index O`Leary decreased, which indicated an improvement in the hygienic condition of the oral cavity. In patients of the main subgroup, the periodontal index O`Leary decreased 6.62 times from 70.67±5.7% to 10.67±0.96%. In the case of the first degree of the disease, the value of the O`Leary index decreased 6.45 times from 68.5±5.4% to 10.4±0.92%, in the case of the second degree - it decreased 6.46 times from 75.4±5.8% to 11.7±0.95% (Table 1). In the case of grade I disease in the control subgroup, the value of the periodontal index O`Leary was reduced 6.54 times from 66.4±5.3% to 13.7±0.86%, and in the case of grade II - it was reduced in 5.82 times from 74.8±5.7% to 15.7±1.2%.

Clinically, the improvement of the hygienic state of the oral cavity led to a decrease in the manifestations of inflammation in the gums, as evidenced by the Schiller-Pisarev test. It was negative in 42 (84.0%) patients of the main subgroup: in 26 out of 30 (86.67%) patients with grade I and in 16 out of 20 (80.00%) patients with grade II generalized periodontitis. In numerical terms, it decreased to 1.15±0.09 points (before treatment 2.38±0.25 points) - a decrease of 2.07 times.

The decrease of inflammation in the periodontium was evidenced by changes in the PMA index (Table 1). In patients with stage I generalized periodontitis, the value of the PMA index decreased to 8.2±0.72% (7.57 times); in patients with grade II PMA index decreased to 9.1±0.7% (7.25 times). After complex treatment, its values decreased in patients of the main subgroup in 7.70 times from 64.25±2.45% and amounted to 8.7±0.78%. In the control subgroup, the value of the PMA index decreased 6.44 times from 67.35±3.51% to 10.46±0.98%; in the first degree of the disease - up to 9.8±0.8%, in the second degree - up to 12.3±0.9%) in 6.54 times and 5.63 times, respectively).

After treatment, the state of oral hygiene improved and the manifestations of inflammation decreased. One of the main indicators of inflammation in the periodontium (gums) is the bleeding on probing index (BOP). Its value in patients of the main subgroup decreased from 2.66±0.19 points to 0.61±0.11 points (4.36 times): in patients with grade I BOP index decreased to 0.54±0.05 points (4.78 times), in the case of the second degree - up to 0.64±0.05 points (4.29 times). In patients of the control subgroup, the bleeding index BOP decreased from 2.76±0.18 points to 0.89±0.08 points (a decrease of 3.1 times).

The periodontal index (PI) can be used to assess the degree of periodontal damage due to the dystrophic-in-

flammatory process. The complex treatment of generalized periodontitis stabilizes the pathological process in the periodontium and the value of the periodontal index does not increase. In patients of the main subgroup, the value of the PI index, which before treatment was 2.06±0.13 after treatment was 1.88±0.11 points (a decrease of 1.16 times). In patients with grade I generalized periodontitis, the value of the PI index was 1.69±0.11 points (1.97±0.12 points before treatment, a decrease of 1.17 times). In patients with grade II, the PI index was 1.81±0.13 points (2.15±0.12 points before treatment, a decrease of 1.19 times). In the control group, the periodontal index of PI decreased from 2.16±0.14 to 1.98±0.11 (decrease by 1.09 times):

The clinical investigation results are presented in table. I.

After treatment, the content of cortisol in saliva decreased from 41,67±5,67 nmol/L to almost the normal level - 19,35±1,17 nmol/L (Fig. 2). This indicated a favorable effect during treatment of the adreoblockers complex on the state of psychoemotional stress in patients with generalized periodontitis.

The ratio of CD4+/CD8+ lymphocytes in patients after the treatment rose almost to the level of the norm – 1,84±0,18 (before treatment 1.71±0,17), which indicates at satisfactory level of their immune resistance of the patients organism.

DISCUSSIONS

In clinical investigations D.C. Peruzzo et al. (2007) reported that most studies found a positive association between psychoemotional stress, cortisol levels, and periodontal disease [21, 22]. Manifestations of stress lead to an increase in biomarkers, including cortisol, increased levels of proinflammatory cytokines and blood pressure [23, 24]. High levels of cortisol due to stress adversely affect periodontal tissues.

Our study revealed significant levels of cortisol in saliva in patients with generalized periodontitis and manifestations of psychoemotional stress. In this clinical situation, medical correction of the manifestations of psychoemotional stress is required in the complex treatment of patients with generalized periodontitis. The proposed complex of adrenoblockers can reduce the manifestations of psychoemotional stress in patients, as evidenced by the decrease in cortisol levels in the saliva of patients. After treatment the positive changes of the PMA, OHI-S, BOP, PI indices were revealed. Such combination of adrenoblockers oppresses main symptoms of psychoemotional stress in with generalized periodontitis as evidenced by the decrease of cortisol levels in the patients saliva.

CONCLUSIONS

Patients with chronic periodontitis who are under stress have elevated levels of IL-6 and IL-1β in the gingival fluid. Similarly, patients with aggressive forms of periodontitis have elevated serum levels of IL-6 and IL-1β. In contrast, another study failed to find any correlation between IL-6 levels. IL-1β and cortisol in the peripheral blood of patients with aggressive periodontitis.

The condition of the periodontium is associated with changes in the concentration of corticosteroids of the adrenal glands, which change the reactions of oral tissues to bacterial toxins. There is a correlation between psychoemotional stress, periodontal disease (chronic periodontitis) and cortisol levels in the oral fluid, which increases when patients have a state of psychological stress. High levels of cortisol due to stress have a negative effect on periodontal tissues.

As a result of researches the obtained data testify to achievement of stabilization of pathological process in a periodontium. All this together demonstrates the beneficial effect of the proposed complex of adrenoblockers on the dystrophic-inflammatory process in the periodontium. All this together demonstrates the beneficial effect of the proposed complex of adrenoblockers on the dystrophic-inflammatory process in the periodontium. Decreased levels of cortisol in saliva indicate a decrease in the manifestations of psychoemotional stress in patients with generalized periodontitis.

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ORCID and contributionship:
Oksana V. Kononova: 0000-0002-7099-5168 [A- F]
Tetiana O. Timokhina: 0000-0002-0220-0220 [B, C, E]
Anatoliy V.Borysenko 0000-0002-0220-0220 [B-D, F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Tetiana O. Timokhina
Bogomolets National Medical University
1 Zoologichna st., 03057 Kyiv, Ukraine
tel: +380961111122
e-mail: tanyatimokhina@gmail.com

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ORIGINAL ARTICLE

APPROPRIATE LEVELS OF PHYSICAL CAPACITIES DEVELOPMENT IN ADOLESCENTS WITH DIFFERENT STATE OF HEALTH

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Valery G. Arefiev[1], Viktor G. Riabchenko[2], Volodymyr M. Piddiachyi[3], Iryna V. Zenina[4], Mariia A. Redkina[1], Serhii M. Novik[5], Vasyl D. Hohots[5]

[1]NATIONAL PEDAGOGICAL DRAGOMANOV UNIVERSITY, KYIV, UKRAINE
[2]ACADEMY OF THE STATE PENITENTIARY SERVICE, CHERNIHIV, UKRAINE
[3]NATIONAL ACADEMY OF EDUCATIONAL SCIENCES OF UKRAINE, KYIV, UKRAINE
[4]NATIONAL TECHNICAL UNIVERSITY OF UKRAINE "IGOR SIKORSKY KYIV POLYTECHNIC INSTITUTE", KYIV, UKRAINE
[5]POLTAVA V.G. KOROLENKO NATIONAL PEDAGOGICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To justify the appropriate levels of physical capabilities development in 12-13-years-old girls with different levels of physical health.

Materials and methods: The research involved 101 12-13-years-old female high-school students. The choice of the female high-school students of this age is due to the greatest variability of their morphofunctional state. The physical health of the girls was assessed according to the method of H. L. Apanasenko. Physical fitness was assessed with the help of 13 motor tests that determine different aspects of girls' physical capabilities.

Results: Appropriate normative standards of physical fitness for 12-13-years-old girls with different levels of health and rational parameters of physical activity were determined. It was established that a rational option for planning physical training for 12-13-years-old girls is: 26 % of time should be spent on strength development; speed and strength qualities and agility – by 22 %; endurance – 18 % and speed qualities – 12 %.

Conclusions: It was found that the main principle of the implementation of developmental and health-oriented training sessions for physical education of adolescents is the differentiated use of loads and assessment of their physical fitness. Calculated with the help of correlation coefficients and regression equations, the appropriate values of physical development in 12-13-years-old girls with different levels of physical health make it possible, using appropriate exercises, to eliminate deviations in their health indicators.

KEY WORDS: physical capabilities, health, developmental and health-oriented training sessions, adolescents

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INTRODUCTION

The theory and methodology of physical education involves determining the rational set and scope of special tools and methods, the sequence of their application at different stages of the health process in accordance with the goals and objectives of exercise implementation for people of different ages, levels of health and fitness [1, 2].

Programs of physical education training sessions for those involved are drawn up for people of the same age, gender, level of physical well-being, etc. The following forms of organization are used: school lesson, sectional training sessions and classes in health groups. Programs are also drawn up for a specific person who is engaged, taking into account individual characteristics as part of fixed forms both in terms of individual tasks and unfixed, organized and independent ones [3, 4]. The problem of programming in physical education has been studied by many scientists [5-7]. According to the results of their development, it has been established that: programming is one of the options for normative predictive modelling, as the norm is the goal of physical education i. e. achievement of the optimal level of physical health; normative levels of physical well-being can be presented in the form of models, the characteristics of which constitute indicators of physical working capacity, physical development, physical fitness, etc.

The generalization of scientific and methodological sources on the programming of developmental and health-oriented training sessions shows that the effective solution of this problem depends on the research of the peculiarities of adaptive responses to the proposed load in homogeneous groups of involved people in terms of their physical health level (PHL). Such research is important for adolescent high-school students, because the heterochronic nature of biological development affects the variability of the manifestation of their physical capabilities [8-10].

THE AIM

The aim of this article is to justify the appropriate levels of physical capabilities development in 12-13-years-old girls with different levels of physical health.

Table I. Regression between the indicators of physical fitness (x) and physical health (y) of 12-13-years-old girls

Indicators	r	R	y	x
Below-average level of physical health				
Push-ups (x), times Strength index (y), %	0.719	x = (y-31.62/1.17) ± 1.97	43	10 ± 2
Standing long jump, (x), cm Robinson Index (y), c. u.	0.521	x = (y-90.21/0.007) ± 9.6	91	157 ± 10
Lifting the torso to the sitting position, (x), times Rufier index (y), c. u.	-0.581	x = (y-17.77/-0.23) ± 1.67	12	25 ± 2
60 m run (x), s Vital index (y), ml/kg	-0.362	x = (y-41.86/3.06) ± 0.40	44	9.6 ± 0.4
1500 m run (x), min, s Robinson Index (y), c. u.	0.637	x = (y-97.86/-0.01) ± 10	92	9 min 45 s ± 10 s
4 x 9 m shuttle run (x), s Vital index (y), ml/kg	-0.687	x = (y-14.2/2.51) ± 0.2	44	11 9 ± 0.2
Torso flexion (x), cm Kettle Index (y), g/cm	0.355	x = (y-1.03/0.02) ± 1.2	-0.9	7 ± 0.1
Average level of physical health				
Push-ups (x), times Strength index (y), %	-0.696	x = (y-8.59/0.03) ± 1.3	9	14 ± 1
Standing long jump, (x), cm Robinson Index (y), c. u.	0.699	x = (y-52.84/0.001) ± 5.4	53	160 ± 5
Lifting the torso to the sitting position, (x), times Rufier index (y), c. u.	0.688	x = (y-31.54/0.61) ± 2.1	50	30 ± 2
60 m run (x), s Vital index (y), ml/kg	-0.397	x = (y-86.33/-3.43) ± 0.2	53	9.7 ± 0.2
1500 m run (x), min, s Robinson Index (y), c. u.	0.773	x = (y-53.52/-0.001) ± 5.3	53	8 min 05 s ± 5 s
4 x 9 m shuttle run (x), s Vital index (y), ml/kg	-0.707	x = (y-84.28/-2.74) ± 0.2	53	11.4 ± 0.2
Torso flexion (x), cm Kettle Index (y), g/cm	0.398	x = (y-0.02/-0.007) ± 1.1	-0.05	10 ± 1

Legend: x – appropriate normative standard of physical fitness, y – indicator of physical health, r – correlation coefficient, R – regression equation

MATERIALS AND METHODS

The research involved 101 12-13-years-old female students. The choice of these high-school students is due to the greatest variability of their morphofunctional state among all female high-school students.

The determination of the level of physical health is based on the assessment of the strength and efficiency of aerobic energy supply. In physiology, this indicator integrally characterizes the state of respiratory, circulatory and metabolic functions, and in biology – the degree of stability of a living organism.

The method of quantitative rapid assessment of physical health, proposed by Professor H. L. Apanasenko, includes registration of the indicators of anthropometry (length and body weight), physiometry (vital capacity of the lungs and dynamometry), as well as analysis of the cardiovascular system. The criterion for reserving and economizing the functions of the cardiovascular system are the indicators of the Rufier index and the Robinson index. The Rufier index was defined as the sum of three heart rate values (at rest for 15 seconds, for the first 15 and last 15 seconds of the first minute of recovery after 30 squats for 45 seconds) multiplied by 4, minus 200 and divided by 4. The Robinson index was determined by the ratio of the product of heart rate and systolic arterial blood pressure to 100. The criterion for the reserve of external respiration is the indicator of the vital index, which was determined by the ratio of vital capacity of the lungs to body weight. The criterion of the effectiveness of the muscular system is the strength index, which was determined by the ratio of the dynamometry of the stronger hand to body weight. The correspondence of body weight to body length (the Kettle index) was also evaluated. All indicators were ranked. The total amount of points was determined after calculating each index, which was used to assess the level of physical health [11].

To determine the level of manifestation of the basic physical capabilities of girls, motor tests were selected, which determine different aspects of the physical capabilities of 12-13-years-old girls, and were tested for validity, reproducibility and objectivity. A total of 13 motor tests were used. The most significant of them, as well as the specific weight of individual capabilities in the overall structure

Table II. Factor structure of physical capabilities of 12-13-years-old girls

No.	Motor tests on physical fitness	Factors				
		1	2	3	4	5
1.	Physical working capacity (PWC150)	029	341	012	751	146
2.	Maximum oxygen consumption	-122	034	036	734	140
3.	The strength of the hand flexors	747	047	-102	067	109
4.	The strength of the shoulder flexors	759	200	-029	138	005
5.	The strength of the torso extensors	654	030	261	015	168
6.	Long standing jump	044	683	263	106	111
7.	High standing jump	078	800	-122	068	014
8.	Throw a stuffed ball weighing 1 kg	639	045	210	012	113
9.	Running for 5 seconds (maximum rate)	002	157	-156	-219	860
10.	Running 70% of the maximum rate	067	-318	284	634	479
11.	Spinal mobility	586	-074	-073	041	-073
12.	Time difference in 3 x 10 m and 30 m run	-057	-145	808	094	-242
13.	30 m run	-189	-336	-730	052	-418
	Specific weight of factors (%)	26.0	19.0	18.0	16.3	10.3

Note: lines 1-13 show only decimal places of correlation coefficients

of physical capabilities of girls were identified by factor analysis (principal components method).

The research methods included the analysis and generalization of data from special literature (30 sources on the topic of the article from the scientometric databases PubMed, Scopus, Web of Science Core Collection and others were used), anthropometry, physiometry, methods of mathematical statistics (correlation and factor analyses).

The procedure for organizing the research was previously agreed with the Committee on compliance with Academic Integrity and Ethics of the National Pedagogical Drahomanov University. Prior consent to participate in the research was obtained from all the participants.

RESULTS

The first task of this research was to determine the appropriate values of physical fitness indicators in the group of girls of interest. To do this, based on the correlation between motor test indicators and physical health indicators, regression equations were calculated separately for girls with below-average and average PHL (Table I).

In the equations, the variable "y" is replaced by the quantitative value of the corresponding physical health indicator (below-average or average) from the table of PHL assessment. These values in the equations are given in parentheses. The variable "x" indicates the indicators of physical fitness, the appropriate values of which are given with the standard error of the equation in the last column. The equations were calculated for adolescent girls with below-average and average PHL. This is due to the fact that no girls with higher PHL were identified within the research. The main difference between the developed normative standards and those existing in the "State Tests and Standards of Physical Fitness of the Population of Ukraine" is that they are designed for 12-13-years-old girls with low and below-average PHL.

Comparing the initial values of motor tests (for example, in girls with low PHL) with the appropriate values (for girls with below-average PHL) will help the teacher (instructor, parents) to identify weaknesses in children's physical health and to eliminate deficiencies by means of exercise.

In addition to assessing the level of physical fitness, we studied the factor structure of girls' physical capabilities in order to justify the rational planning of physical training of the studied contingent (Table II).

The elaboration of rational parameters of developmental and health-oriented training sessions for 12-13-years-old girls was carried out with the help of:

- reasonable ratio of physical activity of various orientations for a given contingent of high-school students;
- pulse regimes of physical activity, which determine the training effect for 12-13-years-old girls with different levels of their physical health.

The problems of reasonable ratio of physical activity of various orientations in the course of developmental and health-oriented training sessions of 12-13-years-old adolescent girls were solved with the help of factor analysis. The expediency of the latter for such problems has been proven repeatedly.

As a result of factoring the matrix of intercorrelations of 13 indicators of physical capabilities, 5 statistically independent factors were identified: muscle strength, speed and strength qualities, agility, endurance and speed. The total contribution of these factors to the generalized variance of the sample made 89.6 %.

The first factor i. e. muscle strength (26.0 % of the total variance of the sample) combined control tests for the dynamometry of the shoulder flexors, which is most closely related to this factor; for the dynamometry of the hand

flexors and extensors of the torso; throwing a stuffed ball weighing 1 kg over the head from a sitting position with legs apart.

The second factor i. e. speed and strength qualities (the contribution to the generalized variance of the sample is 19.0 %) is characterised by high factor weights represented by a high standing jump (the most informative indicator) and a long standing jump.

The *third factor* i. e. agility (specific weight of 18.0 %) is represented by the time difference in 3 × 10 m and 30 m run.

The *fourth factor* i. e. endurance (contribution to the generalized variance of the sample of 16.3 %) has high correlations with relative working capacity (PWC_{150} test), maximal oxygen consumption and running results at a rate of 70 % of maximal. Physical working capacity according to the PWC_{150} test is the most informative indicator in the fourth factor.

The *fifth factor* i. e. speed accounts for 10.3 % of the generalized variance of the sample. It combined the rate of movements (run in place for 5 seconds) and the result in running 30 m. The first indicator has the largest factor weight here.

Thus, among the studied physical capabilities of 12-13-years-old girls, the most statistically informative are: to assess muscle strength – dynamometry of the shoulder flexors; speed and strength qualities – standing high jump; agility – time difference in 3 × 10 m and 30 m run; endurance – physical working capacity (according to the PWC_{150} test), speed – run in place for 5 seconds at maximum speed. These tests can be used as objective criteria for qualitative changes in the physical fitness of 12-13-years-old girls in the process of experimental research.

Hypothetically, a rational option for planning the physical training of 12-13-years-old girls is when 29 % of the total time planned for physical training is devoted to the development of muscular strength, for example, for a month or six months; to the development of speed and strength qualities and agility – by 22 %, to endurance – 18 %, to speed – 11 %.

For developmental and health-oriented training sessions, in addition to knowledge of the reasonable ratio of motor activity of various orientations, it is important to choose pulse modes in the process of these loads, which determine the training (health) and effective impact. In the special literature, such modes are developed according to special equations for persons from 20 years of age. Therefore, the calculation of effective working heart rate for primary school students was carried out according to the equations adequate for this age, according to which:

$\text{Heart rate}_{max} = 208 - (0.7 \times \text{age})$,

$\text{Heart rate}_{training}$ (bottom level) $= 0.65 \times \text{heart rate}_{max}$,

$\text{Heart rate}_{training}$ (top level) $= 0.75 \times \text{heart rate}_{max}$,

The choice of these equations for teenage girls is explained by the fact that physical education of schoolchildren, especially during puberty, prohibites the use of extreme and almost extreme loads. Therefore, the pulse range, which determines the health effects on the body, is 130-150 beats / min^{-1}.

DISCUSSION

Today, the amount of scientific information that characterizes the relationship between the health of schoolchildren, students and their physical activity has increased significantly [12-14]. However, only a small part of it is reflected in the theory and methods of physical education for the purpose of its practical application. Most authors consider this problem without regard to gender, physical development and puberty. There are also gaps in the study of the peculiarities of adaptation of schoolchildren and students to physical activity. There is an ongoing discussion about the existence of phases in the period of formation of the high-school student, during which his / her certain capabilities are most (or least) influenced by external stimuli [15, 16].

Motor activity can be considered from the standpoint of biomechanics and physiology. Motor activity in biomechanics is characterized by such indicators as strength, speed, acceleration, inertia, mechanical force or mechanical work. Physiology analyses motor activity using metabolic indicators such as oxygen consumption, metabolic energy (e. g., in kilocalories or kilojoules), etc. [17, 18].

In 2004, the World Health Assembly adopted the WHO Global Strategy on Nutrition, Physical Activity and Health, which emphasized that motor activity is a key tool for improving a person's physical and mental health. Each individual is recommended to ensure an adequate level of motor activity [19].

The mechanisms of the relationship between motor activity and functional capabilities have been and are the subject of research for many scientists [20-22]. The physiological nature of the positive effects of motor activity on the human body is due to the complex interdependent relationships between the muscular system and internal organs. These relationships are explained by the presence of two types of reflex effects: from the internal organs to the muscles i. e. viscero-motor reflexes and from the muscles to the internal organs i. e. motor-visceral reflexes. According to the needs of the organism in the activity of vegetative systems (respiration, blood circulation, etc.) motor-visceral reflexes are directed (by changing the metabolism) to change the functional state of these systems. Thus, along with the contraction of muscles that occur when the motor zone of the cerebral cortex is excited, nerves are stimulated, which increase blood circulation in working muscles [23]. In the case of insufficient human motor activity (hypodynamia), as well as excessive nervous and emotional stress, according to the experts [24], the functional state of the CNS as a mediator between muscles and internal organs is broken down. This causes a violation of the functional state of certain organs and systems of the body and the emergence of diseases. According to modern research [11], the deficit of muscular activity results in the following consequences: only 1.3 % of school-age children, according to an express assessment of the level of somatic health by Professor H. L. Apanasenko, can be considered healthy; 22.6 % are in the "risk group"; "sick" – 76.0 % of children. More than half of children have low levels of cardiovas-

cular and respiratory systems [25, 26]. The consequences of hypodynamics of high-schools students are disorders of the cardiovascular and respiratory systems, obesity, posture disorders, endocrine and mental diseases. Current research shows that only 15 % of high school graduates are healthy, the remaining 85 % have some deviation from the normative standard [15, 23].

How do the levels of physical fitness assessed by physical tests interact with the levels of physical health? To what extent are the former a reflection of health and can be an indicator of it? And if we assume that there is a statistical relationship between them, then the question arises – what quantity amount for each component of physical fitness will be the normative standard that corresponds to the average (and above) level of physical health? The latter is important for physical education, and therefore for everyone who is engaged in organized or independent physical exercises for health purposes. The results of the research of these issues on the example of 12-13-years-old girls are presented in this article. The precondition for asking these questions was the following judgment: the levels of development of certain motor qualities achieved by a particular individual are a consequence of the state of the individual body systems and, ultimately, other things being equal, determine the level of his / her physical health.

It should be noted that no research to assess the interaction of motor normative standards to determine physical fitness with the level of physical health of high-school students has been conducted, and therefore the answers to these questions are of both theoretical and practical interest. The obtained results expand and deepen the results of research by other authors [27-30].

CONCLUSIONS

1. It was found that the main principle of the implementation of developmental and health-oriented training sessions for physical education of adolescents is the differentiated use of loads and assessment of their physical fitness.
2. Calculated with the help of correlation coefficients and regression equations, the appropriate values of physical development in 12-13-years-old girls with different levels of physical health make it possible, using appropriate exercises, to eliminate deviations in their health indicators.
3. A rational option for planning developmental and health-oriented training sessions for 12-13-years-old girls is one in which 26 % of time should be spent on strength development; speed and strength qualities and agility – by 22 %; endurance – 18 % and speed qualities – 12 %. The developmental and health pulse regime for girls with low and below average levels of physical health is 163-176 beats / min, and for girls with average level of health – 167-190 beats / min. There were no girls with higher levels of health in this research.

Prospects for further research are to substantiate the appropriate levels of development of physical capabilities of adolescent boys with different levels of health.

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ORCID and contributionship:
Valery G. Arefiev: 0000-0002-1531-3523[A]
Viktor G. Riabchenko: 0000-0002-5630-9459[C]
Volodymyr M. Piddiachyi: 0000-0002-8596-6749[F]
Iryna V. Zenina: 0000-0001-5917-3203[D]
Mariia A. Redkina: 0000-0002-2474-1001[B]
Serhii M. Novik: 0000-0001-8718-6271[E]
Vasyl D. Hohots: 0000-0002-5915-1095[E]

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CORRESPONDING AUTHOR
Valery G. Arefiev
National Pedagogical Dragomanov University
9 Pirogova st., 02000 Kyiv, Ukraine
tel: +380978281281
e-mail: Physical_education_2020@ukr.net

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ORIGINAL ARTICLE

COMPLICATIONS AND EVALUATION OF QUALITY OF LIFE IN PATIENTS AFTER LESS-INVASIVE TREATMENT OF VARICOSE VEINS OF THE LOWER EXTREMITIES

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Vitalii I. Liakhovskyi, Arkhyp V. Sydorenko, Roman M. Riabushko
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To analyze the occurrence of complications and evaluate the quality of life in patients who got less-invasive treatment methods using endovenous laser ablation of varicose veins of the lower extremities in the early and late postoperative periods.

Materials and methods: The study was conducted with the participation of 100 patients treated in 2019-2020 by one team of surgeons for varicose veins of the lower extremities with symptoms of chronic venous insufficiency C_2-C_4 (CEAP classification). Depending on the performance of endovenous surgical interventions, all patients were divided into two study groups.

Results: In assessing the quality of life associated with health, according to the CIVIQ 2 questionnaire, it was found that in the presence of varicose veins in the superficial veins of the lower extremities, indicators decrease both in general and on all studied scales (pain, physical, psychological and social). However, when using endovenous laser ablation without miniphlebectomy, after 6 months of observation, recurrence of varicose veins of the lower extremities was noted, which was not observed in patients of the first group.

Conclusions: The use of less-invasive interventions with ultrasound guidance positively affects patients' quality of life with varicose veins of the lower extremities, both in the early and prolonged postoperative periods.

KEY WORDS: varicose veins, less-invasive treatment, complications, assessment of the quality of life of patients

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INTRODUCTION

Varicose veins of the lower extremities occur in 20-60% of the population of developed countries [1, 2]. Currently, there is a tendency to increase by 60-76% incidence in people of working age, and the first signs of pathological reflux in the veins of the lower extremities are found even in 1015% of students 1213 years [3, 4].

In case of untimely and insufficient treatment of varicose veins of the lower extremities, patients may experience trophic and thrombotic complications, which often lead to disability and even death [1, 5]. Treatment of this pathology is mostly performed surgically and is quite expensive [6].

Nowadays, the surgical correction of blood flow through subcutaneous veins is mainly performed using modern methods of endovenous thermal ablation or glueing in combination with less-invasive and sclerosing interventions [7, 8]. The development and improvement of new approaches to thermal and sclerosing ablation are aimed at achieving irreversible occlusion of veins while minimizing the trauma of such operations [9]. To improve the results of treatment of varicose veins, it is necessary to use ultrasound in the preoperative period to identify the cause of pathological reflux and blood flow in the veins of the lower extremities and under ultrasound accompanied by surgical correction [10].

The main goal of modern endovenous surgery is to choose the optimal methods of intervention and energy modes of radiation that would be effective for irreversible occlusion of veins with minimal damage to blood vessels and surrounding tissues. Therefore, to improve the results of treatment of varicose veins of the lower extremities, it is necessary to identify complications after surgery, which can occur in both early and prolonged postoperative periods, analyze them and assess their impact on the quality of life of patients [11, 12].

Thus, the great prevalence of this pathology, as well as the presence of various methods of treatment and the occurrence of severe complications of its course, refers to varicose veins of the lower extremities to topical medical and social problems.

THE AIM

To analyze the rate of complications and assess the quality of life in patients with minimally less-invasive treatments using endovenous laser ablation of varicose veins of the lower extremities in the early and prolonged postoperative periods.

MATERIALS AND METHODS

The study was conducted with the participation of 100 patients who got surgical treatment in 2019-2020 by one team of surgeons in the Department of Vascular Surgery

CE "Poltava Regional Clinical Hospital M.V. Sklifosovsky PRC" on varicose veins of the lower extremities with the sings of chronic venous insufficiency C2-C4 (CEAP classification). Patients were selected by random sampling. All of them performed endovascular surgery using a laser coagulator "Lika-surgeon" ("Fotonica-plus", Ukraine) with a wavelength of 1470nm, power up to 10W, a linear energy density of up to 100J/cm and radial fibre. During the preoperative period, patients had clinical and laboratory tests and ultrasound colour scanning (VDUS) of the lower extremities using a machine "Philips" linear multifrequency sensor 7MHz.

Depending on the additional removal of varicose veins from minimal accesses (punctures), all patients were divided into two study groups. The first group included 50 people (38 (76.0%) women and 12 (24.0%) men, whose average age was 48.4 ± 4.82 years). Patients in this group had ultrasound-controlled and tumescent anaesthesia with Klein's solution got endovenous laser ablation (EVLA) of the trunk of the great saphenous vein and insufficient perforating veins on the leg with the removal of varicose tributaries by mini-accesses. The second group of the study also included 50 patients (40 (80.0%) women and 10 (20.0%) men, mean age - 47.4 ± 5.07 years), who underwent EVLA of the trunk of the great saphenous vein, insufficient perforating veins on the shin and varicose tributaries had ultrasound-controlled and tumescent anaesthesia with Klein's solution, but without mini-phlebectomy. In the postoperative period, patients received a prophylactic dose of low molecular weight heparins subcutaneously and, if necessary, painkillers.

Follow-up examinations of patients in both groups were performed during the first 7 days and 6 months after surgery, during which lower extremity ultrasound was performed, pain intensity was determined, and quality of life surveys were conducted based on the Chronic Venous Insufficiency Questionnaire 2 (CIVIQ 2) taking into score physical (9 questions), psychological (4 questions), social (3 questions) and pain (4 questions) factors [13]. Recovery was considered to be an irreversible narrowing of the vein diameter to 1.5-3.0mm or total occlusion of the operated vein or hemodynamically insignificant (up to 0.3s) pathological reflux without clinical manifestations. Then statistical processing of the received data is performing.

RESULTS

According to the survey to assess the quality of life of patients directly before surgery for varicose veins of the lower extremities, the following data were obtained. The average duration of surgery in patients of the first group was 56.3 ± 6.47, and in patients of the second group - 78.6 ± 5.82 minutes ($p < 0.05$).

According to the corresponding scale of the CIVIQ 2 questionnaire on the state of quality of life, which is related to health, patients in the first group average: pain - 4.7 ± 0.43, physical - 5.9 ± 0.52, psychological - 24.1 ± 1.24 and social - 5.2 ± 0.38 points. The total score averaged 39.9 ± 0.88 points. The same indicators of quality of life in patients of the second group, respectively, averaged: 4.3 ± 0.36, 6.2 ± 0.49, 23.5 ± 1.09, 5.4 ± 0.32 points, with a total assessment - 39.4 ± 0.79 points. No significant difference in these indicators of patients of the first and second groups was found ($p > 0.05$). Thus, patients in both study groups were comparable in their assessment of the quality of life associated with their health.

According to the results of the analysis in the early postoperative period, pain was observed in all patients of both groups. However, in the first group it lasted on average 3.2 ± 1.72, and in the second group - 1.7 ± 1.23 days ($p < 0.05$). Its intensity on the first day according to the pain scale of the CIVIQ 2 questionnaire in patients of the first group averaged 6.8 ± 2.01 and in the second - 5.7 ± 1.84 points ($p > 0.05$).

