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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ
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Шнайдер К.В., Моренко М.А., Ковзель Е.Ф., Гагауова М.Р., Усенова О.П. КЛИНИЧЕСКИЙ СЛУЧАЙ ТЯЖЕЛОЙ КОМБИНИРОВАННОЙ ИММУННОЙ НЕДОСТАТОЧНОСТИ.....	107
Fedota O., Roschenyuk L., Tyzhnenko T., Merenkova I., Vorontsov V. PHARMACOGENETIC EFFECTS OF METHOTREXATE IN UKRAINIAN PATIENTS DEPENDING ON THE MTHFR GENOTYPES (CLINICAL CASES)	111
Пилипко И.В., Галлицкая-Хархалис А.Я., Гешик Т.Р., Флекей Н.В., Папчашви Н.Я. МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ ВНУТРЕННЕЙ СТРУКТУРЫ ОРГАНОВ МОЧЕПОЛОВОЙ СИСТЕМЫ КРЫС ПРИ МОДЕЛИРОВАНИИ ПОРТАЛЬНОЙ ГИПЕРТЕНЗИИ	117
Mostovoy Y., Demchuk A., Konstantynovych T., Chichirelo-Konstantynovych K., Demchuk A. FROM THE PERSISTENT EPSTEIN-BARR VIRUS INFECTION TO ANGIOIMMUNOBlastic T-CELL LYMPHOMA - DRAMATIC CONVERGENCE. ANALYSIS OF THE CLINICAL CASE	122
Avilova O., Shyian D., Marakushin D., Erokhina V., Gargin V. ULTRASTRUCTURAL CHANGES IN THE ORGANS OF THE IMMUNE SYSTEM UNDER THE INFLUENCE OF XENOBIOTICS	132
Абхазова М.В., Квачадзе И.Д., Цагарели М.Г., Мжаванадзе Д.Ш., Чичинадзе Г.П. КОРРЕЛЯЦИЯ СТЕПЕНИ МЕХАНИЧЕСКОЙ БОЛЕВОЙ ЧУВСТВИТЕЛЬНОСТИ С КОНЦЕНТРАЦИЕЙ БЕЛКА μ -ОПИОИДНОГО РЕЦЕПТОРА В РАЗЛИЧНЫХ ФАЗАХ ОВАРИАЛЬНО-МЕНСТРУАЛЬНОГО ЦИКЛА	137
Iatsyna O., Vernygorodskiy S., Kostycv F. MORPHOLOGICAL ASSESSMENT OF NO-SYNTASE DISTRIBUTION IN OVERACTIVE BLADDER AND STRESS URINE INCONTINENCE IN ANIMAL MODELS ADMINISTERED WITH EXPERIMENTAL PHARMACOCORRECTION REGIMENS	143
Voloshchuk N., Melnik A., Danchenko O., Nechiporuk V., Kosechenko N. THE STATE OF THE CYSTATIONINE GAMMA-LYASE / H ₂ S SYSTEM IN THE LIVER AND SKELETAL MUSCLES OF RATS WITH HYPERCHOLESTEROLEMIA UNDER SIMVASTATIN ADMINISTRATION.....	150
Karsanidze A., Antelava N., Gorgasledze N., Ghonghadze M., Okudzhava M., Pachkoria K. STATIN-ASSOCIATED INTOLERANCE AND ITS PREVENTION.....	155
Iermolenko T., Krivoshapka A, Shapoval O. DYNAMICS OF INDICATORS OF ANTIOXIDANT PROTECTION IN RESPONSE TO THE APPLICATION OF SODIUM POLY-(2.5- DIHYDROXYPHENILEN)-4- THIOSULFATE ACID IN EXPERIMENTAL ACUTE KIDNEY INJURY	161
Ларина С.Н., Сахарова Т.В., Чебышев Н.В., Беречикидзе И.А., Деркачева Н.И. ОСОБЕННОСТИ МЕТАБОЛИЗМА ПАРАЗИТИЧЕСКИХ ПРОСТЕЙШИХ И ВОЗМОЖНОСТИ РАЗРАБОТКИ АНТИПРОТОЗОЙНЫХ ПРЕПАРАТОВ (ОБЗОР)	171
Kuzminska E, Omelchuk S., Karlova E., Grinzovsky A. DRUG-FREE MODALITIES OF IRON DEFICIENCY CONDITIONS IN UKRAINE	175
Bagmut I., Kolisnyk I., Titkova A., Babi L., Filipchenko S. NITRIC OXIDE SYNTHESIS INTENSITY ASSESSMENT BY THE CONTENT OF ITS TERMINAL STABLE METABOLITES IN THE BLOOD OF RATS UNDER FLUORIDE INTOXICATION	180
Манатова А.М., Семенова Ю.М., Пивниа Л.М., Белыхина Т.И., Булегенов Т.А. ОЦЕНКА КАЧЕСТВА ЖИЗНИ ПОТОМКОВ ЛИЦ ПОДВЕРГШИХСЯ ОБЛУЧЕНИЮ В РЕЗУЛЬТАТЕ ИСПЫТАНИЙ ЯДЕРНОГО ОРУЖИЯ В КАЗАХСТАНЕ.....	184
Korotky O., Vovk A., Kuryk O., Dvorshchenko K., Falalyeyeva T., Ostapchenko L. CO-ADMINISTRATION OF LIVE PROBIOTICS WITH CHONDROPROTECTOR IN MANAGEMENT OF EXPERIMENTAL KNEE OSTEOARTHRITIS	191
Krynytska I., Marushchak M., Svan O., Akimova V., Mazur L., Habor H. THE INDICES OF ENDOGENOUS INTOXICATION IN RATS WITH CARRAGEENAN SOLUTION CONSUMPTION.....	196