At day 7, patients in the first group averaged 5.9 ± 1.26 points, and in patients of the second group, it was significantly lower and averaged 4.7 ± 0.56 ($p < 0.05$). Indicators of other scales of the CIVIQ 2 quality of life questionnaire on day 7 of the study did not differ significantly between patients in both study groups. Thus, in patients of the first group averaged: physical - 6.2 ± 0.48, psychological - 24.7 ± 2.15 and social - 6.7 ± 0.53 points, and patients in the second group - 6, 5 ± 0.37, 24.1 ± 1.54, 6.6 ± 0.42 points, respectively. The total average total assessment of the quality of life in persons of the first group was 43.5 ± 1.92, and in patients of the second group - 41.9 ± 2.14 points. There was no clear difference in these indicators between patients in both study groups ($p > 0.05$).

During this period of monitoring, the following complications of surgical interventions were identified. Clinical manifestations of acute subcutaneous phlebitis occurred in 3 (6.0%) patients in the first and 1 (2.0%) - in the second group. Subcutaneous hematomas of various sizes were observed in 23 (46.0%) persons in the first group and 11 (22.0%) of the second group, while paresthesias occurred in 4 (8.0%) patients in the first group and did not occur in patients of the second group.

Six months after surgery, patients in the first group rated the pain intensity on an average scale of 3.4 ± 0.95 points, while patients in the second group of the study rated the same average of 1.6 ± 0.68 points ($p < 0.05$). Patients of the first group according to the CIVIQ 2 questionnaire assessed the quality of life associated with health and on average it was on the scales: physical - 4.8 ± 0.46, psychological - 13.7 ± 0.39 and social - 7.3 ± 0.62 points. The total score averaged 29.2 ± 0.59 points. Patients of the second group assessed their quality of life the same method. Their mean scores were as follows: 3.9 ± 0.28, 11.8 ± 0.92, 7.8 ± 0.44, and the total average score was 25.1 ± 0.47 points. The level of difference in these indicators between the groups was not significant ($p > 0.05$). In general, the quality of life was assessed as: "satisfactory" - 3 (6.0%), good - 25 (50.0%), excellent - 22 (42%) patients of the first group, and in the second group - 5 (10, 0%), 16 (32.0%), 29 (58.0%), accordingly.

Of the complications of the prolonged postoperative period, only the presence of recurrence of varicose veins of the

superficial extremities in 5 (10.0%) patients of the second group, and in patients of the first group such complications were not observed. Subcutaneous phlebitis in patients of both groups was not observed. According to the VDUS, complete recovery occurred in 46 (92.0%) patients of the first and 44 (88.0%) - of the second study groups.

DISCUSSION

Therefore, the study shows that before surgery it is necessary to conduct an ultrasound examination of the lower extremities and pelvic veins to verify the cause of varicose disease and choose the correct surgical treatment tactics, which reduces the recurrence of varicose veins in the prolonged postoperative period. These data coincide entirely with the opinion of some authors [10]. Also, our opinion coincided with the data of other researchers who recommended improving the results of treating varicose veins of the lower extremities to conduct clinical examinations using ultrasound not only in early but also in prolonged postoperative periods [11, 12]. Thus, according to the gotten data, during the examinations after 6 months, we took on attention to the complications that occur after endovascular surgery, analyzed them, and evaluate their impact on patients' quality of life.

Also, it was found that in patients who had thermal laser ablation with mini-phlebectomy, the average duration of surgery was significantly longer than in the group of patients who had just endovascular surgery without additional incisions.

In the analysis of the obtained statistics of quality assessment of life according to the CIVIQ 2 questionnaire in the early postoperative period, was found that in most cases the average pain, physical, psychological and social scales in patients of the first group were slightly higher than in the second group. In the late postoperative period after 6 months of the study, they almost levelled off and did not differ much. However, in 5 (10.0%) patients of the second group the recurrence of varicose veins of the lower extremities was noted, and in patients of the first group, such a complication was not observed at all. Moreover, according to ultrasound scanning, complete recovery occurred in 46 (92.0%) patients in the first and 44 (88.0%) - the second groups of the study. These data coincide with the data of other authors in their publications [9].

CONCLUSIONS

Less-invasive treatment for varicose veins of the lower extremities with the use of EVLA ultrasound-controlled is easily tolerated by patients, and the pain is most pronounced on the first day after surgery and decreases within the first 7 days.

In the prolonged postoperative period, during the first 6 months, the assessment of the quality of life on the pain, physical and social, and especially - by psychological scales increases. However, when using EVLA without mini-phlebectomy, after 6 months of monitoring there was a recurrence of varicose veins of the lower extremities, which was not observed in patients of the first group.

Thus, the use of less-invasive ultrasound-controlled interventions positively affects patients' quality of life with varicose veins of the lower extremities in both early and prolonged postoperative periods.

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ORCID and contributionship:
Vitalii I. Liakhovskyi: 0000-0003-1551-4891 [B-F]
Roman M. Riabushko: 0000-0002-5073-9095 [B,E,F]
Arkhyp V Sydorenko: 0000-0003-4152-513X [A,B,D,E]

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CORRESPONDING AUTHOR
Arkhyp V. Sydorenko
Poltava State Medical University
23 Shevchenka St., 36011 Poltava, Ukraina
tel: +38 (0532) 561240
e-mail: arkhyp.sydorenko@gmail.com

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ORIGINAL ARTICLE

EXPERIMENTAL ANALYSIS OF WAYS OF VIRAL INFECTIONS INTO THE HUMAN BODY

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Volodymyr Hryn[1], Yurij Kostylenko[1], Viktoriia Pinchuk[1], Valeriy Zhamardiy[1], Viktoriia Donchenko[1], Olha Honchar[1], Oksana Hordiienko[2]

[1] POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

[2] NATIONAL UNIVERSITY «YURI KONDRATYUK POLTAVA POLYTECHNIC», POLTAVA, UKRAINE

ABSTRACT

The aim: The aim of the study is to experimentally test the process of viral infection and determine the ways of its penetration into the human body.

Materials and methods: This experimental analysis is based on systematic research, published peer-reviewed articles, books, textbooks, monographs. It should also be noted that in order to identify some immunocompetent lymph node cells and the ability to visualize certain sites in the lymphoid nodes of Peyer's patches, where the initial processes are presented below, we resorted to sampling anatomical material. The study involved 10 adult albino rats weighing 200.0 ± 20.0 g. The search period covered the period from 2010 to 2021, but the experimental analysis contains some valuable data from previous years, as these literature sources have significant scientific value.

Results: According to immunohistochemical analysis of the epithelium associated with the dome of the lymph nodes of the small intestine of white rats, the bulk was B-lymphocytes (about 47%) and T-lymphocytes (about 35%), while plasma cells, macrophages and dendritic cells accounted for approximately 5% for each of them.

Conclusions: Process of development of viral infection can be represented in the form of the following targeted steps: 1) massive invasion of viruses into the body; 2) the pathway of viruses to the intended target (target cells) is carried out by the blood flow; 3) achieving the target by viruses and their penetration into target cells. In the pathogenesis of viral diseases, the role is played by the preparedness of the particular body, which directly depends on the functional state of its immune system, which determines the possibility, severity and outcome of the disease.

KEY WORDS: virus, Coronavirus infection, COVID-19, entrance gate of infection, immune system

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INTRODUCTION

The paper has been written in response to the ongoing spread of the coronavirus infectious disease (COVID-19) pandemic caused by the novel coronavirus (SARS-CoV-2), causing severe acute respiratory syndrome [1, 2]. Considering that the questions raised in the present paper are common to all types of human viral infections, we can limit ourselves only to a general characteristic of their pathogens.

Coronaviruses (Coronaviridae, CoVs) are a large family of RNA viruses that can cause mild to severe acute respiratory infections in humans such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (Severe Acute Respiratory Syndrome, SARS). Coronaviruses are capable of infecting the respiratory, gastrointestinal tract, liver and central nervous system of humans and many other species of vertebrates, including domestic animals and livestock, birds, bats, etc. [3]. Before the epidemic outbreaks of SARS in 2002 and MERS in 2012, coronaviruses were not considered highly pathogenic for humans, since viruses previously circulating in the human population in immunocompetent individuals mainly caused only mild forms of the disease.

THE AIM

The aim of the study is to experimentally test the process of viral infection and determine the ways of its penetration into the human body.

MATERIALS AND METHODS

This experimental analysis is based on systematic research, published peer-reviewed articles, books, textbooks, monographs. For the purposes of this experimental analysis, a literature search was conducted (to study the development process and identify possible ways of viral infection) using the Internet, domestic and foreign literature, scientific and electronic library of Poltava State Medical University by the following keywords: "virus", "Coronavirus" infection "," COVID-19 "," entrance gate of infection "," mucociliary barrier "," mucous membrane "," follicle-associated epithelium "," immune system ". The search period covered the period from 2010 to 2021, but the experimental analysis contains some valuable data from previous years, as these literature sources have significant scientific value.

The following inclusion and exclusion criteria have been used:
- inclusion criteria: original articles published in journals and conference proceedings, books, study guides, monographs; language of publication: Ukrainian, Russian, English;
- exclusion criteria: reviews, case studies, editorials, letters, etc., not peer-reviewed; language of publication: others.

Also, it should be noted that in order to identify some immunocompetent cells of lymphoid nodules and the possibility of visualizing certain places in the lymphoid nodules of Peyer's patches, where the initial processes presented below occur, we resorted to sampling anatomical material. 10 mature albino male rats weighted 200,0±20,0 g were involved into the study. Before the experiment, all animals were kept in standard conditions of the experimental biological clinic (vivarium) at the Poltava State Medical University in compliance with the regulations on keeping experimental animals, adopted by the European Parliament and Council Directive (2010/63/EU), the Order of the Ministry of Education and Science, Youth and Sports of Ukraine as of 01.03.2012, No. 249 "On approval of the procedure for conducting tests, experiments on animals by research institutions" and "General ethical principles of experiments on animals", adopted by the V National Congress on Bioethics (Kiev, 2013), (Minutes No. 178 as of 24.12.2019 of meeting the Commission on Biomedical Ethics at Poltava State Medical University).

After vivisection made by thiopental anesthesia overdose (75 mg/kg of animal body weight intramuscularly in the upper third of the thigh of the hind paw) in compliance with the requirements for dissection of the abdominal cavity, the entire complex of the gastrointestinal tract was removed, which was fixed in 10% formalin solution for two days. Following a week (after pre-washing in running water) the murine gastrointestinal tract was examined and sections of the small intestine, containing Peyer's patches, were selectively excised. The set of Peyer's patches were clearly visualized along its length beneath the serous membrane (on the side opposite to the mesentery attachment site) in the form of whitish spots, different in shape and size.

The specimens, after washing from formalin and dehydration in alcohol of increasing concentration, were embedded into paraffin blocks, from which serial sections of 4 μm thick (Microm HM 325) were obtained in the cross-section of the small intestine and, subsequently, stained with hematoxylin-eosin. Their study and documentation was carried out using the "Konus" light microscope equipped with the Sigeta DCM-900 9.0MP digital microphoto attachment and the Biorex 3 program (serial number 5604) adapted for these studies. The morphometric characteristics of the tissue structures of the corresponding specimens were obtained using a system of visual analysis of histological specimens, as well as using the Sigeta X 1 mm/100 Div.x0.01mm stage micrometer, the scale of which (equal to 1 mm, where a small step corresponds to 10 μm) was applied to the corresponding microimage obtained in the same magnification.

The Ethics Commission of Poltava State Medical University has no comments on the methods used in this study.

RESULTS

Viruses are known to be non-cellular life forms with their own genome, but not capable of self-reproduction. Therefore, they are able to carry out the process of reproduction of their own kind in generations only due to the synthetic apparatus of cells of all, without exception, plant and animal organisms (including bacteria). According to their structural organization, they are divided into simple and complex forms. The first consists of an outer protein coating called the capsid, which protects the enclosing RNA or DNA nucleic acids. Coronaviruses are single-stranded RNA-containing forms. Such a viral particle is clearly visualized only in an electron microscope. In contrast to them, complex viruses, being larger (some of them are distinguishable in a light microscope), have a complex layer-by-layer structure of the outer shell, a supercapsid, which contains carbohydrates (glycoproteins) and lipids (lipoproteins) in combination with proteins, which have separate antigenic properties [4-6].

But in terms of understanding the development of viral infection, it is more important to know that viruses in general are characterized by two forms of existence in the host body: extracellular, or dormant, and intracellular, multiplying (reproductive). The synonyms of the first form are «viral particle», «viral corpuscle», «virion», and the second – «virus-cell complex» [7, 8].

The intracellular form appears as a result of the penetration of virions into the target cell and reproduction of viruses in it. In this process, the following stages are distinguished: adsorption, penetration of virions into the cell, transcription, translation, replication, assembly of viral particles and release of viral particles from the cell [9].

Most of all we are interested in the first, initial stage. It is believed that at the very beginning, the adsorption process is facilitated by the forces of electrostatic interaction of positively and negatively charged groupings located on the surface of the virus on the one hand, and the cell surface, on the other hand. This nonspecific stage of adsorption is followed by a highly specific one, when the proteins of the surface of the virus combine with matching receptors on the plasma membrane of the cell. It is this local site of interaction of the virus with the cell surface that is currently understood as the gateway to infection [10, 11]. This view is supported by the findings of morphological studies, mainly of cell cultures infected with the virus [12]. However, it should be noted that cells are infected by the nutrient medium in which they are grown, that is, this model is expressed by a simple formula: virus ⟶ nutrient medium ⟶ cell.

This, extremely simplified, model, in principle, can be likened to an animal organism, in the understanding that enclosed diverse numerous cellular structures receive nutrition from its internal (humoral) environment, which is understood as a complex system of recirculating fluids,

Table I. The main immunocompetent cells in group lymphoid nodules small intestine of white rats is normal

Cellular elements	Localization area	n=10
B-lymphocytes	B-zone	40,0-45,0%
	T-zone	<1%
	Dome	before 2,0%
T- lymphocytes	B-zone	<1%
	T-zone	27,6-30,7%
	Dome	3,7-4,1%
Plasmocytes	B-zone	<1%
	T-zone	1,0-1,6%
	Dome	2,8-3,2%
Macrophages	B-zone	1,4-2,2%
	T-zone	1,1-1,8%
	Dome	1,3-1,9%
Dendritic cells	B-zone	5-6,7%
Phagocytic enterocytes	Epithelium	–

Fig. 1. Microscopic structure of lymphoid-associated epithelium of lymphoid nodule of Peyer's patch of small intestine of rat. Paraffin sections; H&E stain; Lens: 100×magnification (author's figure).
ln – lymphoid nodule; pa – parietal area of the small intestine. The border of the intraepithelial lymphoid cell is indicated by a black outline, the presumed M-cell is colored in red.

namely, blood, intercellular (interstitial) fluid, lymph, as well as cerebrospinal and peritoneal fluids. Naturally, the infection of these cellular structures with viruses can be carried out only from the abovementioned humoral environment, where they should not normally be, but they can appear in it, having entered during infection from the external environment. Here, just the key question that interests us arises: how can pathogenic microorganisms enter the internal environment of the body from the outside, if it is known that on their way they will inevitably encounter an insurmountable obstacle in the form of the so-called morphophysiological barrier of the mucous membranes of hollow organs.

Among them, the most important place in this regard belongs to the intestinal tract and the tracheobronchial tree, the mucous membranes of which differ from each other by the covering epithelium, bordering on the external environment, which constitutes the structural base of the morphophysiological barriers. If in the intestinal mucosa it is represented by the polarized monolayer of enterocytes of different specialization, closely conjoined and interconnected by means of intercellular contacts, among which

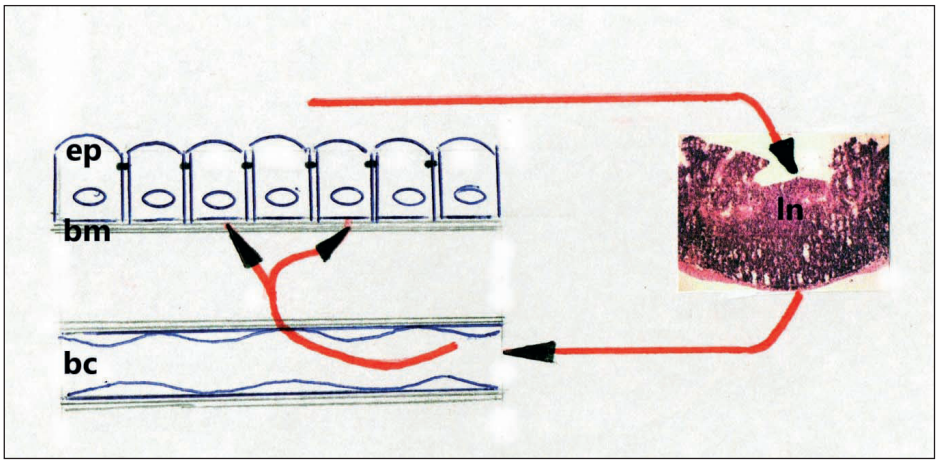

Fig. 2. Scheme of the pathways of viral infection of the epithelium of the mucous membranes (author's figure).
ep – epithelium (target cells); bm – basal membrane; ln – lymphoid nodule; bc – blood capillary. Red lines show the paths of movement of viruses.

absorbing cells predominate, then in the tracheobronchial tree there is pseudostratified (a kind of simple) epithelium with more complex structure, with a quantitative predominance of ciliated cells. Due to the targeted synchronized motor activity of the apically located cilia, a fairly effective continuous translation of a thin layer of mucus along the surface of the mucous membrane towards the pharynx is carried out, in the viscous base of which various dust particles and microorganisms that enter during respiration are stuck. Consequently, the mucous membranes of the respiratory tract, compared to those of the intestinal tract, have an additional active host defense mechanism, which is called the mucociliary barrier [13-16].

The second component of the morphophysiological barrier of the mucous membranes are secretory structures in the form of goblet cells and numerous small (intramural) glands that cover the outer (apical) surface of the covering epithelium with a thin layer of mucus. Notably, in its composition (together with mucins of the corresponding type) there is a bactericidal enzyme lysozyme (mureinase) in the proper concentration, which belongs to humoral factors of innate (nonspecific) immunity, as well as the class A secretory immunoglobulin, which appears as a result of the humoral response of the specific (adaptive) immunity [17, 18]. But all this still needs to be supplemented by the fact that this antiviral active mucin layer, which protects the epithelial layer of the mucous membranes, is, on the one hand, in close connection with the epithelial glycocalyx, and on the other hand, it is associated with the so-called biofilm, which is a specific form of colonization of mucous membranes, mainly by obligate (useful for the body) microflora, in the environment of which pathogenic bacteria and viruses reside in a small amount (about 5 %). Normally, the latter are usually depressed by the obligate microflora, which thus perform a protective function in relation to mucous membranes [19-21].

Therefore, if we add together all the abovementioned protection factors, it becomes obvious that this eliminates not only the possibility of adhesion (sticking) of viruses to the apical surface of epithelial cells, but also their penetration through the epithelium into the mucous membranes, i.e., into the internal environment of the body.

But we paid special attention to immunohistochemical analysis of the epithelium associated with the dome of lymph nodes. According to modern ideas, the intestinal epithelium covering the apical surface of group lymphoid nodules is endowed with the ability to selectively react with the antigenic composition of the contents of the small intestine as an initial link in the formation of immune responses in the gastrointestinal tract (table I).

According to these data, the bulk of them were B-lymphocytes (about 47%) and T-lymphocytes (about 35%), while the share of plasma cells, macrophages and dendritic cells accounted for about 5% of each.

Currently, we can clearly visualize those places in the lymphoid nodules of Peyer's patches, where these initial processes occur (Fig. 1).

It is noteworthy that due to them, according to the literature, in the intestine, slow inflammatory processes constantly take place, which is a physiological norm [27]. Apparently, the respiratory pathways are not an exception in this respect, because in their mucous membrane, as noted above, there are lymphoid nodules. Recently, interest in these formations has increased, because it is believed that they mediate the mechanism of the formation of acquired immunity in oral use of a live vaccine, which is considered more effective compared to other forms of vaccination. In this regard, it is reasonable to recall the history of the creation of the vaccine against poliomyelitis [28, 29].

Generally, the issue on structured lymphoepithelial formations in the form of single and grouped lymphoid nodules arises, which perform the function of immune surveillance of the parietal microbiota of hollow organs, thus being the outposts and the so called «portals» of the immune system of mucous membranes. However, in some extreme situations, for example, in an excessive load of viral infection on the mucous membranes of the intestine or respiratory tract, these formations become the weakest places for the massive entry of viruses into the internal environment of the body. From here, that is, from this source of invasion, they will be carried by the bloodstream throughout the body, reaching their «selected» target cells. For example, in COVID-19 they are mainly alveolocytes of the first and second type, in which coronaviruses penetrate after preliminary adhesion with their basement plasma membrane. But to do this, they have to overcome the basement membrane that underlies these cells. We do not know how this happens, because this issue is not elucidated in the literature. But in general, the whole process of infection of the target cells and reproduction of viruses in them is carried out in the sequential order presented at the beginning of our paper. We only specify that for the strictly polarized cells, which are part of epithelial layers, the entrance gate of an infection is not any of their surface, but only that by which this cell is adhered to in the internal environment of the body (Fig. 2).

DISCUSSION

There must be some special places in this continuum of the morphophysiological barrier of the mucous membranes, potentially accessible for infection, ie some gaps. This point of view is not new. For example, back in the middle of the last century, some authors postulated the presence of special tubules in the mucous membrane of the intestinal and respiratory tracts, through which various microorganisms can enter it [22]. Later, in the process of targeted search for information, our attention was attracted by some reports in the literature that relate to the study of the functional purpose of the well-known structured lymphoepithelial formations related to peripheral organs of the immune system, such as lymphoid nodules. Some of them, individual (solitary) nodules, occur both in the tracheobronchial tree and in the intestinal tract, while the others, grouped nodules (Peyer's patches), are found only in the intestine. But it should be noted that the tonsils, which are located at the very beginning of the digestive and respiratory systems, can be considered similar to the latter in morphology and function. These formations, by

their nature, are normally intended to notify the immune system of the mucous membranes about newly appeared pathogens in their proximity (parietally) [23, 24].

According to the current dogma, the transporters of all antigens from the cavity, for example, from the intestine to its mucous membrane, are the so-called M-cells, which are localized among the polarized monolayer of enterocytes covering the apical sections of the lymphoid nodules, in connection with which it received the name of follicle-associated epithelium [25, 26]. Obviously, M-cells are capable to transcytotic transfer and delivery intact pathogens to dendritic macrophages localized beneath them (subepithelially), which, after processing, present this pathogen to T-lymphocytes, initiating host immune responses, transferring them to the systemic level.

CONCLUSIONS

Thus, based on the above, we believe that the process of development of viral infection can be represented in the form of the following targeted steps:

1. Massive invasion of viruses into the body, that is, into its internal environment. The follicle-associated epithelium of the lymphoid nodules of the mucous membranes serves as a gap for this invasion.
2. The pathway of viruses to the intended target (target cells) is carried out by the blood flow.
3. Achieving the target by viruses and their penetration into target cells.

But in the very pathogenesis of viral diseases, the role is played not so much by the viruses themselves, but by the preparedness of the particular body, which directly depends on the functional state of its immune system, which determines the possibility, severity and outcome of the disease.

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ORCID and contributionship:
Volodymyr Hryn: 0000-0001-5894-4416[A,B,D]
Yurij Kostylenko: 0000-0001-9491-2040[B,D-F]
Viktoriia Pinchuk: 0000-0003-0622-0322[E,F]
Valeriy Zhamardiy: 0000-0002-3579-6112 [A,E,F]
Viktoriia Donchenko: 0000-0002-9665-7204[A,E,F]
Olha Honchar: 0000-0003-4779-2773[E,F]
Oksana Hordiienko: 0000-0003-3207-8497[E,F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Viktoriia Donchenko
Poltava State Medical University
23 Shevchenko st., 36011 Poltava, Ukraine
tel: +380662674172
e-mail: vik.donchenko@gmail.com

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ORIGINAL ARTICLE

PROGRAMMED LAPAROSCOPY IN THE OF DIFFUSE APPENDICULAR PERITONITIS TREATMENT OF CHILDREN

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Ihor V. Ksonz, Denys V. Khmilevskyi, Ievhen M. Grytsenko
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To analyze the implementation of programmed laparoscopy with the criteria definition for its termination in the treatment of diffuse appendicular peritonitis in children.

Materials and methods: Since 2017, the programmed laparoscopy in the treatment of diffuse appendicular peritonitis has been used in 28 children aged 1 to 16 years.

Results: The programmed laparoscopy allows assessing the dynamics of the intra-abdominal infectious-inflammatory process and monitoring the treatment effectiveness. The modified abdominal index (AI) was determined based on integrated assessment of degree and nature of abdominal organs` damage during the first and repeated surgeries, the modified abdominal index (AI) was determined. AI identified during the primary laparoscopic intervention ranged from 14 up to 22 points and on average it was 17.5 ± 1.3 points, during the programmed laparoscopy AI was from 3 to 11 points, on average it was 9.15 ± 1.48 points.

Conclusions: The programmed laparoscopy for diffuse peritonitis in children allows controlling the pathological process in the abdominal cavity and promptly eliminate intra-abdominal complications. Determination of AI allows objectifying the nature of the lesion and the dynamics of changes in the abdominal cavity.

KEY WORDS: diffuse peritonitis, programmed laparoscopy, children

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INTRODUCTION

Complete rehabilitation of the abdominal cavity is the key to successful treatment of all peritonitis forms. After all, in the future it is insufficient or inadequate primary rehabilitation of the abdominal cavity leads to the progression of peritonitis, the formation of demarcated abscesses, which requires relaparotomies and significantly worsens the prognosis [1].

But radical sanation is not always possible during primary surgery in cases of abrupt inflammatory changes of the visceral peritoneum with massive purulent-fibrinous layers and the connective process. To solve this problem, it is proposed to conduct planned (programmed) sanation of the abdominal cavity, with their implementation in 48-72 hours [2].

Currently, a lot of authors consider the laparoscopic sanation as an alternative to the method of programmed revisions and sanations of the abdominal cavity. The advantages of laparoscopic interventions over traditional ones are more accurate determination of peritonitis prevalence at the diagnostic stage, less traumatic intervention, significant reduction of wounds, especially infectious complications, early activation and rehabilitation of patients, good cosmetic effect [3].

THE AIM

The aim to analyze the experience of performing the programmed laparoscopy with defining criteria for its termination in the treatment of diffuse appendicular peritonitis in children.

MATERIALS AND METHODS

Before 2017, in cases of impossibility of full sanation of the abdominal cavity with diffuse peritonitis in children, programmed relaparotomies were performed. 1 to 6 programmed relaparotomies were performed in children with common forms of peritonitis. The effectiveness of the first sanative relaparotomies to reduce the effectiveness of each subsequent one is noted [2].

Since 2017, programmed laparoscopy in the treatment of diffuse appendicular peritonitis has been used in 28 children aged 1 to 16, boys 19, girls 9. Laparoscopic surgery was performed using laparoscopic equipment "Richard Wolf", designed especially for children. The need for conversion arose in 1 patient. Adequate laparoscopic sanation of the abdominal cavity was considered impossible due to the presence of dense massive layers of fibrin and intestinal paresis.

The study was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee (LEC) of all the institutions mentioned in the work. The informed consent of the children's parents (or their guardians) was obtained.

RESULTS

Based on an integrated assessment of the degree and nature of damage to the abdominal organs during the first and repeated operations, a modified abdominal index (AI) was determined by VS Savelyev et al. (1998).

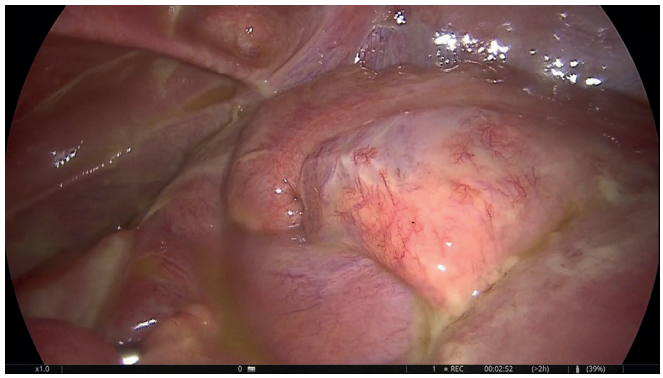

Fig. 1. Patient with perforated appendicitis and diffuse peritonitis operated on laparoscopy

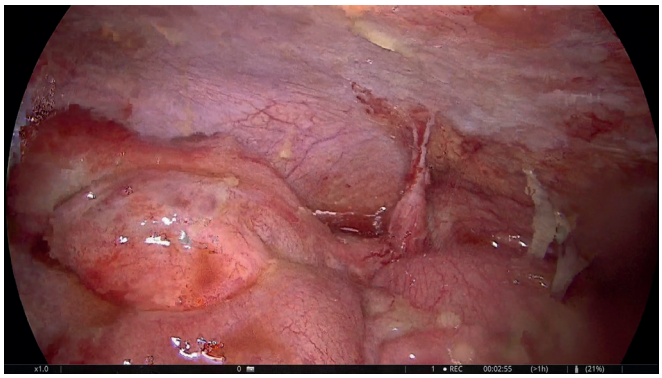

Fig. 2. The planned laparoscopic sanation after 48 hours after the first surgery

Table I. Criteria for intraoperative assessment of the nature of the lesion of the abdominal cavity

Criteria	Points
Prevalence of peritoneal inflammation:	
- local (abscess)	1
- spread	3
The nature of the exudate:	
-serous	1
-purulent	3
-hemorrhagic	4
-fecal	4
Fibrin layers:	
- in the form of loose masses	1
- in the form of a shell	4
State of intestinal - intestinal dilatation	3
- lack of peristalsis	3
- failure of the intestinal wall	4
Total quantity of points – TQP	

Criteria for intraoperative assessment of the nature of the lesion of the abdominal cavity (in points) are shown in Table I. The results were processed using Student's t-test. Differences were considered statistically significant at $p \leq 0,05$.

In all children during primary surgery the significant inflammatory changes of the visceral peritoneum, massive purulent-fibrinous layers, pronounced connective tissue from the formation of multiple abscesses corresponded to the 5th class of the laparoscopic system of acute appendicitis according to Gomes et al [4] (Fig. 1). AI was determined during the primary laparoscopic intervention, ranged from 14 to 22 points and averaged 17.5±1.3 points.

In all children with common forms of peritonitis one programmed laparoscopic sanation of the abdominal cavity was performed. During the programmed laparoscopy, the AI ranged from 3 to 11 points that on average is of 9.15 ± 1.48 points (Fig. 2).

In only one case, during the first programmed laparosanation the AI was 15 points and it was decided to perform the next planned laparosanation. All children underwent the prolonged epidural anesthesia in the postoperative period.

DISCUSSION

Endovideosurgical method allows a thorough revision of the abdominal cavity to assess the nature and amount of exudate, its location, the presence and nature of fibrin layers, the process of commissural formation, the condition of parietal and visceral peritoneum, the formation of intra-abdominal abscesses, intestinal hemorrhage, The color, the state of the intestinal wall, the presence of peristalsis was examined [5].

At the same time, it is noted that the opportunities of endovideosurgery are limited by a number of circumstances that are difficult to predict in advance. They can often be seen during surgery. As a rule, these circumstances are due to technical difficulties in performing a particular stage of the operation. Sometimes it is impossible even a full revision of the abdominal organs, especially the elimination of peritonitis and sanation of the abdominal cavity. This may be due to the process of commissural formation, terminal peritonitis with the formation of strong fibrous commissures and multiple inter-loop abscesses, severe intestinal paresis, technical difficulties of surgical removal of the organic substrate of the disease [6].

P.S. Rusak [7] as the criteria to imply the programmed laparosanations considers signs of further development of peritonitis according to the results of monitoring the postoperative period. In our observations, the decision to perform re-laparosanation was made during the initial surgery in the absence of radical sanation of the abdominal cavity and was not subject to revision.