РЕЗИОМЕ

ОСОБЕННОСТИ МЕТАБОЛИЗМА ПАРАЗИТИЧЕСКИХ ПРОСТЕЙШИХ И ВОЗМОЖНОСТИ РАЗРАБОТКИ АНТИПРОТОЗОЙНЫХ ПРЕПАРАТОВ (ОБЗОР)

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Малоизученным разделом протозоологии являются метаболические процессы паразитических простейших. Исследования биохимии паразитов необходимы для разработки эффективной химиотерапии протозоозов. Некоторые амитохондриальные паразиты человека, такие как *Giardia intestinalis*, *Entamoeba histolytica*, *Trichomonas sp.*, обитающие в среде с пониженным содержанием кислорода, имеют специализированные клеточные органеллы – гидрогеносомы, подобно митохондриям, обеспечивающие энергией клетки простейших. Изучение функционирования этих органелл позволяет рассматривать их в качестве мишеней для разработки антипротозойных препаратов. Мишенью для химиотерапии при лечении трипаносомозов могут служить процессы, связанные с особенностями гликолитического пути или уменьшением уровня энергетического субстрата, такого как глюкоза. Это приводит к быстрому снижению уровня АТФ в клетке паразита, общей потере подвижности и исчезновению трипаносом из кровотока инвазированного хозяина. Также мишенями для применения лекарств могут стать белки-транспортеры глюкозы расположенные в мембране паразита. В будущем исследования в области биохимии паразитических простейших могут привести к разработке эффективной химиотерапии протозоозов.

რეზიუმე

პარაზიტული უმარტივესების მეტაბოლიზმის თავისებურებანი და ანტიპროტოზოული პრეპარატების შემუშავების შესაძლებლობანი (მიმოხილვა)

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პროტოზოოლოგიის ერთ-ერთი ყველაზე ნაკლებად შესწავლილ სფეროს წარმოადგენს პარაზიტული უმარტივესების მეტაბოლური პროცესები. პარაზიტების ბიოქიმიის კვლევა აუცილებელია პროტოზოოზების ეფექტური ქიმიოთერაპიის შემუშავებისათვის. დაქვეითებული ჟანგბადიან გარემოში მცხოვრებ ზოგიერთ ამიტოქონდრიულ ადამიანის პარაზიტს, როგორებიცაა *Giardia intestinalis*, *Entamoeba histolytica*, *Trichomonas sp.* აქვს სპეციალიზებული უჯრედული ორგანელები – ჰიდროგენოსომები. ისინი, მიტოქონდრიების მსგავსად, უმარტივესების უჯრედებს უზრუნველყოფს ენერგიით. ამ ორგანელების ფუნქციონირების შესწავლა შესაძლებელს ხდის მათ განხილვას ანტიპროტოზოული პრეპარატების შემუშავების სამიზნედ. ტრიპანოსომების ქიმიოთერაპიის სამიზნედ შეიძლება განხილული იყოს გლიკოლიზის თავისებურებებთან, ან ენერგეტიკული სუბსტრატის - გლუკოზის შემცირებასთან დაკავშირებული პროცესები. ყოველივე ზემოაღნიშნული პარაზიტის უჯრედში იწვევს ატფ-ის დონის მკვეთრ შემცირებას, მოძრაობის უნარის ზოგად დაქვეითებას და ტრიპანოსომების გაქრობას ინვაზირებული მასპინძლის სისხლის მიმოქცევიდან. პრეპარატების გამოყენების სამიზნედ, ასევე, შეიძლება ჩაითვალოს პარაზიტის მემბრანაში განთავსებული გლუკოზის გადამტანი ცილები.

DRUG-FREE MODALITIES OF IRON DEFICIENCY CONDITIONS IN UKRAINE

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In recent years, the attention of specialists, working in various fields of health care, to the problem of healthy nutrition is growing rapidly. Acquiring modern knowledge and implementation of scientific developments and achievements

of the science of nutrition and dietology are a powerful factor in the prevention and treatment of non-communicable diseases (NCD), active longevity prolongation, and maintaining the emotional and mental well-being of the population [1].

Therefore, nutrition and its rational adjustment are given priority in various regions of the world, as reflected in the principles of European Policy "Health -2020: a European Policy Framework in Supporting Action Across Government and Society for Health and Well-Being" concerning non-communicable diseases for the period up to 2020 [11].

Therefore, many countries cultivate positive attitude of society to the need to prevent disease and behavior that will help to reduce the frequency and prevalence of pathologies caused by nutrition, including a numerous class of diseases of microelement etiology – a shortage of essential minerals in a body. The most well-known hypomicroelementosis is iron deficiency, leading to the development of iron deficiency states (IDS), which every fifth inhabitant of the planet suffers from. Therefore, the prevention of IDS is one of the most topical and urgent issues of modern medicine [1-3,8,12-14].

Most commonly, iron deficiency (ID) occurs in women of childbearing age [1,2,5,7,9,12,14], who due to their physiological characteristics have hemoglobin concentration rates on average 10-15% lower than in men. An average woman spends about 40 mg of iron during a normal menstrual period.

Taking into account the abovementioned information and the fact that iron absorption in the gastrointestinal tract is limited and normally constitutes up to 2 mg per day, it can be concluded that in the absence of adequate intake of iron, the deficiency in this trace mineral in women constitutes 10-20 mg per month, and 120-240 mg per year. All this leads to the fact that a woman may become to suffer from anemia in a few years. A requirement of iron for adult men does not exceed the intake, and they can live on iron deficiency diet for 6 years before becoming to suffer from IDS. The occurrence of anemia in men can be explained by chronic blood losses or iron absorption inability, rather than iron deficiency diet.

Therefore, a significant number of cases of IDS, such as iron deficiency anemia (IDA) and latent (hidden) iron deficiency (LID), is accounted for women of childbearing age, that has a negative impact on their immunity, physical and mental activity, violation of the cardiovascular, reproductive, hematopoietic and other systems [4,5,7,8,11,13].

So IDS is caused by many external and internal factors, among which a dietary factor is the most important, namely the lack of iron income to the gastrointestinal tract together with food.

The purpose of the study was a scientific justification of recommendations for public and individual primary and secondary prevention of IDS of nutritional origin in young women based on the identification of nutritional risk factors.

Material and methods. The object of the study were 204 women living in Kyiv city (Ukraine), aged from 16 to 29 years with no obvious non-nutritional factors of iron deficiency (pregnancy, childbirth, infant feeding, abnormal bleeding, injuries, surgery, organ donation, diseases related to ID, etc.), and were studying or working at the time of the survey.

We used three kinds of polling cards (open active; anonymous and open passive questionnaires with a weekly set of basic foodstuffs and with a 7-day diet of the surveyed – to obtain data on body iron intake in the diet), samples of peripheral red blood cells (hemoglobin, erythrocytes, cell-color ratio, the average content of hemoglobin, etc.), and samples of venous blood of the surveyed (biochemical indicators of iron metabolism: serum iron, total serum iron-binding capacity, latent (indirect) serum iron-binding capacity, transferrin saturation ratio) –to diagnose the iron deficiency degree in women. 2083 laboratory investigations were conducted in total.