Programmed laparoscopy allows not only to assess the dynamics of intra-abdominal infectious-inflammatory process and monitor the treatment of effectiveness, but also to sanate the abdominal cavity, including separation of commissures in the abdominal cavity to prevent early intestinal obstruction, abdominal abscess accumulation with local washing of the affected areas, if necessary, control and correction of the location of drainages. [5,8].

The number of repeated sanative laparoscopic interventions is on average 2-3, although if necessary it can be increased to 7-8 [5]. In our observations, only one repeated sanative laparoscopy was performed, only in one case there was a need for 2 repeated laparoscopic interventions.

CONCLUSIONS

The programmed laparoscopy for diffuse peritonitis in children allows controlling the pathological process in the abdominal cavity and promptly eliminate intra-abdominal complications. Determination of AI allows objectifying the nature of the lesion and the dynamics of changes in the abdominal cavity. The indication for termination of programmed laparoscopy is AI in the range of 3-11 points.

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ORCID and contributionship:
Ihor V. Ksonz: 0000-0002-7703-1759[A,E,F]
Ievhen M. Grytsenko: 0000-0003-3173-3859[A,D]
Denys V. Khmilevskyi: 0000-0002-5499-1343[A,B,C]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Ievhen M. Grytsenko
Poltava State Medical University
23 Shevchenko st., 36011 Poltava, Ukraine
tel: +380667137283
e-mail: doc.grytsenko74@gmail.com

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ORIGINAL ARTICLE

THE EFFECT OF S-ADEMETIONINE ON PLASMA CITRULLINE LEVEL DURING CHEMOTHERAPY-INDUCED OXIDATIVE STRESS IN PATIENTS WITH CHRONIC LYMPHOPROLIFERATIVE DISORDERS

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Roman I. Skrypnyk, Ganna S. Maslova, Igor N. Skrypnyk
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate the effect of S-ademetionine on plasma citrulline level in patients with chronic lymphoproliferative disorders (CLPD) during chemotherapy-induced oxidative stress.

Materials and methods: 25 patients with CLPD were examined. Examinations were conducted twice: before chemotherapy (CT) and after 3 courses of CT. Several biochemical markers in the blood were determined: the activity of catalase, the level of plasma citrulline, the concentration of N-acetylneuraminic acid (NANA) and the concentration of substances that form a trimethine complex (TBARS) with 2-thiobarbituric acid. Patients were divided into groups: I (n=14) – patients who underwent only CT; II (n=16) – patients who during CT received S-ademetionine, at a dose of 1000 mg/day intravenously for 10 days, then 500 mg twice a day for 20 days. III (n=20) –the control group of 20 practically healthy individuals.

Results: Patients in both groups with CLPD had pre-existed mucosal injury that was characterized by 1.25 (p=0.0025) and 1.26 times (p=0.006) higher blood NANA concentration compared to the control group. The conduction of CT was associated with enterocytes dysfunction, which was characterized by 1,66 times (p=0,0002) lower plasma citrulline level in patients of group I compared to the initial examination. The infusion of S-ademetionine attenuated intestinal dysfunction that was associated with 1,23 times (p=0,0005) higher blood citrulline level after the CT as compared to group I.

Conclusions: The infusion of S-ademetionine as adjuvant treatment in patients with CLPD provided effective prophylaxis of intestinal injury that was associated with higher blood citrulline level after the conduction of CT.

KEY WORDS: S-ademetionine, mucositis, oxidative stress, citrulline

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INTRODUCTION

The major treatment option in patients with chronic lymphoproliferative disorders is chemotherapy (CLPD). The major concept in chemotherapy (CT) is to provide the infusion of chemotherapeutic drugs according to the dose-effectiveness principle. According to this principle, CT agents should be prescribed strictly according to the current standards of treatment provided by modern guidelines. At the same time infusion of CT agents in high doses is associated with a high risk of chemotherapy-induced injury of multiple organs and systems throughout the body. Nowadays, it is determined that many CT agents can cause inflammation and dysfunction of the entire gastrointestinal tract (GIT) [1].

The mucosal injury of GIT during CT is caused by the detrimental effect of CT agents on all rapidly proliferating cells. According to the current concepts, chemotherapy-induced mucositis can be divided into 2 groups: oral mucositis and intestinal mucositis. Most of the researchers dedicate their studies to oral mucositis, mostly because patients with oncological malignancies usually have numerous contraindications that make impossible the invasive assessment of small and large intestines [2]. Because of the impossibility to assess the status of small and large intestines by invasive methods, the diagnosis of intestinal mucositis requires a complex assessment of clinical symptoms simultaneously with an evaluation of specific intestinal biomarkers [3].

The state of GIT mucous membrane and chemotherapy-induced injury of the mucous membrane can be assessed by the level of N-acetylneuraminic acid (NANA) in the blood [4].

Currently, blood citrulline level is considered one of the most promising potential biomarkers in the assessment of intestinal injury. Citrulline is the amino acid, that is produced practically exclusively by enterocytes, thereby the assessment of blood citrulline level can be used in clinical management as a marker of enterocytes functional state [5].

Intestinal mucositis (IM) is one of the most common complications during the conduction of CT [6]. According to modern concepts, the resistance of the intestinal mucosal barrier is provided by 3 lines of defense: intestinal microbiota, mucosal layer and epithelium. One of the most important GIT barrier components – is the mucosal layer that provides dynamic and reciprocal interactions with various barrier components including intestinal microbi-

ota. Thus, the mucous layer provides physical, biochemical and biological defense against various aggressive factors and bacteria [7].

Among the agents, that are widely used in the treatment of CLPD is cyclophosphamide. Cyclophosphamide injection is associated with dangerous side effects such as bone marrow suppression simultaneously with suppression of the immune system, which results in the injury of the entire GIT. Dysfunction of the intestinal barrier is also considered one of the major side effects of cyclophosphamide. Cyclophosphamide causes disruption of the functional integrity and functional capacity of the intestinal mucosal layer, which affects tolerability to CT agents and prognosis in patients that ongoing CT [8].

In patients with CLPD the injections of Vincristine can also cause GIT injury. Vincristine causes disruption of GIT motility that clinically manifests with nausea, anorexia and paralytic intestinal obstruction [9].

The injection of Doxorubicin is also strongly associated with GIT injury, which manifests with clinical symptoms such as nausea and mucositis [10].

One of the major pathological mechanisms of CT-induced intestinal mucositis is oxidative stress [1]. Oxidative stress develops when the production of reactive oxygen species (ROS) prevails over the capacity of antioxidant defense to eliminate them [11].

It was determined that exactly the cytotoxic properties of CT agents are strongly associated with oxidative stress [12]. But also, the production of ROS during CT, potentiates various processes, that lead to cellular death including apoptosis [13].

From this perspective, the prophylaxis of CT-induced complications should include the agents that potentiate antioxidant defense. According to several clinical types of research in oncological practice to prevent chemotherapy-induced reactions, S-ademetionine can be used, as entroprotective agent [14]. Due to a systemic effect, S-ademetionine potentially can prevent oxidative injury to multiple organs and systems throughout the body, including the intestine.

It should be noticed, that currently, the application of S-ademetionine in oncological practice remains largely unstudied.

THE AIM

The aim is to investigate the effect of S-ademetionine on plasma citrulline level in patients with chronic lymphoproliferative disorders during chemotherapy-induced oxidative stress.

MATERIALS AND METHODS

24 patients with CLPD were studied: 15 (75%) patients with B-cell CLL and 10 (25%) patients with Small B-cell NHL. All patients were treated in the Hematology Department of M.V. Sklifosovsky Poltava Regional Clinical Hospital during 2018–2021 years. 7 (28 %) females and 18 (72 %) males, ages 30-76. The criteria of inclusion were the progression of B cell CLL, Small B-cell NHL; ECOG performance status – I-II, and Karnofsky Performance Status – 60-80%. All patients were diagnosed with B-CLL, Small B-cell NHL, indications for CT were determined, CT was appointed according to the current standards of treatment of patients with oncohematological malignancies with acute and chronic hemoblastosis, according to the order № 647 of the Ministry of Health of Ukraine since 30.07.2010, European Society for Medical oncology [15]. All patients whose CT has been complicated by diarrhea syndrome were enrolled into the study. The examinations were conducted twice: before CT and after 3 courses of CT. Patients were analysed for the following biochemical markers: the severity of the oxidative stress, which was determined by the concentration of substances, that form a trimethine complex (TBARS) with 2-thiobarbituric acid and the state of the antioxidant system (AOS) was analysed by catalase activity. Resistance of the mucous barrier of the intestine was determined by the concentration of NANA in the blood [16]. The enterocytes functional state was determined by the concentration of the citrulline in the plasma [17].

All patients received CT according to current standards, specifically, the following combinations were used: BR (bendamustine, rituximab), FCR (fludarabine, cyclophosphamide, rituximab), R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone).

Depending on the inclusion of S-ademetionine as an adjuvant treatment, patients were divided into groups:

I (n=13) – patients with B-cell CLL and Small B-cell NHL, who received only CT.

II (n=14) – patients with B-cell CLL and Small B-cell NHL, who received S-ademetionine at a dose of 1000 mg/day intravenously for 10 days, then 500 mg twice a day for 20 days.

III (n=20) – the control group of 20 practically healthy individuals (9 (45 %) females and 11 (55 %) males, ages 22–26).

GraphPad Prism version 5.00 (GraphPad Software, Inc., San Diego, CA, USA) was applied for statistical analysis software. Normally, distributed data were expressed as mean ± standard deviation. Students criteria were used for normally distributed data. Non-parametric Wilcoxon-Mann-Whitney test was used for the analysis of unevenly distributed data. Spearman's rank correlation coefficients were used to assess the correlations between the results. For studies comparing prevalence between two groups, p value of < 0.05 was considered statistically significant.

RESULTS

On the initial examination in patients with CLPD of groups I and II the level of NANA was in 1.25 times (p=0,0025) and 1.26 times (p=0,006) respectively higher as compared to the control group (table I, II). A significant increase in NANA can be a sign of the detrimental effect of the oncohematological process on GIT mucose membrane.

In patients of both group I and group II on initial examination, the concentration of TBARS in the blood was in 1.39 times (p=0.0479) and 1,3 times (p=0.0122) respec-

Table I. Biochemical values in patients of the I group before and after treatment, M±m

Values	I (n=12)		III (n=20)
	V1	V2	
NANA, μmol/g	2,41±0,19* 95%CI 2,30-2,53	2,99±0,19& 95%CI 2,88- 3,11	1,93±0,19# 95%CI 1,845-2,029
Catalase, μmol/g	13,47±2,03* 95%CI 12,24-14,70	11,94± 2,23 95%CI 10,59- 13,29	12,98±2,19 95%CI 11,95-14,01
TBARS, nkat/g	1,56 ± 0,14* 95%CI 1,478-1,65	2,00± 0,16& 95%CI 1,90- 2,10	1,13 ± 0,55# 95%CI 0,87- 1,39
Plasma citrulline, μmol/l	47,39±3,86* 95%CI 45,06-49,73	28,58± 3,41& 95%CI 26,51- 30,64	57,20±9,88# 95%CI 52,70-61,70

Note: V1 – the first examination, V2 – the second examination, * - statistically significant difference between V1 and V2 values in patients of the I group (p<0,05), &- statistically significant difference between V1 values in patients of the I group and the III group (p<0,05), # - statistically significant difference between V2 values in patients of the I group and the III group (p<0,05).

Table II. Biochemical values in patients of the II group before and after treatment, M±m

Values	I (n=12)		III (n=20)
	V1	V2	
NANA, μmol/g	2,44±0,26 95%CI 2,27-2,60	2,63± 5,81& 95%CI 2,54-2,72	1,93±0,19# 95%CI 1,84-2,02
Catalase, μmol/g	12,92±2,25* 95%CI 11,49-14,35	11,80± 1,68 95%CI 10,73- 12,87	12,98±2,19 95%CI 11,95-14,01
TBARS, nkat/g	1,47±0,22 95%CI 1,33-1,61	1,43± 0,14& 95%CI 1,34-1,52	1,13 ± 0,55# 95%CI 0,87- 1,39
Plasma citrulline, μmol/l	49,85±5,22* 95%CI 46,53-53,17	35,22± 2,08 95%CI 33,89- 36,55	57,20±9,88# 95%CI 52,70-61,70

Note: V1 – the first examination, V2 – the second examination, * - statistically significant difference between V1 and V2 values in patients of the I group (p<0,05), &- statistically significant difference between V1 values in patients of the I group and the III group (p<0,05), # - statistically significant difference between V2 values in patients of the I group and the III group

tively higher compared to the control group (table I, II), which can be a sign of oxidative stress that was induced by the oncological process.

Simultaneously the citrulline concentration in the blood in patients of group I was 1.2 times (p=0.0161) lower compared to the control group. This can be explained by moderate functional dysfunction of enterocytes.

After the third course of CT in patients of group I, that underwent CT without the inclusion of S-ademetionine for adjuvant treatment, the level of NANA was in 1.24 times (p=0.0025) higher compared to the initial examination and 1,55 times (p=0.0017) higher (p=0.0017) compared to the control group (table I, II).

In patients of group II, that received S-ademetionine for adjuvant treatment, after the third course of CT the level of NANA was in 1.36 (p=0,0025) times higher compared to the control group (table I, II). The elevation of NANA in the blood can be a marker of chemotherapy-induced mucosal injury of the intestine. It should be noted that in patients of group II that received S-ademetionine the level of NANA was in 1.14 times (p=0,0059) lower compared to group I (table I, II), which can be a sign of mild enteroprotective effect of S-ademetionine.

After the secondary examination in patients of groups I and II the activity of catalase in the blood was in 1.13 times (p=0.0144) and in 1.1 times (p=0.0106), respectively lower compared to the initial examination (table I, II). That can be explained by the depletion of the antioxidant system during the CT.

During the conduction of CT in patients of group I the level of TBARS in the blood was in 1.28 times (p=0.0002) higher than on the initial examination (table I, II). The elevation of TBARS concentration in the blood can be explained by the development of chemotherapy-induced oxidative stress. The infusion of S-ademetionine as an adjuvant treatment to patients of group II, caused a decrease in 1.4 times (p=0.0005) of the TBARS concentration in the blood (table I, II), which can be a marker of a decrease in the severity of oxidative stress.

The conduction of the CT was associated with a decrease of citrulline in blood concentration in patients of both groups I and II, in 1.66 times (p=0.0002) and 1.42 times (p=0.0025) respectively, compared to the initial examination (table I, II). The decrease in citrulline level can be a marker of the enterocyte dysfunction, that was caused by the toxicity of CT. It should be noted that on the second examination, in patients of group II that received S-ademetionine as adjuvant treatment blood citrulline level was in 1.23 times (p=0,0005) higher compared to group I, that received only CT (table I, II). The possible reason for a

higher citrulline level in group II, can be enteroprotective effect of S-ademetionine.

DISCUSSION

In patients with CLPD pre-existed mucosal injury was determined, which was characterized by high blood NANA concentration. Pre-existed mucosal injury in oncohematological patients can be caused by the detrimental effect of malignancy itself that initially disrupt the mucosal functional state, which potentially can result in morphological injuries such as erosions or ulcers. One of the major mechanisms of mucosal injury in patients with CLPD is oxidative stress [6]. Oncological malignancy creates a prooxidative state, that in patients with CLPD was characterized by high TBARS levels in the blood [11]. Pre-existed mucosal injury and prooxidative state combined can significantly affect the functional state of enterocytes. The level of blood citrulline is used to assess the functional state of enterocytes. Because in several cases it's impossible to assess the status of small and large intestines by invasive methods, biomarkers such as citrulline can be the optimal choice [3]. Blood citrulline is produced practically exclusively by enterocytes, thus decrease in blood citrulline level can be a marker of a moderate functional dysfunction of enterocytes [5]. It was determined that patients with CLPD have decreased blood citrulline level. In patients with CLPD the pre-existed enterocytes dysfunction most probably was caused by malignancy-induced oxidative stress and was associated with mucosal injury.

The conduction of CT was associated with a further increase in blood NANA concentration, which can be a sign of aggravation of the pre-existing mucosal injury. Most probably mucosal injury was caused by CT-induced oxidative stress because most agents that are used in CT can induce inflammation and dysfunction of the entire GIT [1]. The infusion of CT agents creates a significant prooxidative state. The prooxidative state was created by an increase in reactive oxygen species (ROS) production, which was determined by the elevation of blood TBARS concentration, simultaneously with depletion of the antioxidant system, which was determined by a decrease in blood catalase concentration. The combination of an increase in ROS production with a decrease in ROS elimination causes severe oxidative stress that with time results in the oxidative injury of multiple cells in the human body, including enterocytes [11]. Oxidative injury of enterocytes caused severe functional dysfunction of enterocytes that was determined by decrease in blood citrulline level.

In patients of group II that received S-ademetionine as adjuvant treatment after CT the levels of NANA and TBARS were significantly lower compared to group I, which can be a marker of a milder mucosal and oxidative injury, respectively. Simultaneously in patients that received S-ademetionine the level of citrulline was significantly higher as compared to group I, which can be explained by the enteroprotective effect of S-ademetionine.

Thus, the infusion of S-ademetionine in patients of group II as adjuvant treatment provided the effective prophylaxis of chemotherapy-induced intestinal injury, due to its antioxidant and enteroprotective features.

CONCLUSIONS

Currently, the only treatment option for patients with CLPD is CT. However, many cytostatic drugs that are used in the treatment of CLPD have a significant enterotoxicity. Because sometimes in patients with CLPD, especially during CT, it's impossible to assess the status of small and large intestines the evaluation of specific intestinal biomarkers such as citrulline can be the optimal choice. The infusion of S-ademetionine as adjuvant treatment in patients with CLPD provided effective prophylaxis of intestinal injury that was associated with higher blood citrulline level after the conduction of CT. The enteroprotective effect of S-ademetionine most probably is provided by its potent antioxidant properties. Because the major pathogenic mechanism of mucosal injury in patients that receive CT agents is oxidative stress, attenuation of oxidative injury by S-ademetionine antioxidant properties can provide effective prophylaxis of chemotherapy-induced enterocytes dysfunction.

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ORCID and contributionship:
Roman I. Skrypnyk: 0000-0003-1828-3371 [B-E]
Ganna S. Maslova: 0000-0002-4729-1736 [B, D]
Igor M. Skrypnyk: 0000-0002-3426-3429 [A, F]

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CORRESPONDING AUTHOR
Igor M. Skrypnyk
Poltava State Medical University
23 Shevchenko St.,36011 Poltava, Ukraine
tel: +380505974908
e-mail: inskrypnyk@gmail.com

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ORIGINAL ARTICLE

MORPHOMETRIC FEATURES OF THE ELEMENTS OF THE HEMOMICROCIRCULATORY BED IN THE CORTEX OF THE ADRENAL GLANDS INFLUENCED BY THE FOOD ADDITIVES COMPLEX

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Serhii M. Bilash[1], Svitlana V. Donchenko[1], Olena M. Pronina[1], Mykhailo M. Koptev[1], Yaryna O. Oliinichenko[1], Valentyna V. Onipko[2], Volodymyr I. Ischenko[2]

[1]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

[2]POLTAVA V. G. KOROLENKO NATIONAL PEDAGOGICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To establish the dynamics of changes in the average total diameter, the diameter of the lumen of microvessels in the cortex of the rats' adrenal glands influenced by the long-term action food additives complex.

Materials and methods: To determine the structural changes of the vessels of the hemomicrocirculatory bed of the cortex of the adrenal glands of rats in our study, we used histological, morphometric and statistical methods.

Results: During the study, we found that the effect of a food additive complex on the vessels of the adrenal glands cortex of rats leads to a violation of hemodynamic conditions in the early stages of the experiment.

Conclusions: arterioles, venules and capillaries as a capacitive link of the hemomicrocirculatory bed are actively involved in response to exogenous administration of a complex of food additives (sodium glutamate, sodium nitrite, and ponso 4 R). Processes of change of morphometric indicators of vessels are observed mainly from the fourth week of the experiment.

KEY WORDS: food supplements, adrenal glands, cortex, medulla, endocrinocytes

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INTRODUCTION

The value of taste will play a significant role in everyone's life. Recognition of the suitability of food, protection against harmful substances, regulation of food consumption - all this is regulated by our taste buds [1]. People always enjoy delicious food, and sweet substances only cause positive emotions. Every day a person, without hesitation, eats food filled with many food additives and preservatives but is in no hurry to give it up, although everyone knows that this dish is harmful. Delicious but unhealthy food has become so common and available that it is difficult for anyone to resist the temptation to eat at least a piece. Many food supplements have emerged in response to the needs of the food industry, as mass production of food is different from home-cooked food. Nutritional supplements are necessary to preserve the appearance of products but in no way should mislead or harm the health of customers [2]. Today, there are several thousand food additives that the consumer is unaware of in foods and that can affect human organs, in our case the adrenal glands. Sodium glutamate (E 621), sodium nitrite (E 250), and Ponceau 4R (E 124) are some of the most common dietary supplements we are studying. The main consequences of taking many supplements are the following symptoms: chest and abdominal pain, migraine, nausea, tachycardia, obesity, weakness, and allergies. We should pay particular attention to the effect of these supplements on the adrenal glands, which can cause organ dysfunction and lead to cancer [3].

THE AIM

To determine morphometric changes in the structural components of the microcirculatory bed of the cortex (zona glomerulosa, zona fasciculata, zona reticularis) of the adrenal glands of rats under the influence of food supplements complex.

MATERIALS AND METHODS

The study was performed on white outbred rats weighing 0,350 ± 0,15 g, kept in standard vivarium conditions of Poltava State Medical University. Experimental studies were conducted in compliance with the requirements of humane treatment of experimental animals, regulated by the Law of Ukraine "On Protection of Animals from Cruelty", 2006 and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

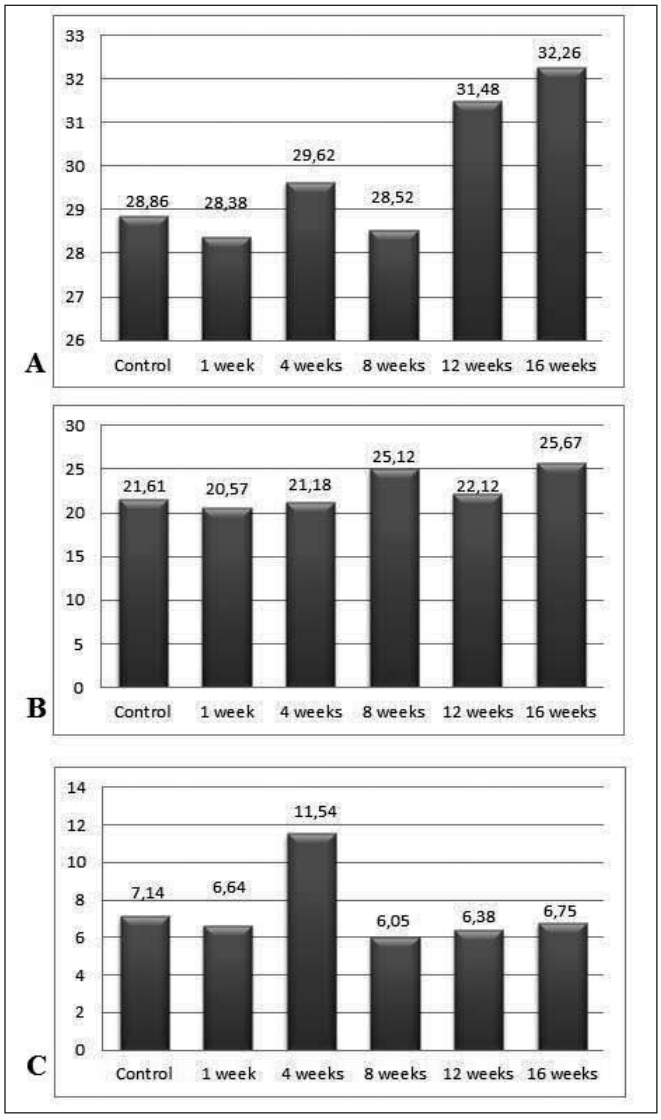

Fig. 1. Morphometric indicators of the total diameter of the hemomicrocirculatory bed of the zona glomerulosa of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

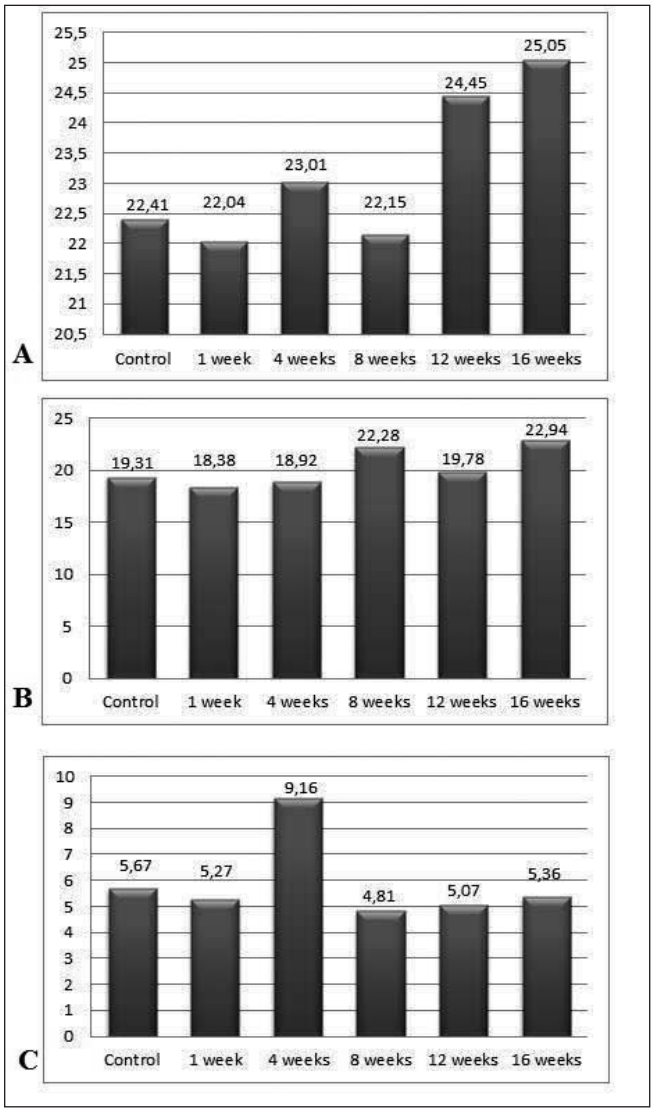

Fig. 2. Morphometric indicators of the lumen of the hemomicrocirculatory bed of the zona glomerulosa of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

A control group of rats consumed drinking water and saline orally. Rats from the experimental group were orally administered 10% sodium nitrite solution (E 250). Sodium glutamate (E621) was administered at a dose of 20 mg/kg in 0,5 ml of distilled water, Ponceau 4R - at a quantity of 5 mg/kg in 0,5 ml of distilled water once a day. Dosages of food additives were twice lower than the acceptable norm in food products. Rats were removed from the experiment at 1, 4, 8, 12, and 16 weeks by thiopental anesthesia overdose. Subsequently, adrenal fragments fixed in neutral formalin solution were sealed in paraffin. Histological sections made of paraffin blocks, colored with hematoxylin and eosin. Sections were studied using a Viorech light microscope with a digital micro photo attachment DSM 900. To obtain semi-thin sections, the test material was fixed in glutaraldehyde and compacted in epon-8. The finished sections were colored toluidine blue. The morphometric method was used to determine the thickness of arteries, venules, and capillaries of the cortex (zona glomerulosa, zona fasciculata, zona reticularis). Then we used a system of visual analysis of histological specimens. Images of histological specimens were displayed on a computer monitor using a microscope and a Vision CCD camera. Morphometric studies were performed using VideoTest-5.0, KAAPA Image Baseta Microsoft Excel on a personal computer. We examined the total diameter, lumen, and wall thickness of arterioles, venules, and capillaries and statistically processed data using Statistica 10 BiostatPro 6 software and Microsoft Excel 2019. The samples' calculations and indicators were verified using the Shapiro-Wilk test. Quantitative evaluation of the data included the determination of the arithmetic mean of the variance series (M) and its standard error (m). To compare the quantitative values in pair rows, we used Student's t-test. The difference was considered significant at $p < 0.05$.

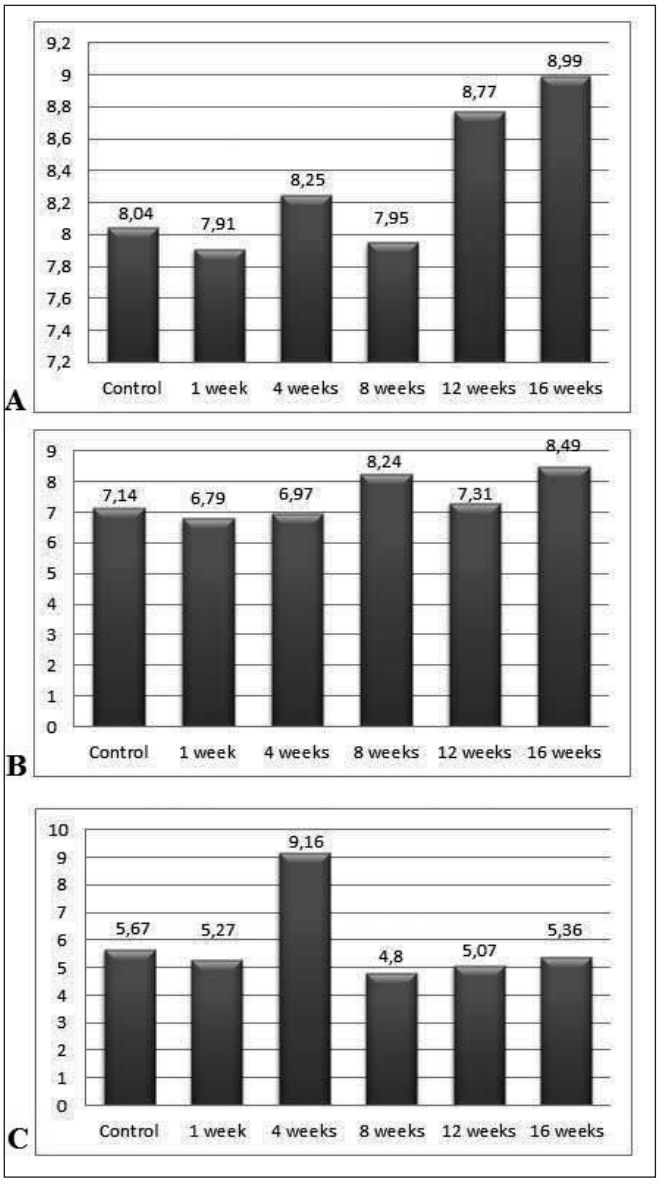

Fig. 3. Morphometric indicators of the total diameter of the hemomicrocirculatory bed of the zona fasciculata of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

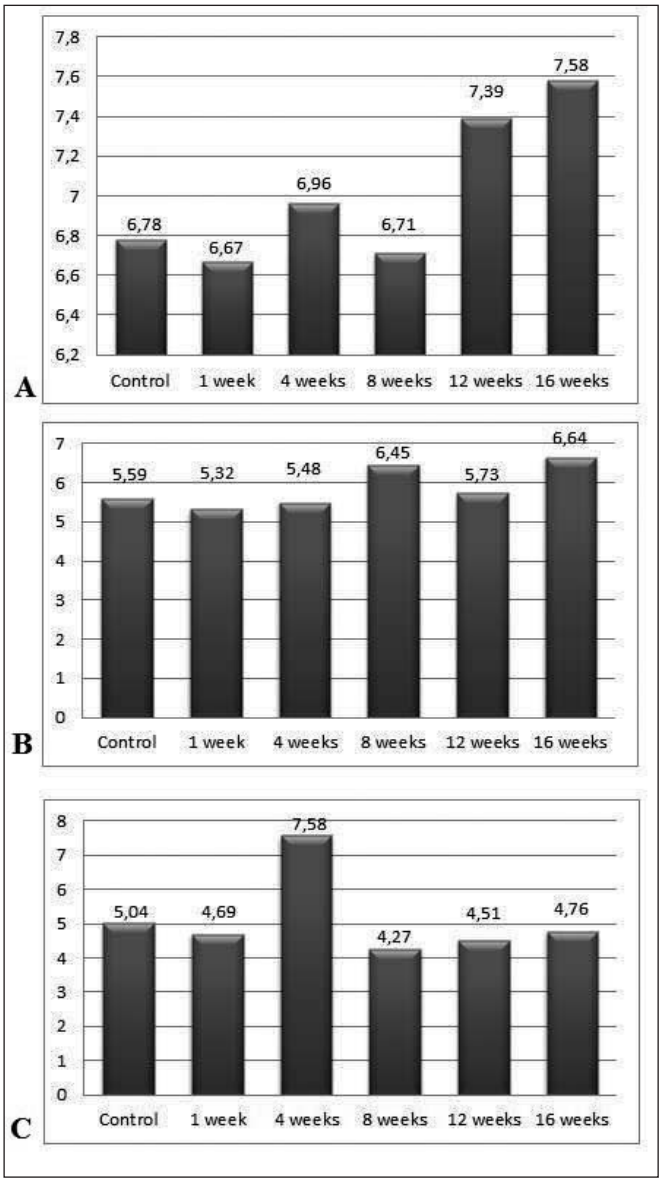

Fig. 4. Morphometric indicators of the lumen of the hemomicrocirculatory bed of the zona fasciculata of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

RESULTS

Morphometric studies have shown that the hemomicrocirculatory bed (HMCB) of the rat adrenal glands is well developed and multicomponent. After modeling the experimental effect of food supplements on the adrenal glands, we found common reactions of cortex vessels and their structural rearrangement. According to the literature, the response of the HMCB to the influence of external and internal factors is quite specific [4,5]. Therefore, during the morphological study of HMCB elements, we analyzed the total diameter, lumen of arteries, venules, and capillaries. In particular, we noted the uneven thickening of the walls of arterioles, venules and capillaries, which was swelling and disorganization of the connective tissue surrounding the vessels. An increase of blood flow and vasodilation were also observed.