By using computer processing, 446 card profiles and 728 nutritious rations of the surveyed were analyzed for 40 nutrients identified as the most important parameters influencing the development of the IDS.

Thus, the scientific data were obtained by three-stage questioning, primary and secondary screening including clinical and physiological, physical and chemical, laboratory and statistical research methods (to identify and to analyze correlation and results reliability degree).

Results and their discussion. It is established that the IDS incidence reaches 41.6% of the surveyed group. IDA have been registered for 31.1% of the surveyed subjects.

According to the degree of iron deficiency, anemia in women are distributed as follows: mild - 96.9%; average - 3.1%; severe - is absent.

Evaluation of actual nutrition of women indicates insufficient intake of easily digestible iron consumed with food (meat and meat products, liver, fish). Thus, the average daily consumption of meat and meat products is 15.3% below physiological levels of food consumption in Ukraine, fish – 50.8%.

According to nutrimental composition evaluation of the actual daily average diet of a woman in comparison to adequate physiological needs of the population in the nutrients and energy, it was found that protein intake is increased by 11.5%, mainly due to plant products. Fats consumption exceeds the normal rate by 34.2%, mainly due to plant products (by 37.6%) too. Also, consumption of simple carbohydrates is increased by 40.3%. It was found out an insufficient intake of complex carbohydrates, potassium, magnesium, riboflavin, biotin, pantothenic acid, folacin, which are iron absorption synergists.

Though women diet has sufficient iron content (20.02 mg), but its quality characteristic does not meet the needs of a body in the required amount of iron. The amount of easily digestible (heme) iron is only 13.9%. The greatest amount of iron income to the respondents' bodies together with: vegetables (19.4%), fruit and berries (17.3%), rye bread (13.8%), tea (9.3%) and cereals (6.7%). Thus, only 2/3 of a total amount of diet iron (66.5%) incomes to a digestive tract together with the above food. But, the impact of that amount of iron on the state of red blood cells is negligible. Iron of milk, eggs, bread, bakery products, cereals, vegetables, and beverages such as tea, coffee is poorly absorbed in the gastrointestinal tract – only 0.5-6%.

This is caused by intake of a significant amount of non-nutritional iron absorption factors, such as phytin compounds, tannins, phosphates, excessive inflow of fiber, fats, unfavorable nutrients ratio, together with the above food. Iron of meat has a much higher absorption - up to 20%. But in respect of sausages, one must pay attention to muscle protein content (not less than 15%), as adding low-grade conjugate tissue protein, plant protein (legumes), dairy product casein-calcium phosphate complex (combine with iron into insoluble compounds) and egg products (presence of phosphytin) to ground beef impairs the body absorption of iron. A weaker influence of blood pudding iron-on red blood compared to meat and liver iron may be due to sporadicness and a very small number of actual consumption of blood pudding by women (7.4 g per week) ($p>0.05$), while rather long inflow of this product to the body is needed for the manifestation of positive action. Generation of poorly soluble muriatic hematin in the stomach, preventing proper absorption of iron, make a contribution to the above effect.

A correlation analysis clearly highlights non-nutritional factors ($p<0.01$), which negatively interfere with the processes of iron absorption and metabolism in a woman's body. This includes beverages such as tea, coffee (Table 1).

This is due to the presence of powerful iron absorption antagonists - tannin, oxalic acid, - in these drinks (diet factors reducing Iron absorption - tannins, excessive income of dietary fiber, fat; alkaline mineral water, salts of phytic, phosphoric, oxalic acids; polyphenol compounds, soy protein, vitamin deficiencies, antacids, etc.).

A number of meat consumption by women has a statistically significant direct impact on all indicators of a body iron supply (Table 1). A significant contribution to a red blood status makes a consumption of liver, sausages of minced meat and fish (diet factors increasing iron absorption - sulfur-containing amino acids of meat and fish; ascorbic and citric acids, retinol, folic acid, riboflavin, cyanocobalamin; cobalt, copper, etc).