To determine the structural and functional changes after exposure to a complex of food additives, we determined the total diameter, lumen diameter of arteries, venules and capillaries. During the morphometric examination of the vessels of the zona glomerulosa of the cortex in the control group, it was found that the total diameter of the arterioles is 28,86 μm, and the diameter of the lumen - is 22,41 μm. After the influence of food supplements, the morphometric parameters of the total diameter of arteries, venules, and capillaries change significantly [6,7]. Starting from the 4th week, there is a gradual increase in the total diameter of the arterioles compared with the control group, and it is 29,62 μm - an increased of 2,61%. At the 8th week, the total diameter reached almost baseline, but at the 16th week, the total diameter of the arterioles was 32,26 μm, which is 11,8% higher than the control values. At the 8th week,

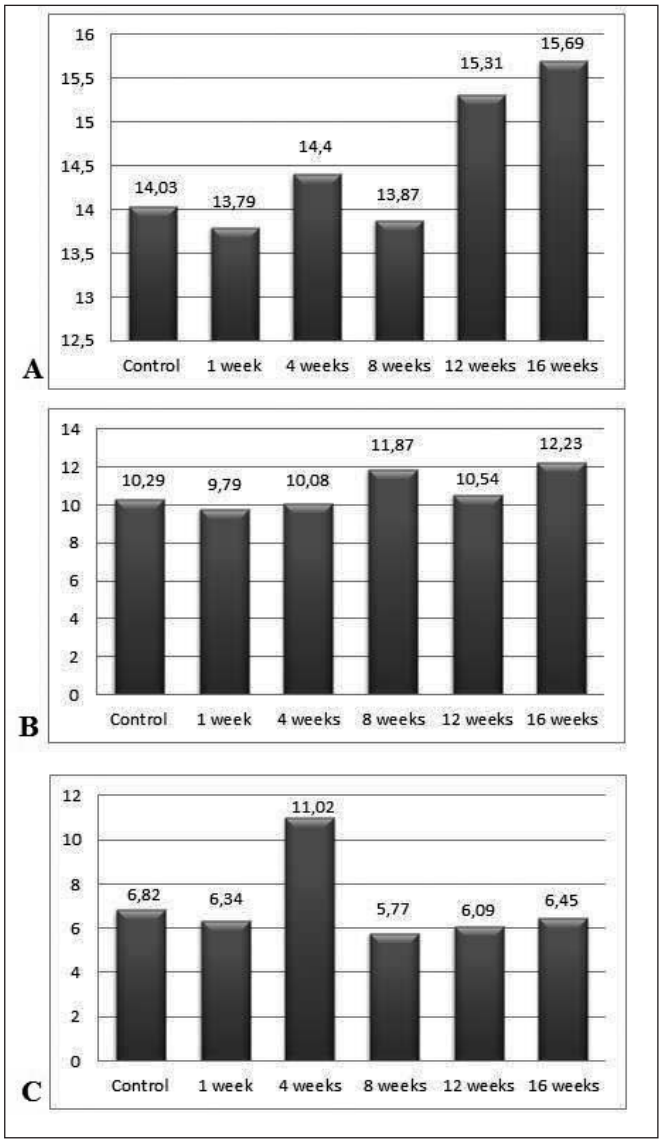

Fig. 5. Morphometric indicators of the total diameter of the hemomicrocirculatory bed of the zona reticularis of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

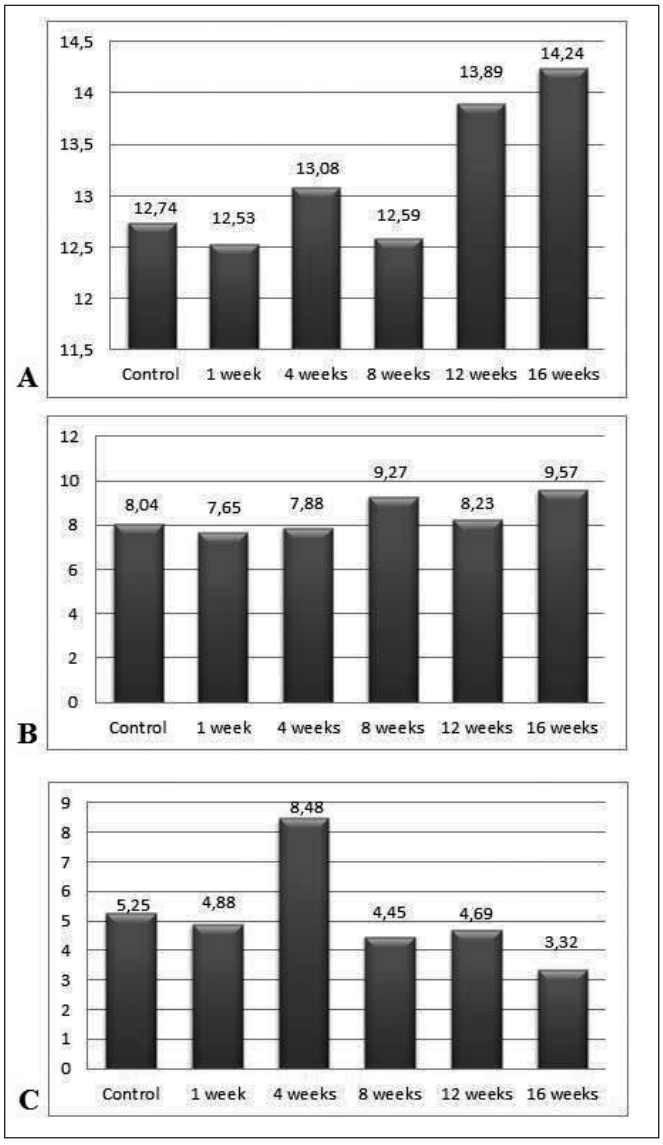

Fig. 6. Morphometric indicators of the lumen of the hemomicrocirculatory bed of the zona reticularis of the adrenal glands cortex of rats, μm: A - arterioles; B - venules; C – capillaries

the total diameter reached almost baseline, but at the 16th week, the total diameter of the arterioles was 32,26 μm, which is 11,8% higher than the control values.

The total diameter of the glomerular zone venules of the control group cortex was 21,61 μm. During the four weeks of the experiment, the indicators did not change significantly. However, starting from the 8th week, the total diameter of the venules is 25,12 μm, which is 16,2% more than the control value. At the 16th week of the experiment, the total diameter of the venules increased and was 25,67 μm – 18,8% higher than the control value.

The morphological analysis of the total diameter of the capillaries set control values – 7,14 μm. Starting from the 4th week, the value changes sharply and is 11,54 μm, which is 61,6% more than the control value. At week 8, this value returned to baseline and did not change significantly until the end of the experiment (Fig. 1). This phenomenon can be explained by the fact that the use of food supplements (monosodium glutamate, sodium nitrite and Ponceau 4R) directly affects the walls of the adrenal vessels, causing hypertrophy and p erivascular edema in the early stages of the experiment.

The average diameter of the arterioles lumen of the glomerular zone of the cortex in the control group was 22,41 μm. At the 4th week, this figure was 23,01 μm, which is 2,72% higher than the control value. At the 12th and 16th weeks, the average diameter of the lumen of the arterioles changed significantly and was 24,45 μm and 25,05 μm, which is higher than baseline by 9,13% and 11,8%, respectively. The average diameter of the lumen of the venules of the glomerular zone of the cortex in the control group was 19,31 μm. During the experiment, the indicator did not change significantly. Only at the 8th and 16th weeks, there was an increase in the lumen of the venules 22,28

μm and 22,94 μm, respectively, which is higher than the control value of 15,4% and 18,8%. The average diameter of the lumen of the capillaries of the glomerular zone of the cortex in the control group was 5,67 μm. Abrupt changes in indicators were noticed in the 4th week of the experiment. The indicator was 9,16 μm, which is higher than the control group by 61,6% (Fig. 2).

During the morphometric analysis of the total diameter of the arteries of the hemomicrocirculatory bed of the zona fasciculata of the adrenal glands cortex of rats, the control group was 8.04 μm. At 1st week, the indicators decreased to 7,91 μm. Starting from the 12th week of the experiment, the total diameter of the arteries of the zona fasciculata was 8,77 μm, which is 9,07% more than the initial value, and at the 16th week - 8,99 μm, which is 11,81% higher than the control value.

Indicators of the total diameter of the venules of the zona fasciculata adrenal glands cortex of the control group were 7,14 μm. In the 1st and 4th weeks, the indicators were close to the control ones. However, starting from the 8th week, the average total diameter of the venules was 8,24 μm, and at the 16th week - 8,49 μm, which is higher than the control indicators by 15,4% and 18,9%, respectively.

The total average diameter of the capillaries of the zona fasciculata adrenal glands cortex of the control group was 5,67 μm. Morphometric analysis of indicators at 1, 12, and 16 weeks did not differ significantly from the control. However, at the 4th week, this indicator was 9,16 μm, which is 61,6% higher than the initial parameters (Fig. 3).

The average diameter of the arterioles lumen of the zona fasciculata of the cortex of the adrenal glands of rats in the control group was 6,78 μm. From the 1st to the 8th weeks of the experiment, the indicators remained similar. At the 12th and 16th weeks, the values were 7,39 μm and 7,58 μm, which is 8,98% and 11,8% higher than the control values, respectively.

The average diameter of the venules lumen of the zona fasciculata of the cortex in the control group was 5,59 μm. During the experiment, the morphometric parameters of these vessels did not change; only slight changes were observed at 8 and 16 weeks and were 6,45 μm (above the control values by 15,6%) and 6,64 μm (above the control values by 18,8%).

Morphometric research of the average diameter of the capillaries lumen of the zona fasciculata of the cortex in the control group was 5,05 μm. However, a significant increase in indicators was noticed in the 4th week of the study, which reached 7,58 μm - 50,4% higher than the control value (Fig. 4).

The average indicator of the total diameter of the hemomicrocirculatory bed of the arterioles of the zona reticularis of the adrenal glands cortex of rats was 14,04 μm. There were minor changes in the indicators from the 1st to the 8th week. At week 12 of the experiment, the rate was 15,31 μm, which is 9,26% higher than the control. At week 15, the indicator was 11,8% higher and was 15,69 μm.

The average diameter of the venules of the zona reticularis of the adrenal glands cortex of the control group was 10,29 μm. During the experiment, the indicators did not change significantly. Only changes were observed at 8 and 16 weeks, which were 11,87 μm and 12,23 μm, respectively, increased by 15,3% and 18,9%.

The average diameter of the capillaries of the zona reticularis of the adrenal glands cortex of the control group was 6,82 μm. During the experiment, the indicators did not deviate significantly. However, at the 4th week, significant changes were observed in the indicators, which amounted to 11,02 μm, which is 61,6% higher than the control values (Fig. 5).

The average diameter of the arterioles lumen of the zona reticularis of the cortex of the adrenal glands in the control group was 12,74 μm. At the 4th week of the experiment, this indicator was 13,08 μm (2,67% higher than the control). At the 12th and 16th weeks, there was an increase of 9,02% and 11,8%, which amounted to 13,89 μm and 14,24 μm, respectively.

The average diameter of the venules lumen of the zona reticularis of the cortex of the adrenal glands of rats in the control group was 8,04 μm. However, significant changes were observed at 8 and 16 weeks of the experiment. Morphometric parameters were 9,27 μm and 9,57 μm, which was higher than the control values by 15,3% and 19,1%, respectively.

Morphometric parameters of the average diameter of the arterioles lumen of the zona reticularis of the cortex of the adrenal glands were: 5,25 μm - control, at 4th week the rate increased to 8,48 μm (61,5%), at 16 weeks, the rate decreased to 3,32 μm, which is less than the control value by 36,8% (Fig. 6).

DISCUSSION

The data obtained during the experiment allow us to conclude that the action of a food additives complex of glutamate sodium, sodium nitrite, and Ponceau 4R are triggers for activating the inflammatory focus, as well as changes in structural components of the hemomicrocirculatory bed, namely arterioles, capillaries, and venules.

The average values of the total diameter, the diameter of the lumen of the walls of the microvessels varied in the dynamics of the experiment (from the 4th to the 16th week) and corresponded to the phases of the inflammatory reaction and the timing of reparative and regenerative processes, which is related to the direct effect of food additives on the vascular wall and equates to the effect of this complex of food additives on the vascular walls of other organs according to the authors [8] and the reaction of the vascular bed to the action of exogenous factors. Large vessels responded by increasing the diameter of the resistive and capacitive links due to impaired hemodynamic conditions, which is reflected in studies previously conducted to study the response of the vascular bed to the action of food additives complex [9]. Subsequently, due to the action of food additives, there is an inflammatory reaction with edema, which is confirmed by a decrease in the vascular lumen. This leads to the activation of arterio-venular anastomoses

to release blood into the vessels of the capacitive link and, consequently, increase the diameter of the venules of the adrenal cortex of rats.

Restorative-compensatory reactions aimed at neutralizing the source of alteration and restoring the morphofunctional state of blood vessels did not lead to complete restoration of normal hemodynamic parameters, which in recent weeks is reflected in increased vascular lumen and decompensation, decreased in the cortex of the adrenal glands, as a consequence of impaired hemodynamic conditions.

CONCLUSIONS

The effect of the food additives complex on the vessels of the cortex of the adrenal glands of rats in the early stages of the study was expressed by vascular spasm of the hemomicrocirculatory bed due to the damage action of food additives and increasing the diameter of the vascular lumen as a result of hemodynamic conditions. In the later stages of the experiment, the development of inflammatory reactions and hypoxia was observed, which led to the development of restorative and compensatory responses, but complete recovery did not occur.

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ORCID and contributionship:
Serhii M. Bilash: 0000-0002-8351-6090 [A,C,E]
Svitlana V. Donchenko: 0000-0001-7411-9897 [A,C,D]
Olena M. Pronina 0000-0002-8242-6798 [A,D,F]
Mykhailo M. Koptev 0000-0002-3726-8911 [B-D]
Yaryna O. Oliinichenko 0000-0001-7724-7333 [B-D]
Valentyna V. Onipko 0000-0002-2260-971X [B-D]
Volodymyr I. Ischenko 0000-0003-3513-2110 [B-D]

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CORRESPONDING AUTHOR
Svitlana V. Donchenko
Poltava State Medical University
23 Shevchenko st., 36024 Poltava, Ukraine
tel: +380955699434
e-mail: donchsveta77@gmail.com

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ORIGINAL ARTICLE

RISK-ORIENTED ANALYSIS OF LIMB LOSS IN VICTIMS OF MODERN HOSTILITIES

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Sergei O. Guryev[1], Olexiy S. Solovyov[1], Dmitriy M. Lysun[1], Natalia I. Iskra[1], Vitaly A. Kushnir[1], Andriy I. Tsvyakh[2], Nataliia O. Marchenkova[2]

[1]UKRAINIAN SCIENTIFIC AND PRACTICAL CENTRE OF EMERGENCY AND DISASTER MEDICINE MINISTRY OF HEALTH OF UKRAINE, KYIV, UKRAINE
[2]I. HORBACHEVSKYY TERNOPIL NATIONAL MEDICAL UNIVERSITY, TERNOPIL, UKRAINE

ABSTRACT

The aim: Identification, verification and analysis of clinically effective risks of limb amputation as a basis for the formation of risk-oriented treatment and diagnostic tactics in victims with limb injuries due to modern hostilities.

Materials and methods: This research is based on a study of 1,072 cases of limb damage due to modern hostilities in eastern Ukraine in 2014-2020. All injuries were gunshot (bullet and mine injuries). According to the concept of Clinical Risk Management, Clinical Result Risk was chosen for evaluation and analysis. Risk factors - epidemiological and anatomical signs of damage.

Results: Quantitative indicators of the clinical effective risk of limb loss are generally small and range from minimal to significant values (0.01-0.24). In some cases - up to 0.4 (significant), and are not critical and catastrophic. Of practical importance are only the risk factors associated with the nature of participation in hostilities and the anatomical characteristics of the injury. Among the immediate causes of limb loss, only primary traumatic amputation matters. Damage to vascular and nerve structures is not critical for limb loss. The impact of other risk factors may be reduced or eliminated if adequate care is provided.

Conclusions: The risks of limb loss in victims of modern hostilities vary within the qualitative characteristics of the minimum-significant risk. The greatest importance in the clinical implementation of risks are risk factors related to the performance of functional duties of servicemen and anatomical features. he use of risk-based analysis must be taken into account in the formation of standards of medical care and treatment protocols for victims of modern hostilities.

KEY WORDS: limb amputation, damage, risk-oriented treatment

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INTRODUCTION

The fighting in eastern Ukraine has resulted in large and varied damage, and such damage differs to some extent from that caused during previous military conflicts [1-5]. The above is due to a number of factors, primarily the hybrid nature of hostilities and the use of modern weapons [6-9]. One of the most severe and common injuries as a result of modern hostilities is the injury of the limbs with the possibility of their loss [10, 11]. Unfortunately, no modern approach to assessing the possibility of limb preservation based on objective criteria has yet been developed [12-14]. In accordance with the requirements of evidence-based medicine, one of such criteria is the result of risk-based analysis and substantiation of relevant conclusions. Therefore, we considered it appropriate to conduct a risk-based analysis of the need for amputation of limbs in case of damage as a result of modern hostilities, which will form a modern risk-oriented treatment and diagnostic tactics, including rehabilitation measures.

THE AIM

The aim of the research - identification, verification and analysis of clinically effective risks of limb amputation as a basis for the formation of risk-oriented treatment and diagnostic tactics in victims with limb injuries due to modern hostilities.

MATERIALS AND METHODS

This research is based on a study of 1,072 cases of limb damage due to modern hostilities in eastern Ukraine in 2014-2020. Both primary (limb separation) and secondary limb loss (amputation) were considered. The actual material of the research was obtained as a result of studying and analyzing the official medical documentation and the authors' own experience. The material was copied and stored on electronic media. Subsequently, it was subjected to statistical analysis in accordance with the requirements of evidence-based medicine. According to the concept of Clinical Risk Management, the risk of limb loss, the anatomical result of the traumatic process, was chosen for evaluation and analysis. This risk was interpreted as Clinical Result Risk. Epidemiological and anatomical signs of damage, as well as clinical and anatomical signs of limbs unviability were identified as risk factors. Interpretation of risk indicators (as the probability of limb loss) was in

Table I. Classification and description of risks

Coefficients	Description of mathematical expectation of events (qualitative characteristic of risk)	Percentage of uncompleted tasks from their total number (%)
0	Theoretically impossible	0
1	Minimal	Less than 0,1
2	Unsignificant	From 0,1 through 0,25
3	Significant	From 0,25 through 0,50
4	Critical	From 0, 50 through 0,80
5	Catastrophic	More than 0,80

Table II. Effective risk of limb loss due to damage, by age

Age	Men	Characteristics of mathematical expectation of events	Women	Characteristics of mathematical expectation of events
18-20	0,05	minimal	0,0009	minimal
20-30	0,35	significant	0,0078	minimal
30-40	0,33	significant	0,0049	minimal
40-50	0,19	non-significant	0,0031	minimal
Older than 50	0,058	minimal	-	
Unknown	0,0053	minimal	-	
Total				

Table III. Effective risks of limb loss according to the anatomical basis of the injury

Anatomical area	Percentage of uncompleted tasks from their total number (%)	Characteristics of mathematical expectation of events
Hand	0,076	Minimal
Forearm	0,034	Minimal
Shoulder	0,094	Minimal
Hip	0,16	Insignificant
Fibia	0,14	Insignificant
Foot	0,05	Minimal

accordance with the classification of risks in the modification S.Guryev, P.Volyanskiy, A.Terentieva (2008) (Table I).

The conclusion of the commission on bioethics of the Ukrainian scientific and practical center of emergency medical care and disaster medicine is positive in terms of materials and research methods (meets the requirements of bioethics).

RESULTS

Assessment of the relative risk of injury from the risk factor "age" indicates that a significant risk of injury have persons aged 20 to 40, not significant – persons aged 40-50, the personal risk of other categories is minimal. This is due to the active participation of people aged 20-40, as well as less active participation of people aged 40-50 in hostilities. An almost similar picture of risk realization by age groups is observed in women. Women aged 20-30 have a significant risk at a rate close to critical. Also a significant risk, but with a lower rate, have women aged 40-50 years, others have minimal risks. This is also due to the fact that mostly young women take part in hostilities. The results of the analysis are shown in Table II.

An analysis of the effective risks of limb loss by the risk factor "anatomical structure (area) of the wound" in the total array of wounded as a result of modern hostilities was also conducted. The data are shown in Table III.

Analysis of the effective risks of limb loss on the basis of "anatomical sign of damage" allows to determine the following: the overall risk of limb damage is 0.46, which is a significant qualitative characteristic close to critical. The lower limbs have a total risk of injury of 0.35, ie significant, and the upper limbs - 0.25, ie the ratio of the risks of damage to the upper and lower limbs is 1 to 2. There is also a tendency of increase of the damage from the proximal to the distal parts. Of course, the occurrence of injuries is of great importance for the full characterization of the risks of loss of limbs, depending on the participation in hostilities, which is determined primarily by the military rank, ie the functional responsibilities of the victim. In order to more thoroughly study the impact of the functional responsibilities of the victim on the risk of limb loss, a risk analysis was performed on the basis of rank in

Table IV. Analysis of the clinical effective risk of limb loss in victims in groups on the basis of rank and clinical and anatomical features

	Hand	Forearm	Shoulder	Hip	Tibia	Foot	Total
Soldiers	0,068	0,13	0,011	0,05	0,08	0,13	0,06
Sergeants	0,16	0,06	-	0,15	0,13	0,07	0,12
Ensigns	-	-	-	-	-	-	-
Junior officers	-	0,2	-	0,13	0,3	0,4	0,15
Senior officers	0,33	-	-		0,2	0,5	0,09
Higher officers	-	-	-	-	-	-	-
Unknown	-	-	0,04	0,04	-	-	0,02

Table V. Risk-oriented analysis of limb loss in victims of the risk factor "immediate cause of limb loss"

Damaged anatomical areas	Component that was decisive in the loss of the limb (amputation)							
	Traumatic amputation		Vascular component		Vascular and nerve component		Infectious	
	*	**	*	**	*	**	*	**
Upper limb	0,28	significant	0,01	minimal	-	-	-	-
Lower limb	0,43	significant	0,07	minimal	0,17	insignificant	0,01	minimal

nosological groups in relation to limb loss. Also, to carefully study the relationship between limb loss (amputation) and the military rank of the victims, we analyzed the clinical performance risks in the victims in the arrays on a clinical and anatomical basis, as shown in Table IV.

Analysis of the risks of limb loss, depending on the performance of functional duties, is shown in Table IV, indicating that there is a significant difference in the implementation of risks in nosological groups.

Analysis of the definition of risks in clinical and anatomical groups by the risk-creating factor "military rank" allows us to establish the following:

In soldiers, the greatest risk of limb loss occurs with injuries of the forearm and foot (0.13 - insignificant risk). All other risks are either in the category of minimal or in the category of insignificant, close to minimal.

Sergeants have an insignificant clinically effective risk of limb loss for injuries to the hand, thigh and lower leg - 0.6, and a critical clinical risk for the injuries to the forearm.

Junior officers have an insignificant clinical effective risk of limb loss for forearm and hip injuries, and a significant clinical risk for lower leg and foot injuries.

Senior officers have a significant risk of limb loss due to damage to the distal limbs, ie the foot and hand, and the risk of foot damage is close to critical. This indicates that in the presence of injuries, officers have a higher risk of limb loss in certain clinical and anatomical forms of injury, namely - damage to the hand, lower leg and foot.

In total, in the general array of this group, soldiers have a clinically effective risk of limb loss of 0.06, ie minimal, sergeants - 0.12, ie insignificant, junior officers - 0.15, ie insignificant, senior officers - 0.09, ie minimal, closer to insignificant.

In general, the analysis of the clinical effective risk of limb loss in victims in the arrays on a clinical and anatomical basis allows us to establish the following pattern: the risk of amputations in the array with the loss of limbs is in soldiers - 0.48, ie significant, close to critical, in sergeants - 0.25, ie on the border of significant and insignificant, in junior officers - 0.13, ie insignificant, in senior officers - 0.03, ie minimal, which indirectly indicates the severity of the damage.

There is also a difference in the structure of risks between groups on the basis of military rank. Thus, among soldiers there is an insignificant risk of limb loss for victims with hip and leg injuries - 0.11 and 0.14, respectively. Other categories have a minimal risk of limb loss. All other groups on the basis of rank have minimal risks of limb loss, but the risk indicators are generally lower in junior and senior officers, and in ensigns they belong to the category of theoretically impossible.

Thus, it can be argued that the nature of the functional responsibilities of the victim directly affects the level and nature of the risk of limb loss from injury due to modern hostilities.

In order to determine the immediate cause of limb loss, a risk analysis was performed on this basis with a division into upper and lower limbs. This risk is mainly realized in secondary amputation. The data are shown in Table V.

The results of a risk-oriented analysis of limb loss in victims of the risk factor "immediate cause of limb loss" indicate that the risk of limb loss ranges from minimal to significant. At the same time, such a causal factor as primary traumatic amputation has a significant risk of injuries that led to the loss of the limb, both upper and lower.

Although the relative risk indicators of both the upper and lower limbs are in the only qualitative category of significant risk, the risk index of the lower limbs is 1.75 times higher than the upper ones. The relative risk of amputation due to damage to the vascular component indicates that

in the implementation of risks it is minimal on the upper limbs - 0.01, and is 0.07 on the lower ones.

The risk of amputation due to damage to the vascular-nerve component is insignificant. On the lower limb it is 0.17. The development of the infectious process in the implementation of risk factors is minimal - 0.01.

DISCUSSION

Thus, verification and assessment of the risks of both primary and secondary loss of limbs in victims of modern hostilities suggests that such risks are associated with clinical and epidemiological, clinical and anatomical and clinical risk factors. Of particular importance is the nature of the functional responsibilities during hostilities, which were assessed on the basis of military rank. It was found out that in general, almost all risks are in qualitative categories to significant and below. There are almost no critical and catastrophic risks of limb loss in victims of modern hostilities, which indicates a high probability of limb preservation in the implementation of adequate and effective treatment and diagnostic tactics [4].

The risks of limb loss associated with risk-generating anatomical factors are not decisive and range from minimal to insignificant. That is, the location of the injury is not a decisive factor in the loss of the limb in victims with gunshot wounds. And victims with injuries to the distal limbs have a higher risk of their loss.

The distribution of the implementation of risks associated with risk-creating factors of age and sex, almost coincide with the nature of the distribution of all participants in hostilities. That is, it cannot be said that age and sex are determinants of limb loss in victims of modern hostilities.

Immediate combatants, primarily sergeants and junior officers, have the greatest risk of losing a limb when injured.

Among the immediate causes of limb loss, only primary traumatic amputation (complete or partial) has sufficient effect, and vascular and nerve damage has a much lower impact, and usually minimal risk. This indicates the possibility of preserving the limb with timely and adequate medical care to the victims [6].

The results of risk-oriented analysis of limb loss in victims of modern hostilities suggest that in the vast majority of cases such loss can be prevented, which sets the task of developing and implementing adequate treatment and diagnostic tactics using modern effective medical technologies, especially on prehospital (tactical) and early hospital stages of medical care.

CONCLUSIONS

1. The risks of limb loss in victims of modern hostilities are not too great and vary within the qualitative characteristics of the minimum-significant risk.
2. The greatest importance in the clinical implementation of risks are risk factors related to the performance of functional duties of servicemen and anatomical features.
3. Risk-generating factors related to the immediate causes of limb losses are significant only in the conditions of primary traumatic amputation, and not in a condition of damage to vascular and nerve structures of the limb. This indicates the possibility of preventing limb loss under conditions of adequate time, volume and quality of treatment.
4. The use of risk-based analysis must be taken into account in the formation of standards of medical care and treatment protocols for victims of modern hostilities.

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ORCID and contributionship:
Sergei O. Guryev: 0000-0003-0191-945X [A-F]
Olexiy S. Solovyov: 0000-0002-6615-4868 [A-D, F]
Dmitriy M. Lysun: 0000-0001-9551-6058 [A, B, D-F]
Natalia I. Iskra: 0000-0001-5976-3625 [A-E]
Vitaly A. Kushnir: 0000-0002-6615-4868 [A-D, F]
Andriy I. Tsvyakh: 0000-0003-0884-4024 [A, B, D-F]
Nataliia O. Marchenkova: 0000-0002-3021-8882 [E, F]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Sergei O. Guryev
Ukrainian scientific and practical centre of
emergency and disaster medicine
Ministry of Health of Ukraine
3 Bratislavskaya st., Kyiv 02166, Ukraine.
tel: +38 (067) 735-15-09
e-mail: gurevsergej1959@gmail.com

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ORIGINAL ARTICLE

COMPARATIVE CHARACTERISTICS OF CLINICAL INDICATORS OF THE CONDITION OF SCAR TISSUE OF THE FACIAL SKIN AT DIFFERENT STAGES OF THE POSTOPERATIVE PERIOD DEPENDING ON THE CHRONOTYPE OF THE PERSON

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Liudmyla I. Voloshyna, Oleksandr A. Toropov, Ihor V. Boyko, Pavlo I. Yatsenko, Dmitriy V. Steblovskyi, Olha P. Bukhanchenko, David S. Avetikov
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: The aim of the study was to improve preventive measures aimed at preventing the formation of pathological scarring of the skin in patients after elective surgery by intra- and postoperative use of cryopreserved placental cells.

Materials and methods: The research was conducted in the Department of Maxillofacial Surgery on the basis of the Municipal Enterprise «Poltava Regional Clinical Hospital. M.V. Sklifosovsky» Poltava Regional Council. A total of 60 patients took part in the study, who were hospitalized for planned surgical interventions in the department of maxillofacial surgery

Results: We obtained clinical data on the processes of scar formation in patients with morning and evening chronotype on the background of local intraoperative injection of cryopreserved placenta extract into the wound. We have proved that short people with an established evening chronotype need additional preventive measures, especially on the 90th and 180th days of the postoperative period.

Conclusions: From our study we can say with confidence that the drug "Cryocel" reduces epithelialization time, promotes optimal wound healing and leads to the formation of more aesthetic scars, which creates optimal both functional and cosmetic results.

KEY WORDS: chronotype, scars, cryoextract, placenta

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INTRODUCTION

Atypical wound healing can lead to the formation of pathological scars (hypertrophic and keloid). Thus, postoperative scars in the head and neck can be not only a cosmetic problem, but also a significant psychological trauma for patients, which often leads to long-term mental health dysfunction. According to statistics, about 10% of the world's population suffers from the formation of pathological scars [1]. Analyzing our previous research, we found that the reparative processes in the wound are influenced not only by the topographic area of the wound, but also the human chronotype [2].

Chronotype a term that was proposed to determine the individual characteristics of the organization of human circadian rhythms [3].

Thus, Belfry and the authors in their research proved that biological rhythm affects not only the mental state, but the human condition as a whole [4]. It is biological rhythms that provide a person's ability to adapt to the environment, and of particular interest is the functioning of the organism taking into account its individual characteristics in terms of organization of biorhythmic processes [5,6,7].

THE AIM

The aim of the study was to improve preventive measures aimed at preventing the formation of pathological scarring of the skin in patients after elective surgery by intra- and postoperative use of cryopreserved placental cells.

MATERIALS AND METHODS

The research was conducted in the Department of Maxillofacial Surgery on the basis of the Municipal Enterprise «Poltava Regional Clinical Hospital. M.V. Sklifosovsky» Poltava Regional Council. To study the materials, we conducted an analysis of patients who were hospitalized for planned surgical interventions for congenital neck cysts and tumor-like formations in maxillofacial surgery. A total of 60 patients took part in the study, who were hospitalized for planned surgical interventions in the department of maxillofacial surgery. Patients were interviewed during the hospitalization, as well as questionnaires to determine the chronotype.

We performed clinical examination and photoregistration of patients on the ninetieth day (90 days) after surgery, 180 and 360 days.

Patients were divided into 3 groups after the questionnaire:

The first group – 20 patients, the first group included patients who had improved the protocol of surgical care. We proposed the introduction of the drug "Cryocel – cryoextract of the placenta" (DP "Interdisciplinary Science Center of Cryobiology and Cryomedicine HAH, AMS and Ministry of Health of Ukraine", Ukraine) into the wound during the intraoperative phase.

The first group was divided into 2 subgroups depending on the biorhythm of the person:

The first subgroup (1.a – patients with morning chronotype) consisted of 10 patients.

The second subgroup (1.b are patients with evening chronotype) subgroup consisted of 10 patients.

The second group consisted of 20 patients. In the second group, as in the first group during surgery, the drug "Cryocel" was injected into the wound. It was also used on the 90th and 180th days of scar formation. We performed electrophoresis with the drug mentioned above. Patients in group 2 were also divided into 2 subgroups according to circadian rhythms.

The first subgroup (2.a – with morning chronotype) consisted of 10 people.

The second subgroup (2.b – with the evening chronotype). It consisted of 10 patients.

The third group consisted of 20 patients. This is a control group. We used the standard method of preventing the formation of pathological skin scars. This group was also divided into 2 subgroups.

The first subgroup (3.a) with morning chronotype) consisted of 10 people.

The second subgroup (3.b – with evening chronotype) 10 patients, respectively.

All patients, regardless of group and subgroup, were operated on in the morning.

We used the parameters to obtain results and to assess wound healing and the quality of postoperative scar formation:

P-1 – Vascularization (from 0 to 2 points);
P-2 – Pigmentation (from 0 to 2 points);
P-3 – Height of the scar (from 0 to 2 points);
P-4 – Surface (from 0 to 2 points);
P-5 – Scar density (from 0 to 2 points);
P-6 – Subjective feelings of the patient (itching) (from 0 to 2 points);
P-7 – Subjective feelings of the patient (pain) (from 0 to 2 points).

RESULTS

We analyze seven indicators in 1a group that characterize the condition of scar tissue. Dynamics of changes in indicators (gradual decrease) P1, P2, P6, P7 have the most uniform direct decrease in indicators from the obtained digital value 0 on the 360th day after surgery. It is of interest to change the P4, P5 to the surface of the scar and the density of the scar. They have a smaller decrease curve, especially at 90 and 180 days. This prompted us to create an additional second clinical group to directly affect the scar of the cryopreserved placenta by its active transfer by electrophoresis.

Also noteworthy is a significant decrease in P3 (scar height) by an average of 1 point from the 90th to the 360th day of postoperative intervention. This is probably true for people with a morning chronotype operated on in the morning.

Analyzing the dynamics of changes in all indicators of the first 1a group, the total average for 90 days of the postoperative period is 5.1 ± 0.43. On the 180th day it dynamically decreases to 3.1 ± 0.18, and on the 360th day it is 1.0 ± 0.14. In our opinion, this indicates a positive combination of two factors: intraoperative administration of cryoextract of preserved placenta and the structural structure of the genetic organization of patients with morning chronotype, who were operated on in the morning. This hypothesis is confirmed by the fact that the average quality indicator on the 180th day has already been reduced by 39.1% compared to the 90th day. The 360th indicator decreases by 80.4% without additional preventive measures during these observation periods.

Analyzing the digital data of indicators P1 P7 in 1b, it should be noted that 0 values on the 360th day of postoperative intervention reaches only the indicator P7 in contrast to 4 indicators in subgroup 1a. In our opinion, this indicates the inadequacy of a single intraoperative injection of the drug «Cryocel» into the wound. It should be noted the relatively small dynamics of the decrease in P1, which on the 360th day decreased by 50% compared to the 90th day in contrast to the previous group. Slightly greater dynamics of decrease was recorded in indicator P2. This figure decreases by 66.7%. Slightly greater amplitude of decrease was recorded in the indicator in P3, especially between the 90th and 360th observation days with a difference of 66.7%. Unlike the previous indicator, the P4 indicator decreases by 14.2% between the 90th and 180th days. Then it decreases significantly by 57.1% on the 360th day compared to the 90th.

Slightly similar dynamics of decrease is shown by indicators P5, P6 on the 180th day relative to the 90th. On the 360th day, the P6 indicator significantly decreases by 83.3% compared to the P5 indicator, which has a significant decrease in this observation period of 38.5%. Such a variety of clinical manifestations and cirrhotic values of indicators indicates the unconditional influence of cryopreserved placenta extract on the condition of scar tissue. Its clinical manifestations are diverse and manifest themselves in the form of instability of the dynamics of some clinical indicators.

This indicates the need for additional topical therapy on the 90th and 180th day in patients with detected evening chronotype, who underwent surgery in the morning.

We obtained clinical data on the processes of scar formation in patients with morning and evening chronotype on the background of local intraoperative injection of cryopreserved placenta extract into the wound. We have proved

that short people with an established evening chronotype need additional preventive measures, especially on the 90th and 180th days of the postoperative period.

Analyzing the dynamics of P1 P7 in subgroup 2a, we obtained the best dynamics of normotrophic scar formation among all studied groups.

We found that the indicators P1, P2 and P7 their average value is 0 on the 180th day of postoperative intervention, and the average data of P6 on the 360th day. Also noteworthy are the lowest figures for the 90th day and their sharp decline in the 180th and especially in the 360th in indicators P3, P4, and P5. It should also be noted that the average overall rate is the lowest in all study groups (0.5 ± 0.15) on the 90th day. Analyzing the dynamics of individual indicators, it should be noted a decrease of almost 50% in P3 on the 180th day compared to the 90th, and 90% between the 90th and 360th days.

The digital data of the P4 indicator decreased the slowest, decreasing by 25% on the 180th day, and by 66.7% between the 180th and 360th days. Indicators P5 and P7 also have a rapid decline, especially between the 180th and 360th day. This indicates a positive effect of electrophoresis with the drug «Cryocel», which was performed on the 90th and 180th days.

The dynamics of the P6 indicator changed significantly, the digital indicator of which decreased by 28.6% on the 180th day according to the previous observation period, and on the 36th day it reached zero values, which once again proves the need for preventive action in the near and near future. the late postoperative period is evidenced by the dynamics of the average quality indicator, which decreased by 86.8% on the 360th day compared to the 90th day.

Analysis of digital data of the average score of indicators P1 P7 in group 2b. It should be noted that the average score of P7 reaches zero values on the 180th day, and 360similar values reach P2. It should be noted a rather low average score in indicators P1 and P2 on the 180th day, and indicators P1 and P6 on the 360th day of the postoperative period. This indicates the formation of a normotrophic scar in most cases, but with additional preventive measures that must be carried out in groups of patients with a pronounced evening chronotype.

This is confirmed by the comparative characteristics of the digital data of indicators in groups 1b and 2b, especially on the 180th and 360th days of the postoperative period. The need for preventive action on the 180th day is evidenced by the dynamics of the overall average score of all indicators in group 2b, which on the 90th and 180th day almost did not change and was equal to 0.60 ± 0.14 and 0.60 ± 0.17 , and after additional electrophoresis on the 180th day probably decreased and on the 360th day reached 0.2 ± 0.1.

We performed a digital analysis of P1 P7 in group 3a. It should be noted that none of them reaches zero on the 180th or 360th day. This is conclusive evidence of the effectiveness of the author's method, especially in the 2nd clinical group, regarding the combined use of cryopreserved placenta extract in the form of injections and electrophoresis. A positive point is the relatively low average score of P1 and P7 on the 90th day. But on the 180th and 360th days only the P7 indicator underwent an optimal decrease in contrast to the P1 indicator.

Also, the need for additional preventive action in the protocol of surgical care is evidenced by the overall average value of all seven indicators, which on the 90th day was 1.10 ± 0.18, and on the 360th decreased to only 0.40 ± 0, 12, which correlates with data from other researchers.

We made remarks after analyzing 3b digital data indicators P1-P7. As in the previous subgroup, none of the indicators reached zero at the end of the observation period. The figures for all seven indicators for the 360th day are probably higher than those in Group 3a, which must be taken into account at the planning stage of surgery.

The overall mean value of all indicators probably correlates and coincides with the indicators of group 3a at all stages of observation. which, in our opinion, is due to an increase in digital data indicators that characterize clinical signs and a decrease in indicators that characterize the subjective feelings of patients.

DISCUSSION

Carrying out a comparative characterization of changes in clinical indicators at different stages of scar formation, it should be noted that a person's biorhythm affects not only the mental state, but also the reparative functions during wound healing.

Chronotype plays an important role in everyone's life, it is circadian rhythms that allow organisms to adjust their physiology and behavior.

So Belfry and the authors believe that the human chronotype affects mental illness. In their research, they describe that patients with the evening type of chronotype have increased aggression and personality disorder, which may occur due to reduced sleep time [4, 6].

We found that the time of surgery and the patient's chronotype affect the postoperative period and the wound healing process. Operations performed in accordance with the maximum activity of the patient reduce the time of repair in the wound, which in turn accelerates hemostasis and restores microcirculation in postoperative tissues [7, 8]

Given the data of previous studies [2, 5, 7], we can say that the use of placental cryoextract in the intraoperative and postoperative stage of prevention not only leads to better both functional and aesthetic results, but also significantly improves the quality of life of patients in early and late postoperative periods.

CONCLUSIONS

The following data were obtained by comparing the digital indicators of the three clinical groups and the obtained results of preventive measures. The best aesthetic result was observed in group 2a, in this group the combined use of the drug «Cryocel» was used in the intraoperative stage by

injection and in the postoperative stage by electrophoresis on the 90th and 180th day. We have statistically confirmed that this technique is well suited for patients with evening chronotype type.For patients with a morning-type chronotype who underwent surgery in the first half of the day, using Cryocel by electrophoresis on day 180 is the method of choice. Thus, from the data obtained, it should be noted that a single intraoperative administration of the drug is not enough to form an optimal postoperative scar, especially for patients with evening chronotype, operated in the morning. Our clear digital differences in the clinical parameters of scar tissue in the control group indicate the need for intra- and postoperative prevention of pathological scarring of the skin of cryopreserved placenta extract.

Therefore, from our study we can say with confidence that the drug «Cryocel» reduces the time of epithelialization, promotes optimal wound healing and leads to the formation of more aesthetic scars, which creates optimal both functional and cosmetic results.

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ORCID and contributionship:
Liudmyla I. Voloshyna: 0000-0002-6098-1758 [A, B]
Oleksandr A. Toropov: 0000-0002-9805-5469 [B, D]
Ihor V. Boyko: 0000-0002-6136-3791 [C]
Pavlo I. Yatsenko: 0000-0002-8440-8905 [C]
Dmitriy V. Steblovskyi: 0000-0001-7907-8406 [D]
Olha P. Bukhanchenko: 0000-0002-5736-8442 [E]
David S. Avetikov: 0000-0002-7055-3589 [F]

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CORRESPONDING AUTHOR
Oleksandr A. Toropov
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
tel: +380669095008
e-mail: alexander.toropov.science@gmail.com

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REVIEW ARTICLE

PECULIARITIES IN PERFORMING MEDICAL EXAMINATION TO ASSESS THE EXTENT OF ALCOHOL INTOXICATION OF DRIVERS ACCORDING TO THE LEGISLATION OF UKRAINE AND SOME OTHER COUNTRIES

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Valentin N. Dvornik[1], Nataliia N. Deviatkina[1], Roman N. Opatsky[2], Vyacheslav V. Garkusha[2], Rostislav Yu. Molchanov[2]
[1]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE
[2]DNIPROPETROVSK STATE UNIVERSITY OF INTERNAL AFFAIRS, DNIPRO, UKRAINE

ABSTRACT

The aim: This study is aimed at conducting a comprehensive analysis of the Ukrainian legislation regulating the alcohol testing procedure for drivers, investigating the practice of its implementation, reviewing international experience in this field, and elaborating proposals for its improvement.

Materials and methods: During the writing of the article, the current legislation of Ukraine is regulated, which regulates the procedure for medical examination to establish the state of intoxication of drivers, namely the Code of Ukraine on Administrative Offenses. This work meets the requirements of the Declaration of Helsinki. Methodology of the study includes general scientific methods (dialectic method, inductive and deductive approaches), special investigative techniques.

Conclusions: Our study has underlined the necessity to improve the legal regulation for more effective alcohol testing program for drivers in Ukraine. This implies the elaboration of guideline for alcohol testing procedure and its approval by the Ministry of Health of Ukraine; to specify and legislate maximum permissible indicator values of blood alcohol concentration; to set the list of drugs and other substances through regulation; to adopt administrative responsibility for driving while intoxicated with alcohol (from 0.2 ppm to 1.1), and criminal liability for driving under severe alcoholic intoxication (1.1 ppm and above).

KEY WORDS: medical examination, alcohol and drug intoxication, medications

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INTRODUCTION

Driving under the influence of alcohol is the most serious and dangerous violation of traffic rules. Often such an offense is the cause of traffic accidents, including victims and death. Thus, during 9 months of 2020, 3,286 road accidents were committed in Ukraine through the fault of drunk drivers, in which 81 people died and 1,152 people received injuries of varying severity [1].

To reduce the number of this type of violation and its negative consequences, important is the inevitability of responsibility for its commission. To do this, first of all, it is necessary to have quality legislation that will establish a fair measure of responsibility for driving while intoxicated, the power of the police to prevent, detect such offenses, as well as document them. At the same time, it is important to maintain a fair balance between individual drivers' rights and the public interest within the meaning of the European Convention on Human Rights [2], which is part of Ukrainian law. The public interest in this case is road safety, as well as the protection of life and health of citizens affected by drunk driving. At the same time, drivers of vehicles should not be subjected to arbitrary actions of the police during their medical examination for intoxication.

As practice shows, the legislation of Ukraine, which determines the procedure for conducting a medical examination for intoxication of drivers of vehicles, is imperfect. It lets avoid the responsibility of persons driving while intoxicated. Impunity, above all, provokes repeated similar offenses, as well as offenses with serious consequences.

Thus, there is a need for a comprehensive study of the procedure for medical examination of drivers to determine the state of intoxication and taking into account international experience in developing optimal recommendations for making appropriate changes to current legislation of Ukraine.

THE AIM

The aim of the study was a comprehensive analysis of the legislation that regulates the procedure for reviewing the state of intoxication of drivers, the practice of its application, as well as international experience in reviewing the state of intoxication of drivers and developing proposals for its improvement.

MATERIALS AND METHODS

During the writing of the article, the current legislation of Ukraine was analyzed, which regulates the procedure of

medical examination to establish the state of intoxication of drivers, namely the Code of Ukraine on Administrative Offenses (hereinafter - KUpAP) [3]. The procedure for directing drivers of vehicles for examination in order to identify alcohol, drugs or other intoxication or under the influence of drugs that reduce attention and speed of reaction, and conduct such examination (hereinafter - the Procedure) [4]. Instruction on the procedure for detecting signs of alcohol, drugs or other intoxication in drivers of vehicles or being under the influence of drugs that reduce attention and speed of reaction (hereinafter - the Instruction) [5], Instruction on police registration of materials on administrative offenses in the field of security road safety, recorded not in automatic mode [6]. The case law of Ukraine on consideration of cases of administrative offenses for driving while intoxicated, international experience of the police in conducting and sending for medical examination of drivers to determine the state of intoxication are also analyzed. The article is written taking into account the scientific and practical work of Ukrainian and foreign scientists, such as O.G. Zerenin and S.M. Mostova, who in their manual revealed the legal aspects, methods, devices and methods of determining alcohol in exhaled air and other bioenvironments [7]. R.Yu. Kohan, who conducted a comparative analysis of US and EU legislation on medical examination for drug intoxication [8],

G.Ye. Dudin and S.V. Kalinin, who disclosed the procedure for referral of drivers for intoxication, as well as problematic issues regarding the medical examination of drivers for intoxication in the Russian Federation in terms of proceedings in the case of an administrative offense [9], A.S. Kravets and N.Yu. Veselov, who considered the problematic issues of legislative regulation of medical examination of drivers in Ukraine [10].

This study was conducted on the basis of general scientific and special methods of cognition. Thus, with the help of the dialectical method of scientific cognition, the conceptual apparatus for examining drivers for intoxication has been studied. Methods of deduction and induction allowed to establish practical problems with the procedure for sending drivers for a medical examination to establish the state of intoxication, the preparation of relevant procedural documents. The comparative legal method allowed to consider the foreign experience of medical examination of drivers for intoxication and the possibility of its implementation in the legislation of Ukraine.

REVIEW AND DISCUSSION

It should be noted that the legislation of Ukraine does not define the concept of medical examination to determine the state of intoxication. The Procedure and the Instruction operate with such concepts as inspection by a police officer at the place where the vehicle is stopped and examination by a doctor of a health care institution. The latter is practically called a medical examination. The basis for the driver's examination at the health care facility is the referral of a police officer after the driver refused to conduct an examination for intoxication at the stop of the vehicle or disagreed with the result of such inspection. Also, in accordance with the legislation of Ukraine, the examination may be conducted in specially equipped mobile points (cars) belonging to health care institutions. But in fact it has found its application in practice.

The problems faced by the police in drawing up a report under Article 130 of the Code of Administrative Offenses, which provides for liability for driving while intoxicated, is that the opinion on the results of a medical examination for intoxication is issued only a few days after it. However, in different regions, this period is calculated differently and ranges from 7 to 14 days. This is due to the fact that the method of medical examination state of intoxication is regulated. There are only guidelines for conducting such a review at the regional level. Accordingly, the police have no right to draw up a report on an administrative offense or to take measures to ensure proceedings in an administrative offense case, such as removing the driver from driving, temporarily detaining the vehicle and temporarily revoking the driver's license. However, in some medical institutions in Ukraine the practice is such that the medical examination first reveals signs of intoxication, then examines the air exhaled by the driver, using appropriate technical means. From this, a conclusion is issued about the state of intoxication immediately after the event. At the same time, samples of the body's biological environment are taken from the driver for laboratory testing, after which a second conclusion is issued. Police officers draw up a report on the basis of their initial detention, but do not send the collected materials to the court until they are re-arrested. If the repeated conclusion has a conclusion about the driver's sobriety, the collected materials, including the protocol on administrative offense, are simply written off. However, this practice is isolated and raises questions about the legitimacy of its application. First, this method of examination of the driver is possible only on the grounds of alcohol intoxication, as drug intoxication, as well as the effects of drugs that affect the speed of reaction and attention, can not be detected by examining the driver exhaled air. Secondly, the degree of alcohol intoxication in accordance with the Instruction is determined by the amount of ppm in the blood and not in the exhaled air. The same problem is faced by police officers, who, firstly, do not have the technical ability to examine the driver for drug intoxication, and secondly, do not have the ability to check the level of alcohol in the driver's blood, despite the fact that The instructions prescribe the algorithm of actions of the police during the inspection.

Another problem with the review of intoxication, which, in our opinion, deserves attention, is the lack of a quantitative indicator of the content of narcotic substances in the blood, necessary for bringing to administrative responsibility. Thus, the establishment of any amount of drugs in the driver's body in fact entails administrative liability under the relevant part of Article 130 of the Code of Administrative Offenses, despite the fact that it provides for liability for driving while intoxicated. However, drug intoxication and blood

levels of drugs are different things. Drug intoxication can last for several hours, and the content of drugs in the blood can be several days or more. Therefore, we believe that it is advisable to establish a normative indicator that takes into account the intoxication of the driver while driving due to drug use. The same applies to drugs that reduce attention and speed of reaction. Their quantitative indicator is also not regulated. Article 130 of the Code of Administrative Offenses provides for liability for driving under the influence of such drugs. This means that the drugs should not just be in the blood, but their amount should be such that they affect the condition of the driver while driving, namely reduce his attention and speed of reaction. Therefore, it is necessary to establish a normative quantitative indicator that determines the impact of drugs on the driver, which reduces his attention and speed of reaction while driving.

Consider the international experience of conducting a survey to determine the state of intoxication of drivers of vehicles. In Germany, a slightly different level of blood alcohol content - for novice drivers with experience up to 2 years, as well as for drivers under 21, this is zero, for other drivers this figure is up to 0.3 ppm, but from 0.3 to 0 .5 ppm - this will be a warning if there are no other traffic violations and the driver can safely drive the vehicle. The indicator at which it is considered that the driver cannot safely drive the vehicle is 1.1 ppm of alcohol in the driver's blood. Thus, in the case of the presence of alcohol in the blood from 0.3 to 1.1 ppm, the determination of the ability to drive safely is the competence of the police. If the presence of alcohol in the blood of more than 0.3 ppm and the inability of the police to drive a vehicle safely and regardless of whether the presence of alcohol in the amount of 1.1 ppm in the blood of the driver is grounds for criminal prosecution under Article 316 of the Criminal Code Code of Germany (Strafgesetzbuch), which provides for a fine or imprisonment of up to one year with deprivation of the right to drive vehicles [11]. At the same time, as in Ukraine, the German police can check the level of alcohol in the exhaled air of the driver, which according to German law is less than the level of alcohol in the blood and is 0.25 ppm. However, you can only be prosecuted if your blood alcohol level is measured. Therefore, it is the driver's duty to undergo a medical examination, and if he fails to comply with this duty, the police officer has the right to detain the driver, then by telephone (for efficiency) the police obtain a prosecutor's or court's permission to take blood samples. Oral permission is later confirmed in writing. The same procedure is provided for signs of drug intoxication or other intoxicants. A separate article in the Criminal Code is provided for resisting a police officer during detention [12, 13].

Administrative liability for violation of traffic rules is enshrined in the Law on Traffic in Section 3 Violations and fines [14]. Thus, Article 24 provides for liability for driving a vehicle if the driver has more than 0.25 ppm in the exhaled air or more than 0.5 ppm in the blood. This article also provides for liability for driving under the influence of intoxicants.

In most EU countries, as in Germany, the blood alcohol limit is 0.5 ppm. These countries include Austria, Belgium, Hungary, Greece, Denmark, Spain, Italy, the Netherlands, Norway, Portugal and France. This figure is higher only in countries such as the United Kingdom, Ireland and Switzerland, and is 0.8 ppm. But in Estonia and Sweden this figure is the same as in Ukraine - 0.2 ppm, in the Russian Federation - 0.3 ppm. In a number of such countries, Sweden, Norway, Holland, Austria, Great Britain, the Russian Federation, the United States, Japan, the quantitative indicator of the level of alcohol in the exhaled air is less than in the blood by about half [7, p. 5-6].

As for the medical examination of drivers for drug intoxication, as in Germany, the police have the right to detain the driver in order to take blood samples only after a court order in most EU countries, as well as in the United States.

Most EU countries prohibit drunk driving caused by any drug. This documents the state of intoxication, not the presence of drugs in human biological environments. Some EU countries set limits on the concentration of drugs in the blood, in excess of which no other evidence is required that the driver is intoxicated. Some European countries have a two-tier system, which on the one hand prohibits drunk driving of any substance, and on the other hand for some specific drugs set limits for drug concentration in the blood or zero concentration thresholds [11, 15].

According to Part 2 of Article 9 of the Constitution of Ukraine, the conclusion of international agreements that contradict the Constitution of Ukraine is possible only after the relevant amendments to the Constitution of Ukraine.

In accordance with Part 2 of Article 8 of the Constitution of Ukraine, the Constitution of Ukraine has the highest legal force. Laws and other normative legal acts are adopted on the basis of the Constitution of Ukraine and must comply with it.

Thus the Constitution of Ukraine laws and other regulations must comply with the provisions of international treaties.

Decree of the Presidium of the Verkhovna Rada of the Ukrainian SSR of April 25, 1974 № 2614-VIII ratified the Convention on Road Traffic.

According to Part 1 of Article 15 of the Law of Ukraine "On International Treaties of Ukraine" current international treaties of Ukraine are subject to conscientious compliance with Ukraine in accordance with international law [16].

In accordance with Part 6 of Article 8 of the Convention, national legislation must provide for special provisions relating to the management of alcohol, as well as the legally permissible level of alcohol in the blood and, where appropriate, in exhaled air, the excess of which is incompatible. with driving a vehicle.

The only legal act in Ukraine that determines the permissible blood alcohol content for driving a vehicle is the Instruction on the procedure for detecting drivers of signs of alcohol, drugs or other intoxication or being under the influence of drugs that reduce attention and speed of reaction , approved by the order of the Ministry of Internal Affairs of Ukraine and the Ministry of Health of Ukraine dated 09.11.2015 № 1452/735 [17]. As for the permissible

content of alcohol in exhaled air, this issue is not regulated by any legal act of Ukraine.

In the case of Pravoe Delo and Shtekel v. Ukraine (application no. 33014/05, p 51, 52), there had been a violation of Article 10 of the Convention. in particular, a norm cannot be considered a law until it has been formulated with sufficient precision to enable the citizen to regulate his behavior.

Thus the current legislation does not contain any provisions that set limits on the amount of alcohol in exhaled air, after which driving is not allowed.

CONCLUSIONS

Taking into account the considered problematic issues that arise in the process of examining the driver for intoxication, as well as taking into account international experience, the following measures are proposed to improve the legal regulation of this process in Ukraine:

1) to develop and approve at the level of the order of the Ministry of Health of Ukraine a method of conducting a medical examination for intoxication;

2) at the legislative level to establish the quantitative maximum permissible level of alcohol in the blood, as well as in the exhaled air at which it is allowed to drive a vehicle;

3) normatively approve the list of narcotic drugs and other substances, as well as their quantitative indicator in the blood, at which it is prohibited to drive a vehicle;

4) legally differentiate liability depending on the degree of intoxication of the person driving the vehicle, namely to establish criminal liability for driving under the influence of alcohol, if such intoxication is 1.1 ppm or more, as well as in state of intoxication. Establish administrative liability for driving while intoxicated from 0.2 ppm to 1.1 ppm;

5) abolish the responsibility for refusing to be examined for intoxication and empower the police to detain the driver in order to pass an examination for intoxication if there are signs of intoxication of the driver of the vehicle and he refuses to voluntarily undergo such examination. to establish the possibility of compulsory collection of blood samples for examination on the basis of a court sanction;

6) legally establish the possibility to remove the driver from driving the vehicle until the results of the driver's examination for intoxication, but not more than 24 hours.

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ORCID and contributionship:
Valentin N. Dvornik: 0000-0002-3693-2403[F]
Nataliia N. Deviatkina: 0000-0003-0137-2124[E]
Roman N. Opatsky: 0000-0002-8658-8153[A]
Vyacheslav V. Garkusha: 0000-0003-0982-0825[D]
Rostislav Yu. Molchanov: 0000-0002-1751-9832[B]

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CORRESPONDING AUTHOR
Nataliia N. Devyatkina
Poltava State Medical University
23 Shevchenko st.6 36023 Poltava, Ukraine
tel: +380958451811
e-mail: devyatkinanata87@gmail.com

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REVIEW ARTICLE

INTRODUCTION OF INNOVATIVE TECHNOLOGIES IN EDUCATIONAL PROCESS OF FUTURE SPECIALISTS IN PHYSICAL THERAPY AND ERGO THERAPY

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Anna V. Fastivets[1], Anatoliy V. Emetc[2], Yevheniia O. Skrinnik[2], Oleksandr V. Petryshyn[2]
[1]POLTAVA INSTITUTE OF BUSINESS PHEE «ISTU», POLTAVA, UKRAINE
[2]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: Is scientific substantiation of introduction of innovative technologies in the process of training future specialists in physical therapy and ergo therapy (occupational therapy).
Materials and methods: We used following set of theoretical research methods: analysis and synthesis of scientific and scientific-methodical literature, which made it possible to identify existing contradictions, to formulate the specifics of the introduction of innovative technologies in the process of training of future specialists in physical therapy and occupational therapy and to find possible ways of its improvement. We also used generalization and systematization of research data, which allowed to form the theoretical and methodological basis of the study. We performed a synthesis of scientific theories, approaches and concepts to identify favorable conditions for the formation of future specialists in physical therapy and occupational therapy. Among empirical methods we used observations and surveys.
Conclusions: Our research shows that the use of such interconnected innovative pedagogical technologies as: technologies of personal and professional development, technology of full acquisition of knowledge, information and communication technologies, exploratory research technologies and technologies of contextual education contributes to the effective implementation of the educational process of training specialists in physical therapy and occupational therapy in a medical school.

KEY WORDS: physical therapist, ergo therapist, innovative technologies, training system for physical therapists and ergo therapists, pedagogical process, medical students

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INTRODUCTION

At the beginning of the XXI century traditional forms and methods of teaching in institutions of higher medical education do not allow students to achieve a holistic understanding of the inner essence of processes and phenomena, own reserves of self-development and the appropriate level of readiness for future professional activity. At the same time, research convinces of the expediency of using the interactive organization of the educational process in the training of specialists in physical therapy and ergotherapy (occupational therapy). The development of creative thinking of medical students requires measures that provide personal and professional development and self-development, originality, flexibility and productivity of thinking, professional mobility. This encourages the use of a technological approach in the training of future professionals, which ensures the transformation of the educational process in the educational institution into purposeful activities of all its subjects and ensures its integrity, personal and socio-economic significance.

THE AIM

The purpose of the study is to substantiate the introduction of innovative technologies in educational process of future specialists in physical therapy and occupational therapy.

MATERIALS AND METHODS

To achieve this goal, we used a set of research methods, in particular, theoretical, such as: analysis and synthesis of scientific and scientific-methodical literature, which allowed us to identify existing contradictions, to formulate the specifics of the introduction of innovative technologies in the training of future specialists in physical therapy and occupational therapy. This also allowed us to find possible ways to improve. The generalization and systematization of research data allowed us to form the theoretical and methodological basis of the study. Synthesis of scientific theories, approaches and concepts provided us the ability to identify favorable conditions for the formation of future specialists in physical therapy and occupational therapy. We also used empirical methods of research such as observations and surveys.

REVIEW AND DISCUSSION

The training of specialists in physical therapy and occupational therapy can be qualitatively improved if following conditions are met: the center of the educational system is the student's personality, his educational and cognitive activities, individual psychological mechanisms of knowledge acquisition, the formation of intellectual and professionally important qualities; management of the edu-

cational process is based on continuous diagnostic control over the level of social and professional development and self-development of students and continuous monitoring of their achievements; individual and typological features of each student, individual subjective experience, ability to constructive interpersonal relations are taken into account; in the educational process the basic didactic, organizational-methodical, psychological and technological provisions, requirements of learning patterns, didactic principles and principles of education are followed [1; 2].

In the practice of higher medical education institutions, the technologies of personal and professional development of students are becoming increasingly important. Since an important aspect of the educational process of training a future specialist is the harmonious development of all his talents, we consider elements of developmental learning technology to be effective for students. Their use activates the inner strengths of medical students (their needs, motives, cognitive abilities), which contribute to the self-development of professionally significant personal qualities and the formation of professional skills based on acquired knowledge. Developmental learning is a focus on human potential and their implementation in the educational process.

The most common are interactive technologies that provide training based on the psychology of human relationships and interactions and on dialogue between teachers and students. This dialogue forms and supports joint educational activity, in which the development of the subjects, involved in it, takes place. The communicative space of the lesson requires the establishment of mutual understanding between teacher and students on the basis of humanistic values and tolerance. The set of all the characteristics by which this communicative space is built is called educational discourse. The aim is to create comfortable learning conditions in which the student feels his success, his own intellectual ability, which makes the learning process more productive [3].

One of the most effective and widespread technologies of the organization of active cognitive activity of students, which helps with developing ability for the analysis of real, unsmoothed, unrefined vital and industrial tasks is the analysis of concrete situations. (*case-study*). When studying a specific situation, the student must determine the following: whether there is a problem, what it is and he must determine their attitude to the situation [4]. This technology teaches students to ask questions, distinguish facts from conjectures, identify important and secondary circumstances, analyze and justify their actions and decisions. Situations and cases serve as concrete examples for ideas and generalizations, provide a basis for a high level of abstraction and thinking, demonstrate feelings and emotions, interest students, help to connect learning with real life experience and show the perspective of applying knowledge in medical practice.

In general, interactive technologies allow future specialists in physical therapy and occupational therapy to achieve following: make knowledge acquisition and skills development more accessible; learn to formulate your own opinion, express it correctly, argue and discuss, defend your position or point of view; learn to listen to others, respect alternative opinions or opposite position; to model different social and professional situations, to enrich own social and production experience through inclusion in various life circumstances and their knowledge; learn to build constructive relationships, determine your place in the group, avoid conflicts or resolve them, find compromises, seek dialogue, etc. [5].

Consider in more detail simulation-game learning technologies (situational modeling), which involve learning through simulation games. The specificity of this technology is to model in the learning process of different types of relationships, situations and circumstances of real life. Imitation and game technologies are designed to implement, in addition to the main didactic purpose, a set of additional tasks, for instance: providing control over the output of emotions; giving a person the opportunity for self-determination; inspiration and help to develop the creative imagination; providing opportunities for the development of skills of cooperation in the social aspect; giving the opportunity to express their opinions [6]. Direct emotional involvement in the situation, competitiveness and collectivism in search of better solutions, the possibility of a wide range of situations, mastering new techniques in medicine, business communication, training intuition and imagination, development of improvisational abilities and ability to respond quickly to changing circumstances made educational games quite popular.

Improving the level of professional competence of future professionals contributes to the use of training technologies that can be effectively used to teach medical students methods and techniques of practical work. Training technologies are a model of joint pedagogical activity of a teacher and students in designing, organizing and conducting the educational process with the obligatory creation of a favorable learning environment [7, 8].

One of the problems in the training process is to take into account the manifestation of role positions in the group. The very situation of the training requires flexibility in the behavior of its participants, which means abandoning the template and accepting new, non-standard game roles. One of the tasks of the training of motivation for professional activity is to expand the repertoire of roles, which allows students to function in reality on the basis of tested and consciously chosen roles in the training.

Among the various exercises and techniques of training work, the basic methods of training to motivate the professional activities of future professionals are group discussion and game technology [9]. Group discussion during training is a joint discussion of a controversial issue that allows you to clarify or change the opinion, position and attitude of group members in the process of direct communication. In the training of motivation formation group discussion is used both to enable students to see the problem from different angles, and for group reflection through the analysis of individual experiences.

Technologies of full mastering of knowledge provide ensuring the possibility for students to choose the optimal learning conditions for them in order to achieve maximum results, namely full mastery of the required number of competencies. In practice, this means developing options for achieving the desired learning outcomes for students with different abilities by changing the learning parameters (time, place, method of presenting information), optimally selected for each student [10].

Within this concept, the taxonomy of B. Bloom's goals, used as a scale to measure learning outcomes, has become widespread abroad. Based on the research of American psychologists, as well as V. Bezpalko, the technology of criterion-oriented learning was developed, which is also called the technology of full assimilation, because it is based on the thesis that each individual is able to assimilate certain educational material, however, the amount of time required for this is different, as it corresponds to individual abilities and capabilities.

In the institution of higher medical education, the technology of full acquisition of knowledge is reflected in the individualization of the educational process. Individualized learning is an organization of mastering knowledge, skills, abilities, which allows each student to study according to an individual schedule (plan and programs adapted to it) and at an individual pace. This allows you to choose the optimal difficulty and complexity of educational material, to organize the acquisition of certain knowledge in a much shorter time than planned or, conversely, to extend it, meaning to create optimal conditions for learning in the area of immediate development [11].

The strategic direction of reforming higher education is the active introduction of modern information and communication technologies in educational activities [12].

The general areas of application of information and communication technologies (ICT) are as follows:

In *technologies of educational activity* – training in the use of ICT tools; information and multimedia tools in the educational process; electronic educational resources and electronic educational and methodical complexes; distance learning; electronic library services; medical practice.

In *technologies of research work* – performing calculations, complex computational tasks, modeling; organization of interaction with Ukrainian and foreign colleagues with the help of Internet resources, video conferencing, webinars based on cloud computing and virtualization tools [13].

Research shows that in the training of future professionals the use of ICT opportunities should be carried out in various ways, for instance: independent search by students of information on the Internet, use of thematically selected multimedia, hypertext electronic educational resources from various disciplines, e-mail, work with electronic directories, databases, library catalogs, creation and demonstration of own creative products (developments, presentations, abstracts), etc. [14].

Computer-based learning technologies are aimed at individual and individualized-group forms of learning. New forms of teaching material with the help of interactive equipment allow combining visual, auditory and kinesthetic learning styles.

It is effective to use a computer to present educational information in the presentation of theoretical material. Modern ICT with the help of multimedia provides teachers of higher medical education with the means to demonstrate complex phenomena and processes and allow them to comprehensively illustrate the material with animation, photos, sound clips and video clips. Visual aids facilitate cognitive function, and the process of perception of educational material is significantly accelerated due to the combination of image and word.

In the future, the task is to create electronic educational and methodological complexes (EEMC), able to provide medical students with a full range of electronic educational resources for individual study of the discipline. This allows following: effectively manage the activities of independent study of the discipline; to stimulate educational and cognitive activities; to provide a rational combination of various types of educational and cognitive activities, taking into account the didactic capabilities of each of them in accordance with the level of learning material; rationally combine various technologies of presentation of educational material (text, graphics, audio, video, animation); use posted materials for virtual seminars, business games, work in projects, etc. [12; 13].

Today, the intensive development of the Internet and communication programs have opened up opportunities for real-time communication at a distance. The most widespread in the educational process is Skype, which allows for discussion and exchange of information (communications with the patient or consultations), send files, keep a notebook, receive news and hold Skype conferences, etc. This facilitates the organization of learning in its various forms, saving time and communicating in "live" format and allows you to quickly solve educational issues. Students work in different modes and communication is not limited to only with teachers [15].

The basis of the organization of educational research activities of future doctors are the ideas of problem-based learning. Initiation of independent search of knowledge by the student through problematization by the teacher of educational material assumes that knowledge is got in the course of the decision of problem situations and skills and abilities are formed by solving problems that do not have a defined answer. The main task of organizing such training is to find appropriate problem situations that have the appropriate level of complexity, motivate and provide the opportunity to acquire new knowledge by solving them at the level of accessible and interesting discoveries. The educational problem determines the direction of mental search, encourages the study of the unknown, which leads the student to learn a new concept or mode of action [16].

We see the essence of project technology in the functioning of a holistic system of support for independent activities of medical students and the organization of educational situations in which they pose and solve certain problems. This

involves systematic and consistent modeling of training solutions to problem situations that require search effort, aimed at research and development of optimal ways to solve them (creation of projects), their public protection and analysis of the results of implementation. Project technology requires each participant to become a subject of their own activity and to form competencies at each stage of design.

A project is an activity aimed at solving a specific problem, at achieving a pre-planned result. The problem of the project should be socially significant and include elements of reports, abstracts, research and any other types of independent creative work of students, but only as ways to achieve the result of the project. The teacher does not transfer knowledge, but directs the student's activities, meaning he supports independent work through following actions: counseling (provokes questions, reflections, self-assessment of activities, modeling different situations, transforming the educational environment) and motivation (reveals to students the situation of project activities as a situation of choice and freedom of self-determination) [17].

The technology of research work is associated with the formation of future specialists' knowledge, as well as the development of skills needed in research, which is one of the leading practical tasks of modern education. Mastering these important cognitive competencies is the key to the success of cognitive activity throughout life. We consider the ability to effectively use the relevant knowledge, as well as the developed skills and abilities to perform scientific research as the most important indicator of cognitive motivation and orientation.

Research knowledge should be understood as specific knowledge about conducting research and the operation of research search mechanisms. Under the general research skills and abilities in this context we understand following: ability to see problems; ability to ask questions; ability to make hypotheses; ability to define concepts; ability to classify; observation skills; skills and abilities to conduct experiments; ability to draw conclusions and inferences; skills of structuring the material [18].

Contextual learning involves the creation of an educational situation as close as possible to real life (especially professional). That is, proper preconditions are created for the transformation of educational activities into professional ones. At the same time, there is a natural increase in the share of students' practical activities with an emphasis on applied goals. The main task of contextual learning as a technology is to optimize teaching and learning based not only on the processes of perception or memorization, but primarily on creative, productive thinking, behavior and communication of students [19]. Contextual learning is organized in such a way that knowledge, skills and abilities are given not as a subject to which the activity of medical students is directed, but as a means of solving the problems of their activities as a doctor.

Introduction of educational material in the context of professional activity and "immersion" in it in the learning process increases the effectiveness of professional training of students, because this material and the process of its assimilation acquire for him a personal meaning and significance. Mastering the norms of competent material actions, professional functions and relations of specialists during educational and professional individual and joint analysis and resolution of professional situations, the student develops as a specialist and socializes.

In the current state of education, contextual learning becomes especially relevant because it focuses on the development of personality, which is understood as an internally and externally determined process of becoming a future specialist as a subject of activity. The holistic construction of professional knowledge of the future specialist requires integrative learning, based on the ideas of didactic integration and synergism, provides both semantic and procedural integration. All components of such training are interconnected and form a coherent system [20].

Thus, the contextual learning strategy, in our opinion, focuses on the essence of vocational education, contributes to the awareness of their own professional position and self-actualization of the future specialist. This technology helps to eliminate some "problem areas" of professional training of future professionals and allows to ensure the achievement of expected results of the educational process, improving the level and quality of training of graduates.

CONCLUSIONS

Thus, the training of specialists in physical therapy and occupational therapy for the effective implementation of the educational process in a medical school requires the use of such interconnected innovative pedagogical technologies as: technologies of personal and professional development; full acquisition of knowledge; information and communication; research and contextual learning.

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ORCID and contributionship:
Anna V. Fastivets: 0000-0001-6333-5519 [A,B,D]
Anatoliy V. Emetc: 0000-0002-2088-8428 [B,E]
Yevheniia O. Skrinnik: 0000-0001-5741-4384 [D,F]
Oleksandr V. Petryshyn: 0000-0002-5722-8036 [A,E,F]

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CORRESPONDING AUTHOR
Anna V. Fastivets
Poltava Business Institute of Higher Educational
Institution "Academician Y. Bugay
International Scientific-Technical University
7 Sinna St., 36039 Poltava, Ukraine
tel: +380664292052
e-mail: anna_fast@ukr.net

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REVIEW ARTICLE

EPONYMOUS TERMS IN THE MORPHOLOGY OF ANGIOARCHITECTONICS OF THE HUMAN HEAD

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Volodymyr Hryn[1], Kseniia Yudina[2], Viktoriia Donchenko[1], Valeriy Zhamardiy[1], Viktoriia Horoshko[2]
[1]POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE
[2]NATIONAL UNIVERSITY «YURI KONDRATYUK POLTAVA POLYTECHNIC», POLTAVA, UKRAINE

ABSTRACT

The aim: The aim of the study is to investigate and describe eponymous terms of angioarchitectonics of the human head and to determine their features and possibilities of their functioning in modern medical terminology.

Materials and methods: The work uses general philosophical and general scientific research methods: dialectical, historical-chronological, bibliographic-descriptive, analytical, etc. This bibliographic analysis is based on published peer-reviewed articles, books, textbooks, monographs. The search period covered the period from 2010 to 2021.

Conclusions: The study of eponymous terms contributes to the disclosure of the evolution of clinical disciplines, the diagnostic process of thinking, as well as the formation of terminological competence in applicants for higher medical education, their mastery of the language of the specialty.

KEY WORDS: angioarchitectonics, artery, vein, eponym, eponymous syndrome, eponymous terms, medical terminology

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INTRODUCTION

Due to the development of cognitive orientation in linguistics, close attention is paid to eponymous terms. It is difficult to imagine a branch of medicine in which eponymous names would not be used to one degree or another. The use of eponymous terms or eponymous names derived from proper names is traditional in the «scientific language» and echoes the early periods of its formation [1-4].

Some authors refer to eponymous terms and those formations that are formed on the basis of toponyms [5, 6]. The wide use of eponyms in term formation is explained, first of all, by the existing tradition and the desire to perpetuate the names of doctors and pioneers who contributed to the development of medicine. The translation of eponyms causes certain difficulties, which are connected, first of all, with the national specifics of their use in the medical literature. In particular, very often the names of scientists are omitted when using medical terms or are not used at all [7]. This significantly expands the scope of eponymy, is the subject of discussion and has led to the relevance of this topic.

THE AIM

The aim of the study is to investigate and describe eponymous terms of angioarchitectonics of the human head and to determine their features and possibilities of their functioning in modern medical terminology.

MATERIALS AND METHODS

The work uses general philosophical and general scientific research methods, namely: dialectical, historical-chronological, bibliographic-descriptive, analytical, etc. This bibliographic analysis is based on published peer-reviewed articles, books, textbooks, monographs. For the purposes of this systematic review, a search of the literature (concerning the consideration of eponyms and eponymous syndromes in anatomical terminology in the study of angioarchitectonics of the human head) was carried out on the World Wide Web, domestic sources of literature, scientific and electronic libraries of Poltava State Medical University by the following keywords: «eponym», «eponymous syndrome», «angioarchitectonics», «artery», «vein» and so on. The search period covered the period from 2010 to 2021, but the review includes some valuable data from earlier years, since these literature sources have significant scientific value.

The following inclusion and exclusion criteria have been used:

- inclusion criteria: original articles published in journals and conference proceedings, books, study guides, monographs; language of publication: Ukrainian, Russian, English;
- exclusion criteria: reviews, case studies, editorials, letters, etc., not peer-reviewed; language of publication: others.

The Ethics Commission of Poltava State Medical University has no comments on the methods used in this study.

Fig. 1. Arnold Friedrich

Fig. 2. Vesalius Andrew

Fig. 3. Willis Thomas

Fig. 4. Galen (Galenus) Claudius

Fig. 5. Haller Albrecht

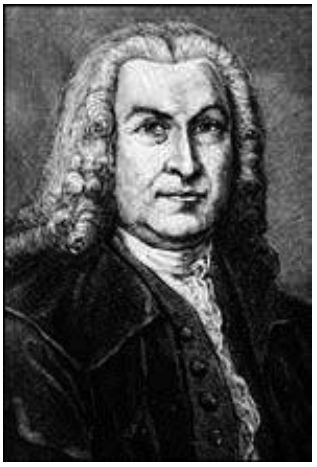

Fig. 6. Heubner Otto

Fig. 7. Dandy Walter

REVIEW AND DISCUSSION

Eponymization in medicine developed gradually, and from the middle of the twentieth century it covered all medical fields. Eponyms are divided into multiple groups, which include biblical, mythological and proper names. It is also possible to divide one's own names into the names of literary heroes, patients, doctors, and scientists [8, 9]. Eponyms can also be divided into such groups as: anatomical terms, names of diseases and syndromes, pathogens, methods of diagnosis and treatment, invasive manipulations, tools and medical devices. The terminology reflects the names of several thousand doctors and scientists from around the world. Such terms may include from one to four names (For instance: Erb-Forster-Barre-Levenstein reflex) [10, 11]. The concept of «eponym» comes from the Greek *eprinymos*, which means «one who gives something or borrows his name from something». This is a concept that is formed from a proper name [12]. Eponyms are most actively used in the morphological field of medical science.

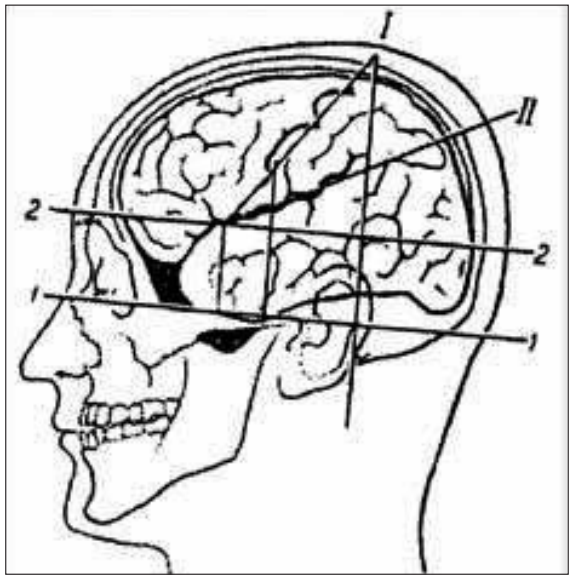

Fig. 8. Krőnlein-Bryussova scheme

Fig. 9. Rauber August

Fig. 10. Ruysch Frederick

This article collects eponymous terms that are used in the study of angioarchitectonics of the human head and are used in both domestic and foreign literature. It is interesting to get acquainted with the portraits of scientists, beacuse some of them are rare in domestic literature.

Fig. 11. Sylvius Francois [Sylvius (De le Boë)]

Fig. 12. Zinn Johann

Fig. 13. Zuckerkandl Emil

Arnold Friedrich (1803–1890), German anatomist. He was born in Landau. He received his medical education in Heidelberg. In 1826 he defended his doctoral dissertation on the structure of the cranial part of the human sympathetic nerve. After that he headed the departments in Zurich (1835–1840), Freiburg (1840-1845), Tübingen (1845–1852) and Heidelberg (1852–1890). His numerous works are devoted to the structure of the brain and peripheral nervous system (Fig. 1).

Arnold's tympanic artery [F. Arnold] (Weber's artery) – anterior tympanic artery (a. tympanica anterior) – branch of the mandibular part of the maxillary artery, which penetrates through the stony-tympanic slit into the tympanic cavity and supplies blood to its mucous membrane. There are options for branching a. tympanica anterior from the

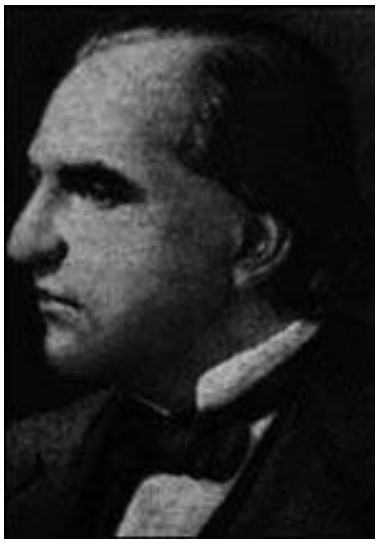

Fig. 14. Charcot Jean

Fig. 15. Schwalbe Gustav

deep auricular artery (mandibular group of branches of the maxillary artery).

Beclard Pierre (1785–1825), French doctor and anatomist. He was born in Angers. He received his medical education in Paris. Doctor and then professor of anatomy at the University of Paris. He studied normal human anatomy and embryology.

Beclard's anastomosis [P. Beclard] – arterial anastomosis within the apex of the tongue between the right and left deep arteries of the tongue.

Breschet Gilbert (1784–1860), French anatomist. He was born in Clermont. In 1818 he was elected professor of anatomy and director of the anatomical laboratory of the University of Paris. He studied the anatomy of the skeletal system, hearing and balance, circulatory system. In 1834 he published a textbook on normal human anatomy.

Breschet's sinus [G. Breschet] – wedge-parietal sinus (sinus sphenoparietalis), steam, located along the posterior edge of the small wing of the cuneiform bone between the leaves of the dura mater, opens into the anterior cavernous sinus.

Browning William (1855–1941), American doctor and anatomist. Born in America. He received his medical education in Leipzig. In 1884–1901 he was a teacher of anatomy and physiology of the nervous system, and from 1901 to 1926 he was a professor of neurology at the hospital's medical college. He studied the blood supply to various parts of the nervous system in normal and in pathology. In 1884 he published a monograph on the anatomy of the venous system of the brain.

Browning's vein (synonym: superior, or large, anastomotic vein, Troll's vein, v. anastomotica superior) – communication path between the middle cerebral vein and the upper longitudinal sinus through the vein of the central (Roland's) furrow.

Vesalius Andrew (1515–1564), scientist of the Renaissance, the founder of modern scientific anatomy. He was born in Brussels to a royal pharmacist. He graduated from the University of Louvain, studied medicine in Paris, where he was a student of the famous anatomist Sylvia J. In 1537 he returned to Louvain, continued to study anatomy, risking his life to extract corpses. In 1537 he went to Padua, received a doctorate in medicine and was appointed professor of surgery and anatomy. In 1538 he published his «Six Anatomical Tables», created in collaboration with the artist Stefan van Kalkar. In 1543 in Basel Vesalius's major work was published, «On the Structure of the Human Body in Seven Books», based on the dissection and study of human corpses and a critique of Galen's erroneous views. In the same year, a short excerpt from this work was published, namely the «Epitom». Fierce attacks by opponents forced A. Vesalius to leave the University of Padua and take the position of court physician of Charles V, and then his son Philip II. In 1559 A. Vesalius moved to Madrid. Deprived of the opportunity to study anatomy, persecuted by slander, he burned some of his manuscripts and in 1564 made a pilgrimage to Palestine. On the way back after the shipwreck he landed on the island of Zante in the Ionian Sea, where he soon died (Fig. 2).

Vesalius's vein [A. Vesalius] – exhaust vein (v. emissaria), penetrates the inconstant hole of the cuneiform bone, connecting the cavernous sinus of the dura mater with the external veins of the head.

Vidius Vidus (1500–1569), Italian anatomist. Born in Florence. He was professor of medicine in Paris, then returned to Italy and from 1548 to 1568 he was Professor of Anatomy and Medicine at the University of Pisa. His work «Seven Books on the Anatomy of the Human Body» (1569) largely repeats the anatomical works of A. Vesalius and G. Fallopus.

Vidius's artery [G. G. Vidianus] (Vidius's artery, Vidianus's artery) – artery of the pterygoid canal (a. canalis pterygoidei) – branch of the descending palatine artery (pterygopalatine group of branches of the maxillary artery), which reaches the ear canal through the wedge-shaped bone canal, supplying blood to its wall.

Vidius's vein [G. G. Vidianus] (Vidius's vein, Vidianus's vein) – vein of the pterygoid canal (v. canalis pterygoidei), accompanies the artery of the same name, collects blood from structures in the area of the torn hole, flows into the pterygoid venous plexus.

Willis Thomas (1621–1675), English doctor and anatomist. Born in Gret Bedwin, Waltshire. He studied theology

first, then medicine at Oxford. In 1660 he became professor of natural philosophy at Oxford, and from 1666 he worked as a physician at London, then the medical physician of King James II. He is the founder of the Royal Medical Society. In 1664 he published his major work «Anatomy of the brain with the addition of a description and function of nerves», which has received wide recognition among doctors (Fig. 3).

Willis's arteria [Th. Willis] – anterior and posterior connecting arteries (aa. communicantes anterior et posterior), involved in the formation of the arterial circuit of the brain. The anterior connecting artery connects the right and left anterior cerebral arteries at the level of the visual junction; the posterior connecting artery connects the posterior cerebral artery to the internal carotid artery.

Willis's circle [Th. Willis] – arterial circle of the brain (circulus arteriosus cerebri), formed on the lower surface of the brain due to the combination of right and left anterior cerebral arteries, posterior connecting (from the system of internal carotid arteries) and right and left posterior cerebral arteries (from the subclavian arteries).

Galen (Galenus) Claudius (131–199), Roman physician and scientist. Born in Pergamum (Asia Minor), he studied philosophy and medicine, studied anatomy in Alexandria. From 158 he worked in his homeland as a doctor at a gladiator school, in 169 he moved to Rome, where he became a court physician. Of his works, of which there are more than 400, half of them have medical content. C. Galen's description of the structure of the human body is a significant step forward in comparison with previous authors, although it contains many errors due to the fact that he studied anatomy mainly in pigs and monkeys. These errors, together with the truths of C. Galen, have been considered an inviolable shrine for many centuries, and it was only after a hard struggle that these mistakes were eliminated. Galen's main work «On the purpose of parts of the human body» was published in Russian in 1971, translated by S. P. Kondratiev and edited by V. N. Ternovsky (Fig. 4).

Galen's great vein [C. Galenus] (Galen's vein) – great vein of the cerebrum (v. magna cerebri), formed by combining the right and left main veins; about 1.0 cm long, located in the transverse slit of the cerebrum, between the lower surface of the corpus callosum (top) and the roof plate of the midbrain (bottom), flows into the right sinus of the dura mater.

Galen's veins [C. Galenus] – veins of the vascular plexus (vv. choroideae), which are tributaries of the deep veins of the cerebrum: the superior vein of the vascular plexus flows into the terminal part of the superior thalamic vein – a tributary of the cerebral great vein, the inferior vena cava is a tributary of the main vein.

Galen's small veins [C. Galenus] – right and left internal veins of the cerebrum (vv. internae cerebri dextra et sinistra), the largest tributaries of the great cerebral vein; each internal vein of the cerebrum is formed in the area of the interventricular orifice, goes back between the two leaves of the vascular layer of the third ventricle, taking numerous tributaries: superior thalamus striatum vein, superior vena cava, etc.

Galen's sinus [C. Galenus] – straight sinus (sinus rectus) of the dura mater, extends in the middle sagittal plane from front to back along the line connecting the posterior part of the cerebral sickle with the cerebellar tent; connects the posterior ends of the upper and lower sinuses, opens into the drain of the sinuses, sometimes falls into the right or left transverse sinuses.

Haller Albrecht (1708–1777), Swiss anatomist and physiologist. He was born in Bern. At the age of 15 he entered the medical faculty of the University of Tübingen, but soon moved to the then famous Leiden University, where he studied under B. Albinus and A. Burgau, and then went to London and Paris, where he studied anatomy with D. Douglas and J. Winslow. In 1727 he received the degree of doctor of medicine (Fig. 5).

After returning home, he studied mathematics from Bernoulli. He traveled many times to the Alps, intensively engaged in botany. In 1736 he was elected professor of anatomy, surgery and botany at Göttingen. He founded a botanical garden, an anatomical theater and the first physiological institute in Germany. He has published many works on anatomy, physiology and embryology («Anatomical drawings», «Anatomical library», «Elements of physiology of the human body», etc.).

Haller's corolla [A. Haller] (Haller's arterial ring, Haller's arterial circle, Zinna's vascular ring) – vascular ring of the optic nerve (circulus vasculosus nervi optici), formed by the posterior short ciliary arteries around the exit of the optic nerve and the central retinal artery.

Heubner Otto (1843-1926), German pediatrician. He received his medical education in Leipzig, where in 1873 he was awarded the title of professor. In 1891 he opened the first modern children's clinic in Leipzig with a department of infants, and in 1894 he took over the Department of Pediatrics in Berlin. With his help, an exemplary children's clinic was built here, headed by O. Geibner until 1913, as well as a mother's and child's home. Among his numerous scientific studies, along with his work in pediatrics, there are important anatomical studies of the central nervous system in children (Fig. 6)

Heubner's artery (synonymous: anterior artery of the striatum, a. striata anterior) – the most permanent large branch of the anterior cerebral artery of the cerebrum; supplies blood to the caudate nucleus and the anterior part of the lenticular nucleus, the anterior leg and the knee of the inner capsule.

Heister's diverticulum [L. Heister] – the upper bulb of the jugular vein (bulbus superior venae jugularis) – dilation of the initial section of the internal jugular vein; contains a jugular ball (glomus jugulare).

Herophilus (Herophilus), ancient Greek physician, born 304 BC. He worked in Alexandria. He was the first to dissect human corpses to study anatomy. Described the meninges, the structure of the medulla oblongata. He knew the ventricles of the brain, vascular plexuses, venous sinuses. He called the initial part of the small intestine the duodenum, observed the lens, eyelids, described the mammary vessels and prostate. The works of this outstanding

scientist are lost in ages. References to his work are found in Celsus, Galen and Rufus.

Herophilus's drainage [Herophilus] (Herophilus's switch, Herophilus's sinus drain) – sinuses drain (confluens sinuum) of the dura mater (well expressed in 30–35 % of people), in which venous blood is collected from the upper and lower arrow sinuses, cerebellar vein and occipital sinus.

Dandy Walter (1886–1946), American neurosurgeon of the late XIX - early XX centuries (Fig. 7).

Dandy's vein – patch vein (v. flocularis) – vein 6–10 mm long, which collects blood from the outer quadrants of the upper and lower surfaces of the cerebellar hemispheres, the medial parts of the bridge, the legs of the brain; flows into the upper stony venous

sinus of the dura mater at a distance of 15 mm from the wedge-shaped process.

Englisch Joseph (1836–1915), Austrian doctor. He taught at the University of Vienna. Known for his work on the clinical anatomy of the human body.

Englisch's sinus [J. Englisch] (Lush sinuses) – the lower stony sinus (sinus petrosus inferior) of the dura mater, placed in the furrow of the same name along the posterior edge of the stony part of the temporal bone, paired, connects the posterior part of the cavernous sinus with the upper bulb of the internal jugular vein (sometimes flows into the sigmoid sinus).

Kiesselbach Wilhelm (1839–1902), German otorhinolaryngologist. He was born in Hanau. Professor of Ear, Nose and Throat Diseases in Erlangen. He studied the pathogenesis and mechanism of diseases of the ear, throat and nose.

Kiesselbach's plexus [W. Kiesselbach] (Kiesselbach's field, Kiesselbach's locus) – venous plexus of the nose (plexus venosus nasi), located in front of the nasal septum, the predominant source of nosebleeds.

Krőnlein-Bryussova scheme [R. U. Krőnlein and S. S. Bryussova] – scheme of craniocerebral topography, for the help of which it is necessary to designate the projection of the main ridges and vessels of the brain on the skin of the brain head. Krőnlein-Bryussova scheme has three horizontal (lower, middle and upper), three vertical (anterior, middle and rear) and one sagittal lines (Fig. 8). The projection of the anterior cerebral artery follows the upper horizontal line, as it is carried out parallel to the middle horizontal line through the point of the crossbar of the projection line and the rear vertical line. The projection of the middle cerebral artery is in the cob sac line of the projection line of the femoral furrow, and the projection under the middle cerebral artery on the main nail shows the crossbar of the anterior vertical and middle horizontal lines. The projection of the posterior cerebral artery is determined above the midline of the horizontal line in its posterior part. The projection of the cerebral part of the internal carotid artery is determined in the square formed by the lower two horizontals and the anterior two verticals. The projection of the trunk of the middle coronary artery is determined at the intersection of the anterior vertical and lower horizontal lines.

Cruveilhier Jean (1791–1874), French anatomist, pathologist and clinician. Born in Limoges, studied theology in Paris, then at the request of his father went to medical school. In 1816 he received the degree of doctor of medicine for his dissertation, in which he proposed to classify diseases not by organs, but by pathological changes in them. In 1825 he was the Professor of Surgery in Montpellier, in 1829 he was Professor of Anatomy there, from 1836 to 1866 he was the Professor of Pathological Anatomy in Paris. He is widely known for his work in the field of normal, comparative and pathological anatomy. He is the author of the well-known textbook on descriptive human anatomy (1834) and the monograph «Anatomy of the Nervous System» (1845).

Cruveilhier's vein [J. Cruveilhier] – mandibular vein (v. retromandibularis), which is a direct extension of the superficial temporal vein; goes down in front of the auricle, penetrates the parotid salivary gland, then goes behind the branches of the mandible and the side of the external carotid artery. At the level of the mandibular angle Cruveilhier's vein turns forward and flows into the facial vein or internal jugular vein.

Labbe Leon (1832–1916), french surgeon. Born in Merlero. Professor of Surgery, Faculty of Medicine, University of Paris. He studied the surgical anatomy of the abdominal cavity. In 1905 he left medicine and became involved in politics.

Labbe's vein [L. Labbe] – inferior connective vein (v. anastomotica inferior) – inflow of the median superficial vein of the cerebrum, going down to the upper lateral surface of the cerebral hemisphere at the border between the temporal and occipital lobes; anastomoses with the inferior veins of the cerebrum and flows into the transverse sinus of the dura.

Rauber August (1841–1917), German anatomist. He was born in Gaardi (Bavaria). He studied at the University of Munich, first at the Faculty of Law, then at the Faculty of Medicine, studied anatomy under N. Rudinger. In 1865 he defended his doctoral dissertation «Fater's nerve bodies, ligaments and periosteum and their relationship to muscle sensation». From 1864 he worked as an assistant in Munich, in 1872 he became an associate professor. During the Franco-Prussian War he served as a surgeon in the army. In 1872, at the invitation of W. His, he went to

Basel, in 1873 he became a professor in Leipzig. In 1886 he came to Russia and until 1911 headed the Department of Anatomy of Yuryevskoho (Tartuskoho) University. He also lectured on microscopic and topographic anatomy. He has published more than 100 works on anatomy, embryology and anthropology. He studied the structure and mechanical properties of bones, spinal and cranial nerves and nodes, the structure of the main part of the sympathetic trunk (Fig. 9).

Rauber's vein [A. A. Rauber] – 1) vein of the pineal body (v. corporis pineale) – collects blood from the pineal gland and flows into the internal vein of the cerebrum; 2) buccal vein (v. buccinatoria), which connects the facial vein with the pterygoid plexus in the buccal muscle.

Ridley Humphrey (1653–1708), English anatomist and general practitioner. He was born in Mansfield. He grad-

uated from the University of London, later improving his skills in Leiden, Oxford and Cambridge. In 1694 he was appointed lecturer in anatomy at the University of London. He is especially known for his research on the anatomy of the brain, its membranes and sinuses. His monograph «Anatomy of the brain, including its mechanics and physiology» (1695) is devoted to these issues.

Ridley's sinus [H. Ridley] – cavernous sinus (sinus cavernosus), steam, placed on the inner base of the skull on both sides of the Turkish saddle. The cavernous part of the internal carotid artery passes through Ridley's sinus surrounded by the sympathetic cavernous plexus and the afferent nerve. The following cranial nerves are located sequentially in the lateral wall of Ridley's sinus: oculomotor (III), block (IV), ocular (VI) and maxillary (VII).

Robinson Frederick (1855–1910), American anatomist and surgeon originally from Wisconsin. In 1882 he graduated from medical school. For 7 years he worked as a general practitioner. During this time, he was improving his skills in surgery, in particular, in 1890 he worked for the famous English surgeon L. Tate in Birmingham. In 1889 he was elected professor of anatomy in Toledo, Ohio, and two years later he became professor of surgery in Chicago. He studied the topographic anatomy of the abdominal cavity and pelvis.

Robinson's duct [F. B. Robinson] – mandibular venous canal, leading from the cell of one of the largest canines to the inner surface of the mandible; the outlet is located near the upper edge of the mandible; observed in fetuses and infants as a variant of the development of venous canals of the mandible.

Rosenthal Friedrich (1780–1829), German anatomist and physiologist. He was born in Greifswald. At first he was a projector of anatomy and physiology in Berlin, and from 1820 he was a professor of anatomy and physiology in Greifswald. Research focuses on the anatomy and pathology of the brain, as well as the organ of hearing and balance.

Rosenthal's vein [F. Ch. Rosenthal] – main vein (v. basalis), paired, formed on the lower surface of the frontal lobe of the cerebral hemisphere in the area of the anterior perforated substance, collects blood from the gray hump and lenticular nucleus and goes back; on the upper surface of the midbrain roof plate, in front of the upper humps, the right and left Rosenthal's veins flow into the cerebral great vein.

Rolando Luigi (1773–1831), Italian anatomist. He was born and educated in Turin. In 1804 he was elected professor of anatomy. Author of works on the structure of the brain and spinal cord.

Rolando's artery [L. Rolando] – artery of the central sulcus (a. sulci centralis), which is a branch of the middle cerebral artery; emerges from the lateral sulcus and enters the central sulcus of the cerebral hemisphere, where it divides and supplies blood to the upper parts of the posterior frontal and anterior parietal lobes of the cerebral hemisphere.

Ruysch Frederick (1638–1731), Dutch anatomist. He was born in The Hague (Fig. 10). He studied medicine at the University of Leiden. In 1666 he was invited to Amsterdam as a pre-lecturer (demonstrator) of the anatomy of the surgical guild, at the same time he was invited to conduct classes at the obstetric school. From 1685 he was a professor of anatomy and botany. In Amsterdam he worked extensively in the field of descriptive human anatomy, as well as in the manufacture of demonstration drugs. He was especially successful in injecting blood vessels. He also achieved brilliant results in embalming corpses. Based on his anatomical preparations, he organized a famous anatomical museum in Amsterdam, which his contemporaries called the «eighth wonder of the world». In 1717, Peter I bought from F. Ruysch a collection of his anatomical preparations, which came to the Kunstkammer (Chamber of Rarities). For his services F. Ruysch was elected a member of the Academy of Natural Researchers of Germany, the Royal Society of Surgeons of England, the French Academy of Sciences.

Ruysch's veins [F. Ruysch] – curly veins (vv. vorticosae), 4–6, are formed in the thickness of the vascular membrane of the eyeball and come out of it along the equator; collect blood from the actual vascular membrane, ciliary body and iris, flow into the upper and lower eye veins, which flow into the cavernous sinuses of the dura mater.

Santorini Giovanni (1681–1737), Italian anatomist, student of M. Malpighi. Born in Venice. He studied medicine in Bologna, Padua and Pisa, where in 1701 he received a doctor's diploma. From 1703 to 1728 he was professor of anatomy and medicine in Venice. He intensively engaged in descriptive human anatomy. He published a major work, «Anatomical Observations» (1714), and a treatise «On the Larynx» (1724); described many small facial muscles.

Santorini's chute [G. D. Santorini] – parietal discharge vein (v. emissaria parietalis), penetrates the parietal opening of the bone of the same name, connects the upper arrow sinus of the dura mater with the superficial temporal vein (inflow of the mandibular vein).

Sviyazheninov's plexus [G. A. Sviyazheninov] – mandibular venous plexus (plexus venosus retromandibularis), formed by veins of the occipital region and papillary process; through the papillary vein these veins connect with the sigmoid sinus of the dura mater.

Sylvius Francois [Sylvius (De le Boë)] (1614–1672), German anatomist. He was born in Frankfurt am Main. He studied medicine at the universities of the Netherlands and Germany, lectured in Paris, where he became famous as a brilliant teacher. From 1632 he worked as a doctor in Amsterdam. From 1658 he was professor of practical medicine in Leiden. He studied the anatomy of the brain, venous sinuses of the brain, variations in the structure of the circulatory system (Fig. 11).

Sylvius's artery [Fr. Sylvius] – middle cerebral artery (a. cerebri media), which is the largest terminal branch of the internal carotid artery; deepens into the lateral sulcus of the cerebral hemisphere, goes up and back in it, goes to the upper side of the hemisphere. Sylvius's artery supplies blood to the upper parts of the frontal, parietal and temporal lobes of the brain (cortex, partially the main nuclei and white matter).

Sylvius's veins [Fr. Sylvius] – middle superficial and deep veins of the cerebrum (vv. mediae superficialis et profunda cerebri): 1) the median superficial vein of the cerebrum is formed from the venous network of the soft membrane on the upper lateral surface of the cerebral hemisphere in the upper part of the central sulcus, anastomoses with the upper boom. In the central sulcus, the vein goes down to the lateral sulcus, which goes forward to the lateral fossa of the cerebrum, reaches the lower surface of the hemisphere and flows into the cavernous or clinotymic sinus of the dura mater; 2) the middle deep vein of the cerebrum originates in the depth of the posterior lateral sulcus of the hemisphere, goes forward, down and medially, collecting blood from adjacent areas of the hemisphere. At the level of the papillary bodies, the middle deep vein of the cerebrum flows into the main vein.

Trolard Paul (1842–1910), French anatomist. Born in Sedan. Professor of Anatomy at the Medical School of Algeria. Scientific research is mainly devoted to the veins of the brain.

Trolard's vein [P. Trolard] (Browning's vein) – superior connecting vein (v. anastomotica superior), which connects the middle superficial vein and the superior veins of the cerebrum; flows into the upper arrow sinus of the dura mater.

Zinn Johann (1727–1759), German anatomist and botanist. He was born in Ansbach (Bavaria). He worked in Göttingen, where he was director of the Botanical Garden. From 1753 he was professor of medicine and director of the Botanical Garden in Berlin. His major work, «An Anatomical Description of the Human Eye Illustrated with Drawings», was published in 1755 (Fig. 12).

Zinn's artery [J. G. Zinn] – central retinal artery (a. centralis retinae), begins at the beginning of the ocular artery, goes forward along the optic nerve; has extraocular and intraocular parts. Approximately 1.0 cm from the posterior pole of the eyeball Zinn's artery penetrates the thickness of the optic nerve and through it enters the eyeball in the depth of the optic disc, where it radiates in the vascular membrane under the retina.

Zinn's vascular ring (synonymous: vascular ring of the optic nerve, circulus vasculosus n. optici), see **Haller's corolla**.

Zuckerkandl Emil (1849–1910), Austrian anatomist, student of I. Girtl. Born in Raab (Austria). In 1874 he graduated from the University of Vienna. He was a searchlight in Amsterdam. After returning home he worked at the Department of Pathological Anatomy under K. Rokytansky. From 1879 he was a professor of anatomy at the University of Vienna, and from 1882 he was a professor at the University of Graz. In 1888 he headed the Department of Anatomy at the University of Vienna. He dealt with issues of descriptive and topographic anatomy. In 1900–1904 he published the «Atlas of Human Topographic Anatomy», which is very popular nowadays (Fig. 13).

Zuckerkandl's veins [E. Zuckerkandl] (Zuckerkandl's venous plexus) – venous anastomoses between nasal veins and cavernous sinuses of the dura mater.

Charcot Jean (1825–1893), French neurologist. Born in Paris. From 1860 he was professor of neuropathology at the University of Paris, and from 1862 he was head of the department of the Salpetrie Hospital, where he worked for 32 years. The early period of scientific activity is connected with works on internal pathology. He has been dealing with special issues of neurology since 1862. He created the doctrine of multiple sclerosis, deepened the information about the clinical picture of Parkinson's disease, and established the connection between polio and damage to the cells of the anterior horns of the spinal cord. He developed the clinical and anatomical direction in neuropathology (Fig. 14).

Charcot's artery [J. M. Charcot] – bleeding artery (a. haemorragica) – one of the branches of the middle central arteries, which start from the middle cerebral artery. Charcot's artery extends along the outer surface of the husk, feeding it and the caudate nucleus and the inner capsule of the terminal brain. The name of the artery is due to its frequent ruptures.

Schwalbe Gustav (1844–1916), German anatomist and anthropologist, a follower of Charles Darwin. He was born in Kedlingburg. He studied medicine in Berlin, Zurich and Bonn. In 1873 he was professor of anatomy in Jena, in 1881 in Königsberg, and in 1883 in Strasbourg. He studied the histology and physiology of muscles, morphology of lymphatic and nervous systems, sense organs. Author of «Textbook of Neurology» (1881) (Fig. 15).

Schwalbe's veins [G. A. Schwalbe] – anterior ciliary veins (vv. ciliares anteriores), which collect blood from the ciliary muscle; they flow into the protein-shell veins, which collect blood from the venous protein-shell sinus of Schlemm-Lyaut. Coming out of the protein shell of the eye, Schwalbe's veins combine with the supraprotein sheath veins, which collect blood from the eyelids and the connective membrane of the eye and enter the veins of the external muscles of the eye, and they, in turn, enter in the upper and lower eye veins.

CONCLUSIONS

Eponyms, as part of the «Scientific language», contribute to a deeper understanding of human activity and culture. The terminology of medicine is the most important source of knowledge about the people who created this science, and the existing trend in modern linguistics to study the human factor allows us to consider eponymous terms in the light of cognitive approach.

Basic eponymous terms that are often used in modern and ancient anatomical literature, and also form the basis for the formation of some clinical terms, have the right to exist, improve in scientific and practical activities of morphologists.

The study of eponymous terms contributes to the disclosure of the evolution of clinical disciplines, the diagnostic process of thinking, as well as the formation of terminological competence in applicants for higher medical education, their mastery of the language of the specialty. Eponyms will always be a significant part of medical terminology.

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ORCID and conrtibutionship:
Volodymyr Hryn: 0000-0001-5894-4416 [B,D, F]
Kseniia Yudina: 0000-0003-3773-8474 [B,E,F]
Viktoriia Donchenko: 0000-0002-9665-7204[A,E,F]
Valeriy Zhamardiy: 0000-0002-3579-6112 [A,E,F]
Viktoriia Horoshko: 0000-0002-5244-5648[E,F]

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The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Viktoriia Donchenko
Poltava State Medical University
23 Shevchenko st., 36011 Poltava, Ukraine
tel: +380662674172
e-mail: vik.donchenko@gmail.com

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REVIEW ARTICLE

STRATEGY FOR THE DEVELOPMENT OF PEDIATRIC SERVICE AT THE LEVEL OF MEDICAL INSTITUTION POLTAVA

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Oksana I. Krasnova, Iryna A. Holovanova, Svitlana M. Tanianskaia, Tetiana V. Pluzhnikova, Mariia O. Rumyantseva, Oleh H. Krasnov
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To analyze the activities of a medical institution in providing medical care to the children's population.

One of the priorities of the work of the Poltava Children's City Clinical Hospital team is close cooperation and contact with the National Health Service of Ukraine under the program of medical guarantees. Since March 2020, on the basis of the Pediatric Department No. 1, infectious and diagnostic beds have been opened for medical care for patients with COVID-19 for residents of the city of Poltava and the Poltava region, which are 100% equipped with a centralized oxygen supply. The main principles for the effective formation and implementation of the strategic tasks of the hospital are: a programmatic and targeted approach to the management of the institution, the implementation of state, regional and local programs. It is important to form a financial, personnel, material and technical plan, to determine the economic efficiency of the measures taken.

The main strategic directions of the hospital are active work on the formation and signing of packages of medical guarantees for 2022 with the National Health Service of Ukraine, carrying out analytical work to comply with quality standards during the treatment and diagnostic process. Important is the high level of surgical activity in the surgical departments with the implementation of modern surgical interventions.

KEY WORDS: medical care, children, reform, development strategy

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INTRODUCTION

One of the important and priority areas of work of the Ministry of Health of Ukraine is the development of a system for providing quality and affordable medical care to children [1]. Children's health is a healthy nation in the future; it is the basis of the country's demographic, economic and intellectual potential. According to statistical data, recently there has been deterioration in medical and demographic indicators [2]. The health status of children and adolescents is also poor, and child morbidity statistics show an increase in non-infectious diseases and disability rates.

All this is a consequence of the adverse impact of environmental and medical factors on children and adolescents, deterioration in the nutrition of children, their sedentary lifestyle, and a decrease in the volume and effectiveness of preventive measures [3, 4]. Today, our state faces the problem of preserving the health of children, namely, reducing infant mortality, childhood morbidity and disability. During the period of reforming the medical sphere, it is especially important to develop the main strategic goals and priority areas in creating an effective system for organizing medical care for the children's population at all levels, which will be aimed at preventive measures, early detection of pathology and maintaining the health of the child.

THE AIM

The aim of our work is to analyze the activities of a medical institution in providing medical care to the children's population.

REVIEW AND DISCUSSION

The process of reforming the health care system in Ukraine has actively affected the pediatric service. The successful development of medical care for children requires comprehensive actions at the level of the state, region and territorial unit, ensuring the use of effective technologies, the systematization of medical processes [5]. The state coordinates all resources and directs them to the development of quality medical care for children. The main strategic directions of the reform include the construction of new modern medical institutions for the provision of medical care to children and the improvement of existing ones [6]. Already today one can observe how new technologies appear in children's medical institutions; new methods of diagnostics and treatment are developed.

Poltava Children's City Clinical Hospital is a medical institution that provides consultative and medical diagnostic assistance to children in the city of Poltava and the Poltava region from birth to 18 years. Outpatient medical

care for the children's population of the city of Poltava is provided on the basis of three children's polyclinic departments - No. 1, No. 2, No. 3 for 240, 300 and 230 visits per medical shift [7, 8].

One of the priorities of the work of the Children's City Clinical Hospital team is close cooperation and contact with the National Health Service of Ukraine under the program of medical guarantees. At the end of 2021, medical care was provided to the population under the medical guarantee program for eleven packages.

This medical institution increases its potential for providing quality medical care through the development of structural units. The medical institution has ten inpatient departments with three hundred beds, of which nine departments serve as regional ones, as well as nine beds there are for intensive care. The admission department provides round-the-clock reception of patients and provides them with emergency medical care in accordance with the protocols approved by the Ministry of Health of Ukraine.

During the COVID-19 pandemic, medical personnel also triage patients into inpatient departments in accordance with their profile. Over the past year, 9206 patients applied to the admission department for medical help (and in 2020 - 8889). At the same time, 8069 patients were hospitalized, which accounted for 78.1% of all visits. The actual work of the bed fund is 133.5 days compared to 146.4 days in 2020. The average length of stay of a patient in a hospital last year was 6.9 (and in 2020 - 7.7). Mortality was 0.25 percent [8].

For of 2019 year, 585 cases of pneumonia were registered, and for of 2020 - 895. For of 2020 year, urgent surgical care was provided to 202 patients, 1873 surgeries were performed [8]. The Early Childhood Department with beds for newborns provides highly qualified medical and diagnostic care from birth to the first three years of age for children with somatic pathologies, including congenital malformations, cardiovascular, endocrine, and gastrointestinal pathologies, prematurely born and newborn children. The Oncohematological Department provides highly qualified specialized care to children with oncological and hematological pathologies under the age of 18 years. The Department is part of the Corporate Group for the Treatment of Leukemia. The Orthopedic and Traumatology Department provides modern diagnostics and treatment of injuries and diseases of the musculoskeletal system. A trauma center for children in Poltava and the Poltava region is open around the clock. The Department of Otolaryngology provides specialized care for children with otorhinolaryngological pathology, including modern surgical interventions.

It should be noted that in the Otolaryngology Department there is an audiology room with appropriate equipment for the early detection of hearing impairment. It is also used by otolaryngologists in outpatient departments. The medical institution has three beds for palliative treatment in the Pediatric, Surgical and Oncohematological Departments, which are equipped with functional beds, all the necessary equipment for treatment and a comfortable stay.

The surgical department provides highly qualified specialized care to children with surgical pathology, including newborns with congenital malformations. There are beds for patients with burns, neurosurgical, maxillofacial, urological, purulent and general surgical beds. The department has an operating unit with modern equipment.

The Department of Anesthesiology and Intensive Care provides intensive treatment of children with various pathological conditions and the postoperative period, provides pain relief during surgical interventions and manipulations in children from birth to eighteen years. Since 2020, intensive care beds have been organized to help patients with COVID-19.

Pediatric Department No. 1 provides medical care to children with complicated forms of acute viral infection, associated viral and bacterial pathology, pneumonia and somatic diseases aged from one month to six years. Since March 2020, on the basis of the Pediatric Department No. 1, infectious and diagnostic beds have been opened for medical care for patients with COVID-19 for residents of the city of Poltava and the Poltava region, which are 100% equipped with a centralized oxygen supply.

The Department of Medical Rehabilitation after the reforms in 2020 develops individual rehabilitation programs for children under the age of eighteen who are under outpatient supervision or inpatient treatment.

In the structural subdivisions of the hospital, the latest technologies and modern standards for the management of patients with various pathological processes are actively introduced into medical practice, new equipment is being mastered, and personnel are being trained to work with it.

So, since 2021, a follow-up room has been operating on the basis of the hospital, which provides medical care to children at risk of developing chronic diseases and developmental delays. Outpatient consultations are carried out for them. Neonatologists, neurologists, ophthalmologists, orthopedists, rehabilitation specialists, and psychologists have created a register of these patients.

The priority direction of work is the work of the department of medical rehabilitation. Rehabilitation is carried out by a professional team, which includes: a doctor of physical and rehabilitation medicine, a physiotherapist, an ergotherapist, a massage nurse, a physical therapy nurse, a speech therapist, a psychologist. The physiotherapist works directly with the child, uses the technique of manual therapy, kinesiotherapy. The occupational therapist teaches the child to perform daily functions, the speech therapist is engaged in the development, restoration of speech and swallowing.

The main achievements of the work of the Children's City Clinical Hospital of the city of Poltava is that the hospital has the status of "Child Friendly Hospital". The hospital has been accredited for the first qualification category, has a license to carry out business activities in medical practice and has the status of "Clean hospital that is safe for the patient."

The hospital has a license for activities related to the circulation of narcotic and psychotropic drugs. This medical

institution actively cooperates with the Poltava State Medical Aid in the main areas of development of the medical industry, under the state programs "Diabetes Mellitus", "HIV/AIDS Prevention" and "Tuberculosis Prevention".

Studies show that the provision of quality medical care to children is the main direction of the work of the Ministry of Health of Ukraine [1]. The country needs a healthy nation, this is the main resource of the country. Unfortunately, the health indicators of children are poor [3, 4]. State authorities should constantly develop measures to improve the health status of children.

The main achievements of the work of the Children's City Clinical Hospital of the city of Poltava is that the hospital has the status of "Child Friendly Hospital". The hospital has been accredited for the first qualification category, has a license to carry out business activities in medical practice and has the status of "Clean hospital that is safe for the patient."

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The main principles for the effective formation and implementation of the strategic tasks of the hospital are: a programmatic and targeted approach to the management of the institution, the implementation of state, regional and local programs. It is important to form a financial, personnel, material and technical plan, to determine the economic efficiency of the measures taken.

The introduction of an effective personnel policy through the planning of material incentives, the development of standards for the provision of medical care, the introduction of modern models of the quality of the activities of a medical institution, and the establishment of relationships between medical workers are widely used. Attention is constantly paid to the continuous professional development of medical personnel, the creation of conditions for the introduction of new medical documents based on the principles of evidence-based medicine.

CONCLUSIONS

The main task of the teamwork of the staff of the Poltava Children's City Hospital is to provide qualified medical care to children and prevent diseases. Therefore, the main strategic directions of the hospital are active work on the formation and signing of packages of medical guarantees for 2022 with the National Health Service of Ukraine, carrying out analytical work to comply with quality standards during the treatment and diagnostic process. Important is the high level of surgical activity in the surgical departments with the implementation of modern surgical interventions. This is impossible without improving the material and technical base, introducing the latest technologies in outpatient and inpatient departments, and mastering new medical equipment. Much attention should be paid to the implementation of state programs and medical guarantees for the children's population of the city and region, continuous professional development of all medical personnel, repairs in all structural divisions to create comfortable conditions for patients. At the same time, it is necessary to constantly monitor the effective use of medical equipment, medicines and material resources of the hospital, expand the information space for working with the population, providing information on priority medical services and the volume of specialized medical care in the institution.

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ORCID and contributionship:
Oksana I. Krasnova: 0000-0001-9819-1818 [B, D]
Iryna A. Holovanova: 0000-0002-8114-8319 [A, F]
Svitlana M. Tanianskaia: 0000-0003-3764-2181 [B]

Tetiana V. Pluzhnikova: 0000-0001-8300-854 [B]
Mariia O. Rumyantseva: 0000-0001-7247-9792 [B]
Oleh H. Krasnov: 0000-0002-8704-1686 [B, D]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Oksana I. Krasnova
Poltava State Mediacal University
23 Shevchenko st., 36000 Poltava, Ukraine
tel: +380984673750
e-mail: krasnovaoksana197@gmail.com

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CASE STUDY

DIFFERENTIAL DIAGNOSIS OF SOFT TISSUE TUMORS

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Denys Kapustianskyi, Ihor Ivanytskyi, Tetiana Ivanytska, Valeriy Zhamardiy, Viktoriia Donchenko
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim of the study is to identify clinical signs of neurilemmoma of the upper limb, its main ultrasound and X-ray distinctions from other benign tumors of soft tissues.
To make a preliminary diagnosis, it is advisable to use different methods of imaging, such as: ultrasound, MRI, radiography. Radiological diagnosis of soft tissue tumors should be based on the integrated use of radiological and ultrasound methods with mandatory consideration of clinical and anamnestic data such as patient age, topographic location of the tumor and its growth rate. Although ultrasound and MRI do not allow to completely differentiate the tumor, but they help to choose the right tactics of the patient. Treatment is to remove the tumor and includes cesium dissection and removal from the nerve bundle, using magnification.

KEY WORDS: neurilemmoma, schwannoma, tumorof the peripheral nerve, tumor of soft tissues, ultrasonography

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INTRODUCTION

Soft tissue tumors are a very common pathological condition. Doctors of various specialties such as surgeons, dermatologists and general practitioners have to diagnose these diseases. The most common among them are fibromas and lipomas, which usually do not cause discomfort, have different localization and slow growth, they rarely acquire characteristics of malignant tumors [1]. Because these tumors are most common, patients are often diagnosed with lipomas or fibromas when soft tissue formations are detected, even without additional examinations, which leads to misdiagnosis and, consequently, incorrect treatment.

Neurilemmomas (schwannomas) account for 5 % of benign soft tissue tumors [2]. Neurilemmoma, also called schwannoma, develops from cells of the Schwann sheath of peripheral nerves. Schwann cells (neurolemocytes) are involved in the formation of nerve fibers, forming their shells, in the peripheral nervous system [3]. In embryogenesis, Schwann cells are of neuroectodermal origin. As peripheral nerves are formed, Schwann cells migrate from the spinal ganglia parallel to the axons and close them within their cytoplasm.

Neurilemmoma is formed in the soft tissues along the nerve trunks and cranial nerves, occasionally it can be formed in the internal organs. Neurilemmoma is the most common benign tumor of the peripheral nerves sheaths. Mainly located on the small and medium-sized nerves of the head, neck, flexor surface of the extremities, sometimes affecting the skin. The presence of a soft tissue tumor near the peripheral nerve gives the doctor grounds to think about the presence of neurilemmoma.

Clinically, schwannoma is a painless encapsulated formation (single or multiple), which is observed mainly under the age of 50, affects men and women with equal frequency. In most cases, neurilemmoma is a solitary tumor, multiple schwannomas are observed in Recklinghausen's disease or schwannomatosis [2, 4]. Elbows and tibial nerves are often affected by neurilemmomas.

Neurilemmomas are the most common benign tumors of peripheral nerves, but to distinguish them from neurofibromas and neurocarcinomas in the preoperative period is quite difficult. Often the final diagnosis is established during surgery or in the postoperative period. To make a preliminary diagnosis, it is advisable to use different methods of imaging, such as: ultrasound, MRI, radiography. Radiological diagnosis of soft tissue tumors should be based on the integrated use of radiological and ultrasound methods with mandatory consideration of clinical and anamnestic data such as patient age, topographic location of the tumor and its growth rate. Although ultrasound and MRI do not allow to completely differentiate the tumor, but they help to choose the right tactics of the patient. Treatment is to remove the tumor and includes cesium dissection and removal from the nerve bundle, using magnification.

THE AIM

The aim of the study is to identify clinical signs of neurilemmoma of the upper limb, its main ultrasound and X-ray distinctions from other benign tumors of soft tissues.

CLINICAL CASE

Given the relatively high percentage of diagnosed neurilemmoma in the postoperative period and the need

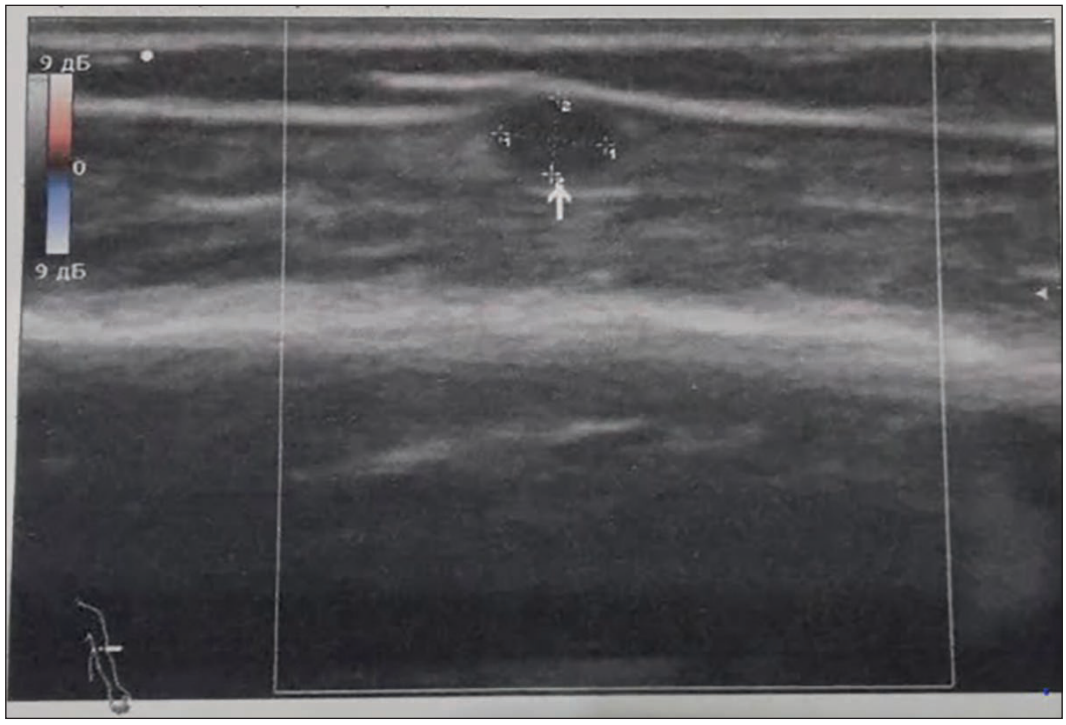

Fig. 1. Ultrasound of shoulder neurilemmoma, showing a hypoechoic encapsulated formation

for great caution in its surgical treatment to preserve the integrity of the nerve, we consider it necessary to describe the clinical case from our own experience.

Patient A, 22 years old, complained to the family doctor about the appearance of a small painful formation in the elbow area on the right. Application of pressure on the formation lead to significant increase in pain which irradiated in the shoulder and forearm, limiting the atient's movements. Patient first noticed a slight pain six months ago after strenuous exercise in the gym (squeezing off the floor). Palpation revealed a small, up to 5 mm, painful formation, the occurrence of which is associated with exercise. On examination: on the extensor surface of the shoulder 2 cm above the elbow joint a formation with a diameter of about 7 mm was palpated, which was sharply painful after slight pressure and percussion, the pain irradiated to the shoulder and fingertips. The patient was referred for soft tissue ultrasonography. Ultrasound examination revealed in subcutaneous adipose tissue a hypoechoic formation of a round shape with clear, smooth contours, homogeneous structure, hyperechoic capsule, not associated with the surrounding soft tissues. The formation was visualized near the triceps tendon. It shifted together with the tendon during active and passive movements. Between the tendon and the formation revealed a thin (diameter less than 1 mm) hyperechoic structure associated with the formation. It was seen by us as *nervus cutaneus brachii posterior* (Fig. 1). When performing compression elastometry, streinratio was 4.8 when compared to adipose tissue and 3.9 when compared to muscle tissue, indicating increased stiffness of tumor tissue. Performing ergot Doppler mapping revealed the absence of blood vessels in the tumor. We concluded that there is a high probability of tumor origin from the *nervus cutaneus brachii posterior* and the need for its surgical removal.

After clarifying the topographic and anatomical features of the location of the tumor it was removed. Under local infiltrative anesthesia with 2 % lidocaine solution, the skin was dissected over the tumor, then with the help of a surgical magnifying glass under visual control the tumor was isolated and removed. We needed to remove the tumor as accurately as possible with minimal nerve damage, to prevent further neurological dysfunction. The removed tumor was placed in a preservative and sent for histological examination. According to the results of histological examination, the diagnosis was «Neurilemmoma». In the early postoperative period, the patient noted the absence of clinical symptoms, the condition improved significantly, the pain disappeared, there was no violation of neurological functions. The postoperative wound healed with primary tension. Sensitivity in the area of innervation of the nervus cutaneus brachii posterior was not disturbed. At next examination of the patient after 1 month any features or pathology in the course of the postoperative period were not revealed.

DISCUSSION

Schwannomas or neurilemmomas are rare tumors. They are often single and benign formations, but can be multiple and associated with neurofibromatosis type 1 and schwannomatosis [5]. Neurilemmomas are most common in the head, neck, including the brachial plexus and spinal nerves. Limbs are affected less often. In this case, tumors are mainly

found on the flexor surfaces of the limbs. Schwannomas of the upper extremities are quite common, manifested by mild symptoms and lack of neurological manifestations [6]. It is important to make a differential diagnosis of neurilemmoma from the most common soft tissue tumors.

The most common benign soft tissue tumors are lipomas formed by matured adipose tissue. They can be single or multiple, including systemic lipomatosis. They are distributed in the population regardless of gender and age. Clinically, these are painless soft-elastic formations. The skin over them is not changed. A common feature of lipoma on radiographs and echograms is the density of the shadow or echogenicity, which is the same as subcutaneous fat. Liposarcomas have increased echogenicity [7, 8].

Benign formations of fibrous origin – desmoids (invasive fibromas). These are peculiar tumors, which are characterized by local infiltrative growth and constant recurrences. A characteristic clinical feature of fibromas is a very dense consistency with limited mobility. Radiologically they are characterized by the density similar to the muscle tissue, elongated shape and infiltration of surrounding tissues, including subcutaneous fat. In ultrasonography, they are homogeneous and hypoechoic.

The main clinical sign of neurilemmoma is pain on pressure with irradiation along the corresponding nerve. The radiograph reveals a small formation with a clear contour of the ovoid shape in the subcutaneous fat or in the muscles in the projection of the main nerve. At ultrasonic research of a schwannoma is revealed as homogeneous hypoechoic formation.

Diagnosis of neurilemmoma at the preoperative stage is quite a difficult task, because the tumor grows slowly and in most cases has few clinical manifestations. Proper diagnosis is essential for proper planning of surgery, which aims not only to remove the tumor, but also to preserve the integrity of the affected nerve. Neurilemmomas have many features in common with soft tissue tumors, which are the cause of misdiagnosis and, accordingly, incorrect treatment tactics. Differential diagnosis of neurilemmoma should also be performed with neurofibromas, ganglion cysts, lipomas, xanthomas and malignant tumors [6]. For example, neurofibroma is indistinguishable from schwannoma during objective examination. The final diagnosis can be established only histologically. There are no specific symptoms to distinguish these tumors. The slow growth of benign tumors of the nervous tissue allows it to adapt to being under pressure without significant dysfunction. The onset of the first symptoms is more related to the location than the size of the tumor, because the symptoms of neuronal compression occur with increasing tumor mass, and this process can take several years. Unlike schwannoma, neurofibroma often becomes malignant, turning into neurosarcoma [8]. Because this process is long and the body adapts to it, it may not cause sufficient vigilance of the primary care physician. Therefore, it is advisable to conduct a comprehensive diagnosis of any detected tumor to prevent adverse effects.

Clinically, neurilemmoma has the appearance of a rounded almost painless formation. For neurilemmoma Tinel's positive symptom is characteristic, there can also be paresthesias and local increase in sensitivity. Sometimes patients complain of spontaneous pain, weakness in the extremities. Often this formation is detected by chance in the absence of clinical symptoms. Neurilemmoma rarely leads to impaired motor activity. Impaired motor function is often caused by neurosarcomas [9]. The presence of the formation that causes pain when pressed, shifts in the transverse direction relative to the axis of the limb and is almost motionless with its longitudinal displacement, percussion of the formation causes paresthesias along the affected nerve, which is analogous to the symptom of Tinel – these are the most characteristic clinical signs of neurilemmoma at the initial examination [10]. Quite often the correct diagnosis is made already in the operative or postoperative period that can have undesirable consequences for the patient. Untimely diagnosis of neurilemmoma in clinical practice is associated with nonspecificity and sometimes absence of symptoms. Schwannomas have a soft consistency, are mobile, grow slowly, and are sometimes completely painless. They are often diagnosed as lipomas, fibroids or xanthomas, which is the reason for their improper management. Visualization of the formation with the help of magnetic resonance imaging, radiography or ultrasonography will allow you to make a correct diagnosis in time. Ultrasonography is the primary method of visualization of soft tissue tumors, as it is widespread, accessible and fast to perform. In ultrasonography neurilemmoma has the form of a clearly defined hypoechoic and homogeneous mass with the presence of acoustic amplification.

Magnetic resonance imaging is the best way to diagnose neurinoma. These tumors may vary in their manifestations but, as a rule, most of them are isointensive in T1 mode and hyperintensive in T2 mode. Variations may be due to the content of fat and melanin in some neurinomas. About 40 % of schwannomas contain a cystic component. All neuromas accumulate contrast [11]. Unfortunately, these patterns of signal intensity do not help to distinguish tumors of neurogenic origin, but make it possible to clarify the neurogenic origin of the tumor. Neurilemmomas have a low risk of recurrence or malignancy. Surgical treatment is the careful removal of the tumor using optical lenses for magnification [10, 11]. After accurate, correctly performed surgery, neurological defects are virtually absent.

CONCLUSIONS

Thus, we conclude that it is necessary to conduct a differential diagnosis of soft tissue tumors using existing imaging methods (radiography, ultrasound, magnetic resonance imaging), which will help prevent misdiagnosis and prevent possible resection of the affected nerve. Peripheral nerve tumors should be included in the list of possible causes of soft tissue tumors. Only the presence of close cooperation between a family doctor, ultrasound diagnostician or radiologist and surgeon will qualitatively increase the possibilities of early diagnosis and treatment of atypical soft tissue diseases. Ultrasound diagnosis allows to identify

the differential signs of soft tissue tumors, the association of a tumor with a peripheral nerve, and to choose the correct tactics of patient management. Treatment of schwannomas is precise dissection and its removal from the nerve bundle, using a magnifying glass.

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ORCID and contributionship:
Denys Kapustianskyi: 0000-0002-7633-7713 [B-D,F]
Ihor Ivanytskyi: 0000-0002-0583-2303 [B-D]
Tetiana Ivanytska: 0000-0002-2556-7658 [B-D]
Valeriy Zhamardiy: 0000-0002-3579-6112 [A,E,F]
Viktoriia Donchenko: 0000-0002-9665-7204 [A,E,F]

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CORRESPONDING AUTHOR
Viktoriia Donchenko
Poltava State Medical University
23 Shevchenko st., 36011 Poltava, Ukraine
tel: +380662674172
e-mail: vik.donchenko@gmail.com

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ABSTRACT BOOK

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ПОЛІТИКА ЄВРОПЕЙСЬКОГО СОЮЗУ ЩОДО ЗДОРОВ'Я ГРОМАДЯН

EUROPEAN UNION POLICY ON PUBLIC HEALTH

Наталія В. Харченко[1], Олександр В. Харченко[2]
[1]ПОЛТАВСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ, ПОЛТАВА, УКРАЇНА
[2]ПОЛТАВСЬКИЙ ДЕРЖАВНИЙ ПЕДАГОГІЧНИЙ УНІВЕРСИТЕТ ІМЕНІ В.Г. КОРОЛЕНКА, ПОЛТАВА, УКРАЇНА

Nataliia V. Kharchenko[1], Oleksandr V. Kharchenko[2]
[1] POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE
[2]POLTAVA STATE PEDAGOGICAL UNIVERSITY NAMED AFTER VG KOROLENKO, POLTAVA, UKRAINE

Вступ: Політика ЄС впливає на здоров'я різними способами.
Мета: Описати політику ЄС в напряму високого рівня захисту здоров'я людини.
Матеріали та методи: Використовувався теоретичний метод дослідження.
Результати: Такими способами можуть бути починаючи від середовища, в якому живуть його громадяни, на роботу, яку вони виконують, і на їжу, яку вони їдять. Лише частина з них належить до сфери діяльності, яку можна описати як політику охорони здоров'я, і в деяких випадках рішення приймаються на інших підставах, які негативно впливають на здоров'я. І це незважаючи на положення, згідно з якого «високий рівень захисту здоров'я людини повинен бути забезпечений при визначенні та здійсненні всіх політик та діяльності Співтовариства».
Більш суперечливим є те, що регулювання реклами продуктів, що містять або потенційно небезпечні для здоров'я, також було прийнято на рівні ЄС. Частиною причин суперечок є відсутність «відповідності» між цим регламентом та його правовою основою у праві ЄС, тобто внутрішньому ринку. Регулювання ЄС щодо оподаткування тютюнових виробів показує подібну відсутність «відповідності» між правовими базами ЄС та цілями охорони здоров'я, що стоять за оподаткуванням тютюнових виробів, які, по суті, мають на меті перешкодити людям кинути палити та заохотити курців кинути палити.
Висновки**:** Тому ми вважаємо, що цінним напрямком політики ЄС у сфері охорони здоров'я в майбутньому буде продовжувати зосереджуватися на конкретних сферах діяльності та розробляти чіткіші та точніші пріоритети за допомогою прозорих процесів на основі даних про тягар хвороб та ефективність політики.

КЛЮЧОВІ СЛОВА: політика ЄС, сфери діяльності, їжа, тютюнові вироби.

KEY WORDS: EU policy, areas of activity, food, tobacco products.

KEY ISSUES AND PUBLIC HEALTH PROJECTS IN UKRAINE

Svitlana V. Kharchenko, Iryna A. Holovanova, Natalia A. Lyakhova
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

Introduction: The health of the population is a determining factor in the progressive development of society, its prospects in social, economic, scientific, cultural and other spheres of life. The science of public health studies the health of the population and its protection system. New challenges and threats, growing demands on public health require modern development strategies and programs.

The aim: Get acquainted with the projects implemented with international partners by the State Institution «Public Health Center of the Ministry of Health of Ukraine», aimed at combating HIV / AIDS, tuberculosis, development of new monitoring and evaluation programs and pharmaceutical management.

Materials and methods: Literary sources, normative-legal base are analyzed. Methods such as sociological, economic, prognostic are used.

Results: Over the past 10 years, Ukraine has adopted 45 national programs and 10 comprehensive government-approved measures aimed at improving and prolonging the life expectancy of citizens, which to some extent duplicate or only complement each other. Thus, in terms of stimulating the birth rate and forming a healthy generation, 15 of them were adopted, on prevention and treatment of AIDS – 5, elimination of the consequences of the Chernobyl accident – 5, tuberculosis control – 4, disaster medicine development – 3, elderly health – 3, drug addiction – 3. At the same time, there were extremely insufficient resources for the effective implementation of the declared programs, as 4 % of them were not funded at all, 6 % funding was limited to one third, 10 % – almost half, 26 % of programs were partially funded. As a result, the implementation of state targeted programs, which were supposed to significantly improve the health of the Ukrainian people, was extremely low.

State Institution «Public Health Center of the Ministry of Health of Ukraine» was established pursuant to the order of the Cabinet of Ministers of the Ministry of Health of Ukraine from 18.09.2015 № 604. «Public Health Center of the Ministry of Health of Ukraine» implements the following projects:

Care & Treatment. Full title of the project: Strengthening the Capacity of HIV / AIDS Treatment in Ukraine within the Framework of the US President's Emergency Initiative on HIV / AIDS (PEPFAR).

SILab. Full title of the project: Supporting the HIV Epidemiological Surveillance and Management System / Improving the Quality of Laboratories of the Ministry of Health of Ukraine, Improving the Use of Strategic Information and Capacity Building of Public Health under the US President's Emergency HIV Assistance Initiative / AIDS (PEPFAR), implemented by the State Institution «Public Health Center of the Ministry of Health of Ukraine».

Projects of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF):

GF Project 2018 – 2020. Full title of the project: Accelerating Ukraine's Progress in Ensuring a Sustainable Health Response to Tuberculosis and HIV.

GF Project 2021 – 2023. Full title of the project: Accelerating Progress in Reducing the Burden of Tuberculosis and HIV in Ukraine.

GFA / THL. Full title of the project: Supporting Ukraine in the Development of a Modern Public Health System.

FHI. Full title of the project: Cooperation with Ukraine in the Field of Health Care.

The Union. Full title of the project: Strengthening the Implementation of the WHO Framework Convention on Tobacco Control in Ukraine.

Conclusions: Implementation of projects, programs, public health measures will reduce the excessive burden on the country's budget, outline the phasing of reforms to assess the effectiveness of each stage to improve public health in Ukraine, taking into account the requirements of present and future generations (individuals) and society as a whole.

KEY WORDS: public health, public health projects, public health programs of Ukraine.

MODERN ASPECTS OF CARE FOR PATIENTS WITH DIABETIC FOOT SYNDROME AT THE PRE-HOSPITAL STAGE

Oleh H. Krasnov, Vitalii I. Liakhovskyi, Ruslan B. Lysenko, Ivan I. Niemchenko, Oksana I. Krasnova
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

Introduction: One of the most severe complications of diabetes mellitus is the Diabetic foot syndrome (DFS). This is a combination of damage to the nerves and main arteries of the lower extremities, with the formation of ulcerative defects and destruction of the foot tissues. Patients have a lifetime risk of developing ulcers about 25%, and the risk of amputation is 22 times higher. In most patients with complications of DFS, these problems can be prevented with proper prevention and timely treatment.
The aim: To improve the results of diagnosis and medical care in patients with DFS at the pre-hospital stage.
Materials and methods: Materials were international clinical protocols, observation methods and analytical.
Results: To improve the results of treatment of patients with DFS, they must be provided with blood glucose correction, medical supervision, timely angiosurgical intervention, wearing orthopedic shoes, and the use of preventive measures. However, in the conditions of the war in Ukraine, the fulfillment of these tasks is a difficult task. The current situation requires the proper organization of outpatient care for these patients. For this purpose, the Diabetic foot clinics are optimally suited, where a vascular surgeon and an endocrinologist work. The patient is diagnosed with sensory disorders, vascular lesions, the presence of foot deformity, and then the treatment is prescribed. It is important to remove hyperkeratosis, which is a therapeutic and preventive measure. During the work of this clinic, the following groups of patients are distinguished: those who need hospitalization in Endocrinology, in the Department of vascular surgery for revascularization, in the Department of surgical infection in the presence of foot tissue infection. Currently, it is very important to properly treat local wounds using modern wound dressings, which makes it possible to suppress the infection and delay the next dressing. Topical for patients is TCC (Total Contact Cast) technology, which allows you to treat ulcers even in active patients, that makes them mobile. To monitor the carbohydrate regime and monitor patients in our time, constant contacts are needed between authorities, volunteers, family doctors and endocrinologists. It is necessary to improve communication between outpatient services with inpatient endocrinological departments, surgical and vascular departments.
Conclusions: Nowadays the solution of these problems will allow us to reduce the rate of complications of DFS and increase the effectiveness of the treatment of such patients. The active work of the Diabetic foot clinics enables patients to receive all the preventive and therapeutic care they need at the pre-hospital stage, to reduce the risk of complications of diabetes mellitus.

KEY WORDS: diabetes mellitus, diabetic foot syndrome, health care, diabetic foot clinic.

REGULATORY REGULATION OF EMPLOYMENT OF INTERNALLY DISPLACED MEDICINES IN OTHER HEALTHCARE INSTITUTIONS DURING THE WAR

Nataliia O. Liakhova, Tetiana V. Pluzhnikova, Maksym V. Khorosh, Inna V. Bielikova
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

Introduction: Due to the military aggression of the Russian Federation, many doctors have lost their jobs and are forced to look for new opportunities to work in safer regions.
The aim: To investigate the mechanism of normative regulation of employment of medical workers from among internally displaced persons.
Materials and methods: Materials: orders of the Ministry of Health of Ukraine for the period 24.02.2022 to 30.05.2022. Methods: bibliosemantic, content analysis.
Results: The Ministry of Health of Ukraine has regulated the employment of medical workers who lost the opportunity to work at their main place of work due to a full-scale war in medical institutions of other regions of Ukraine to provide medical services to the population by issuing an order. In this case, it is a question of temporary involvement of physicians from among internally displaced persons in health care institutions, which is regulated by the order of the Ministry of Health of Ukraine from 04.03.2022 № 414 «On accounting and reporting of medical workers who provide medical care outside the main place of work during martial law on the territory of Ukraine «.
The procedure for employment in another health care facility for internally displaced health workers is the same as for regular employment. That is, the doctor must submit a package of documents consisting of:

- passport or ID-card - an identity document;
- identification number;
- a document confirming education and professional qualification (diploma, certificate of a specialist, certificate of qualification category);
- a document confirming professional experience (employment record book);
- applications for employment.

If available, the candidate may also submit other additional documents.
The simple procedure and the absence of any restrictions have allowed many physicians to find employment: to date, 2,375 internally displaced health workers have taken advantage of the opportunity to find employment in another medical facility.
Conclusions: The Ministry of Health of Ukraine regulates the employment of medical workers who have been forced to change their place of residence due to hostilities, which allows both doctors to work and receive wages in these difficult times, and medical institutions to improve medical care.

KEY WORDS: medical workers, employment, internally displaced persons

ЗАСТОСУВАННЯ «МЕТОДУ ВІДВОЛІКАННЯ» НА ПРИЙОМІ У СТОМАТОЛОГА ДЛЯ ДІТЕЙ, ЩО ЗАЗНАЛИ ВПЛИВУ ВОЄННОГО СТАНУ

THE USE OF «DISTRACTION METHOD» AT THE DENTIST'S RECEPTION OF CHILDREN AFFECTED BY MARTIAL LAW

Ольга В. Шешукова, Валентина П. Труфанова, Тетяна В. Поліщук, Аліна І. Максименко, Софія С. Бауман, Катерина С. Казакова, Анна С. Мосієнко
ПОЛТАВСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ, ПОЛТАВА, УКРАЇНА

Olga V. Sheshukova, Valentina P. Trufanova, Tetyana V. Polishchuk, Alina I. Maksymenko, Sofia S. Bauman, Kateryna S. Kazakova, Anna S. Mosienko
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

Вступ: Під час воєнного стану діти належать до найвразливішої категорії населення. Перебуваючи в небезпеці, зазнаючи впливу тривалого стресового стану, дитина не отримує повноцінних умов для розвитку. Через відчуття тривоги, напруги, страху, невизначеності ускладнюється процес соціалізації дитини. Діти, які вимушені бути переміщеними із зони активних бойових дій, стикаються з проблемою соціальної адаптації, перебуваючи в нових соціальних умовах.

Мета: Ознайомити з особливостями менеджменту поведінки дитини, що зазнала впливу воєнного стану на прийомі у лікаря-стоматолога.

Матеріали та методи: Майже всі батьки погодяться, що часто складно переконати дитину, навіть в мирний час, не боятися лікарів і стоматолога в тому числі. Страх маленького пацієнта перед лікуванням зубів виникає незалежно від можливих відчуттів під час прийому, та від виду виконуваних процедур. Ситуація воєнного стану вкрай негативно впливає на здатність дитини до співпраці з лікарем-стоматологом. Найчастіше в цей період діти контактують з стоматологом вимушено, з приводу нагальної потреби в лікуванні, а не в профілактичних цілях. тому умовах надзвичайної ситуації найбільшої актуальності набуває налагодження системи комунікації між дітьми, їхніми батьками та лікарем – стоматологом, що в подальшому дасть змогу завоювати довіру у дитини. Важливою метою роботи лікаря-стоматолога дитячого є поступове, покрокове проведення дитини через стоматологічне лікування для здобуття нею позитивного відношення до стоматології.

Результати: Від того, чи зуміє лікар завоювати довіру дитини, залежить успіх подальших взаємин із стоматологом. У деяких дітей попередній досвід перебування в стоматологічному кабінеті викликає тривогу та негативне відношення до стоматолога. В більшості випадків такими контрольованими, але наляканими дітьми можна управляти без використання медичних препаратів.

Навіть у екстремальній ситуації лікуванню повинна передувати загальна бесіда, що доведе батькам план лікування дитини,його обсяг та необхідність профілактичних заходів. Поряд з профілактикою карієсу і роз'яснювальними бесідами з батьками, необхідно мотивувати дитину до стоматологічного лікування вже уражених карієсом зубів. Для встановлення довірчих стосунків між маленьким пацієнтом і лікарем-стоматологом надійним другом може стати «Твінкі Стар» - унікальний кольоровий пломбувальний матеріал фірми VOCO (Німеччина). Завдяки застосуванню різнокольорового матеріалу у дитини страх від відвідування клініки поступово змінюється на інтерес. Причиною тому стають кольорові пломби. Від думки про те, що зуб можна розфарбувати, діти перебувають у захваті. вони беруть активну участь в процесі лікування, а саме самостійно вибирають колір майбутньої пломби - рожевий, золотий, зелений, синій, срібний, лимонний або помаранчевий. Вибір кольорової пломби позитивно налаштовує дитину на лікування і вони забувають про страх в кабінеті стоматолога. Твінкі Стар створений на компомерній VOCO-технології, що особливо зарекомендувала себе при лікуванні тимчасових зубів у дітей. Твінкі Стар має наступні характеристики: висока біосумісність, відмінна адгезія і краєва адаптація, низька абразія, вивільнення фтору – профілактика вторинного карієсу,швидке і прости внесення із капсули, добре полірується, вісім яскравих, ефектних і блискучих відтінків. Одним з важливих ефектів від застосування цього матеріалу є те, що діти позбавляються страху до стоматолога.

Як приклад, наводимо клінічну ситуацію: з сімї тимчасово переміщених осіб пацієнт Давид, 6 років, має 8 зубів уражених карієсом. Декілька попередніх візитів до лікаря-стоматолога за місцем проживання не мали успіху. Давид не дозволяв лікарю провести огляд порожнини рота з використанням стоматологічних дзеркала та зонду. До прийому під час очікування дитина без покійна, з насторогою відноситься до медичних працівників, прислуховується до звуків, що долинають з кабінету, насторожено озирається, тримається за руку мами. Асистент запросив Давида до кабінету під час лікування іншої дитини, яка не боїться стоматолога і продовжує лікування. Давид уважно спостерігав за процедурами протягом усього прийому, ми в свою чергу, детально коментували всі свої дії та розповідали про стоматологічний інструмент. Це дозволило нам зробити перший крок у встановленні довірливих стосунків і провести стоматологічне обстеження Давида. Перше відвідування на цьому було завершено, мамі надали рекомендації з гігієни порожнини рота. На наступний день проведене препарування каріозної порожнини в зубі 7 за допомогою екскаватора. До препарування дитині були продемонстровані різнокольорові пломби на моделі щелепи. Наступним кроком у лікуванні був вибір кольору пломби. Давид вибрав першу пломбу зеленого кольору. Результат пломбування дитина могла побачити у люстерці і із задоволенням продемонстрував «кольоровий» зуб мамі. Дитина з нетерпінням чекала наступного візиту до стоматолога. Після остаточного завершення лікування Давид був щасливий і залюбки погодився продемонструвати свої пломби. Санація порожнини рота проведена в чотири відвідування.

Висновки: Лікувальний процес дитини, яка зазнала впливу екстремальної ситуації, у дитячого стоматолога пов'язаний із рядом психологічних проблем і потребує їх методологічно правильного вирішення Лікар - стоматолог дитячий повинен бути хорошим психологом, щоб знайти індивідуальний психологічний підхід, одним з яких є метод відволікання, до кожної дитини і провести якісно лікування .

КЛЮЧОВІ СЛОВА: діти, дистракційний метод, стоматологічна допомога**.**

KEY WORDS: children, distraction method, dental care.

НАДАННЯ СТОМАТОЛОГІЧНОЇ ДОПОМОГИ ДІТЯМ ПІД СЕДАЦІЄЮ В УМОВАХ СЬОГОДЕННЯ

PROVISION OF DENTAL CARE FOR CHILDREN UNDER SEDATION IN TODAY'S CONDITIONS

Ольга В. Шешукова, Тетяна В. Поліщук, Анна С. Мосієнко, Валентина П. Труфанова, Аліна І. Максименко, Катерина С. Казакова, Софія С. Бауман
ПОЛТАВСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ, ПОЛТАВА, УКРАЇНА

Olga V. Sheshukova, Tetyana V. Polishchuk, Anna S. Mosienko, Valentina P. Trufanova, Alina I. Maksymenko, Kateryna S. Kazakova, Sofia S. Bauman
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

Вступ: Дитина є складною біосоціальною істотою, всі органи і системи якої знаходяться в стані постійного розвитку та перебудови, крайньої нестабільної рівноваги. Тому відчуття болю і страху має виражений вплив на його організм.

Більшість стоматологічних втручань супроводжується больовими відчуттями більшої чи меншої інтенсивності, тому знеболення є однією із найбільш актуальних проблем стоматології, а особливо дитячої стоматології. Надзвичайно важливо, щоб візит до стоматолога в дитинстві та підлітковому віці мав позитивний характер, тому що цей дитячий досвід залишає значний слід у дорослому віці відносно сприйняття необхідності відвідування стоматолога.

Завдяки застосуванню седації для препарування зубів у стоматології, багатьом маленьким пацієнтам вдається позбутися страхуперед стоматологічним кабінетом, що роками формувався. Седацію використовують у стоматології в тих випадках, коли дитині має бути відпрепарований не один, а кілька зубів відразу - це скорочує не тільки кількість відвідуваньстоматологічноїклініки, але й кількість препаратів, які використовуються для анестезії, що також сприятливо позначається на здоров'ї пацієнта.

Мета: Вивчити скорочення строків санації дітей із субкомпенсованою та декомпенсованою формами активності карієсу на можливість усунення негативного відношення до стоматологічних маніпуляцій при застосуванні седації.

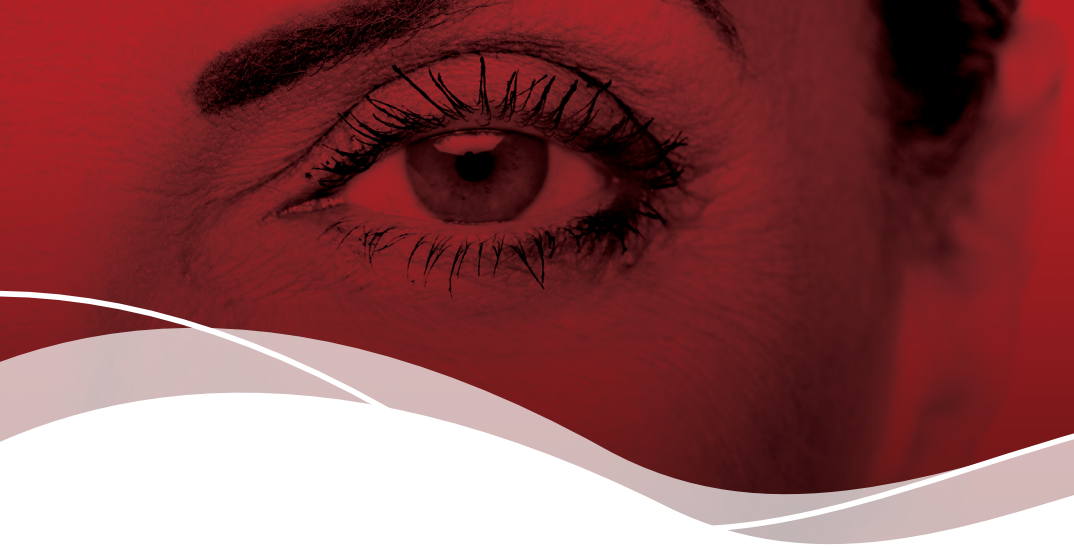
Матеріали та методи: Нами проліковано під седацією 19 пацієнтів із субкомпенсованою та декомпенсованою формами активності карієсу у віці від 2 до 8 років. Дослідження проводилося набазі КП «МДКСП ПМР». Для порівняння були вибрані сліпим методом історії хвороб 38 дітей того ж віку, які лікувалися традиційно.

Результати: Всі діти при первинному зверненні були обстеженні педіатром та виключені всі можливі протипоказання до загального знеболення.Лікування дітей при традиційному методі лікування (тобто без застосування загального знеболення) необхідна кількість відвідувань становила 5-7 прийомів. При лікуванні під седацією скорочувались до 1-2 відвідувань.У 78% дітей не сформувалося негативне відношення до стоматологічних маніпуляцій, що надало можливість проводити подальшу санацію порожнини рота без застосування загального знеболення. Відсутність страху у дитини сприяло в подальшому формуванню довірливих відносинміж лікарем та дитиною, що полегшило виконання лікувальних маніпуляцій, яке, в свою чергу, підвищило якість лікування.

Висновки: Застосування загального знеболення на амбулаторному прийомі дає можливість скоротити кількість відвідувань та підвищити якість лікування із мінімальним психо-емоційним стресом, як для дитини так і для лікаря.

КЛЮЧОВІ СЛОВА: діти, седація, стоматологічна допомога.

KEY WORDS: children,sedation, dental care.



Pallas Kliniken

Kliniki Pallas specjalizują się w okulistyce i medycynie estetycznej. Zatrudniamy ponad 350 pracowników w 18 lokalizacjach i jesteśmy jednym z wiodących świadczeniodawców w Szwajcarii. Poprzez innowacje stale rozwijamy naszą ofertę usług w tych dziedzinach. Czy to poprzez nowe metody leczenia, sprzęt, dodatkowe lokalizacje i współpracę, a może poprzez współpracę z Państwem w najbliższej przyszłości?

W celu uzupełnienia istniejącego zespołu w naszej grupie w lokalizacjach **Olten, Aarau i Solothurn** poszukujemy osoby z inicjatywą i niezależną osobowością na stanowisko

specjalista oftalmologii (k/m/i) 60–100%

Główne obowiązki

Specjalista oftalmologii w naszych placówkach w Olten, Aarau lub Solothurn zapewnia profesjonalną obsługę medycznych konsultacji zachowawczych. Osoba ta będzie kompetentnie wykorzystywać swoje umiejętności we współpracy z obecnymi lekarzami specjalistami. Do jej obowiązków będzie należało zapewnienie naszym pacjentom optymalnej opieki. Wraz ze zgranym zespołem będzie świadczyć usługi medyczne na najwyższym poziomie. Będzie korzystać z szerokiej sieci wybitnych lekarzy, ciągłych szkoleń wewnętrznych i zewnętrznych oraz nowoczesnego środowiska pracy.

Profil kandydata

- Specjalizacja w dziedzinie oftalmologii
- Kilkuletnie doświadczenie w dziedzinie oftalmologii
- Przedsiębiorcze myślenie i działanie zorientowane na sukces i cel, z wysokim zrozumieniem jakości i obsługi
- Wysoka inteligencja emocjonalna i odporność w kontaktach z pacjentami, pracownikami oraz innymi partnerami wewnętrznymi i zewnętrznymi
- Umiejętność szybkiego rozpoznawania problemów i samodzielnego opracowywania rozwiązań
- Wybitne kompetencje doradcze w języku niemieckim, wyrażane w mowie i piśmie w sposób zrozumiały i adekwatny do adresata

Nasza oferta

W ramach udzielania konsultacji udostępniamy nowoczesną infrastrukturę, w której można profesjonalnie leczyć pacjentów, zarówno ambulatoryjnie, jak i stacjonarnie. Zapewniamy optymalne i jak najlepsze wsparcie podczas pracy. Oprócz uregulowanych godzin pracy (brak dyżurów nocnych i niedzielnych), które pozwalają na spędzanie czasu z rodziną i czas wolny, oferujemy także możliwości szkoleń wewnętrznych i zewnętrznych. Chętnie udzielimy dodatkowego wsparcia podczas stawiania pierwszych kroków w Szwajcarii.

Wykorzystując swoje wieloletnie doświadczenie, innowacyjność, a przede wszystkim umiejętność aktywnego słuchania, mogą Państwo naszym pacjentom pozwolić odczuć wyraźną różnicę.

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Dodatkowych informacji udziela pan Melvin Fankhauser, HR Recruiter/doradca HR ds. lekarzy, tel. +41 58 335 31 84 lub e-mail: melvin.fankhauser@pallas-kliniken.ch

Pallas Kliniken AG
Melvin Fankhauser | Louis Giroud-Strasse 26 | CH-4600 Olten | www.pallas-kliniken.ch