This is explained by the presence of readily available iron - a naturally chelated form (Fe^{2+}) - in natural meat and fish. Chelation is a process in which minerals are associated with amino acids and that converts these minerals into the most

digestible form. Assimilation of chelated minerals is three - ten times higher than of non-chelated [1,4,6-8].

The obtained data allowed to make the necessary adjustments in the construction of an adequate and complete product and the nutritional compound of a diet that provides an adequate intake of essential nutrients and allows to prevent nutritional iron deficiency (Table. 2).

However, it should be noted that the abovementioned food package is preventive on the occurrence and progression of nutritional ID and may be recommended as a part of dietary therapy in case of IDS along with drug therapy, which involves the use of iron supplements, multivitamin preparations etc. in order to supplement iron deficiency in the body faster.

A daily food package is developed, which provides the necessary qualitative and quantitative intake of iron given the effect of iron absorption synergists and antagonists.

We conducted a mathematical and statistical analysis of the obtained data and proposed a tentative diet to prevent IDS in women of childbearing age, which is recommended for the prevention and alimentary correction of IDS in this high-risk group.

Approximate diet (menu) to prevent IDS in women of childbearing age:

breakfast: 2 sandwiches: (whole-wheat bread - 80 g, butter- 10 g, cheese- 30 g, boiled or baked meat - 30 g), rose hip tea - 200 mL;

lunch: beetroot soup - 250 mL, bread - 80 g, buckwheat cereal - 300 g, stewed beef - 80 g, stewed fruits compote (dried fruits compote) or juice - 200 mL, cabbage, tomato, cucumber, onion and oil salad (5: 5: 5: 1: 1) - 200g;

afternoon luncheon: cheese casserole with raisins (15:1) - 150 g, fruit and berry jelly - 100 mL, orange - 50 g;

dinner: fried (saltwater) fish with carrots (7:1) - 80g, boiled potatoes - 150 g, seaweed salad - 50 g, rye-wheat bread - 80 g, pomegranate juice - 150 mL. The proposed menu selection is the result of many calculated options that corresponds to the developed food package.

Nutrient composition of the menu allows for developed standards and demonstrates adequate per day intake of iron and other nutrients which are iron assimilation synergists (complete proteins, vitamins C, B₆, B₁₂, A, β -carotene, biotin, folic acid, potassium and other) and

Table 1. The correlation relationship between the IDS and the level of consumption of tea and coffee by women. (r)

Food	Dependent IDS indicators		
	Hemoglobin	Red Blood Cells	Cell-Color Ratio
Meat, g	0.38**	0.18*	0.29**
Liver, g	0.30**	0.19*	0.16*
Sausage (meat protein content of at least 15%), g	0.36**	0.22**	0.19*
Blood pudding, g	0.04	- 0.01	0.05
Fish, g	0.16*	0.03	0.13*
All meat products, g	0.47**	0.24*	0.31**
Tea, mL	- 0.31**	- 0.23**	- 0.22*
Coffee, mL	- 0.15*	0,04*	- 0,11**

note: * - $p<0.05$; ** - $p<0.01$

Table 2. Daily food set (optimum and range of fluctuations in grams (mL)/day) to prevent IDS of nutritional origin in women of childbearing age (in energy consumption of 2500-3000 kcal)

Product Name	Product Consumption (net)	
	Optimum	Fluctuations range
Meat, g	80	60-100
Liver, g	8	5-11
Sausages (the content of meat protein is not less than 15%), g	45	30-60
Meat products, g	130	90-180
Fish, g	30	20-50
Dairy Products (in milk equivalent), mL	400	300-450
Eggs, pcs.	0,5	0.4-0.6
Oil, g	30	27-35
Butter, g	25	20-30
Bread and bakery products, cereals, g	380	340-440
Potatoes, g	250	200-300
Vegetables, except potatoes, g	300	250-350
Sugar (mono or disaccharide), g	73	60-75
Fruits and berries, g	300	240-360
Tea, g	3.5	2.0-4.5
Coffee, g	3.0	2.5-5.0

iodine assimilation synergists, as well reduction of iron absorption antagonists income.

Conclusions. 1. IDS prevalence among women who had no non-alimentary grounds for the occurrence of iron deficiency (pregnancy, childbirth, baby nursing, blood loss, organ donation, surgery, trauma, etc.) is 41.6 of the group, including clear iron deficiency - iron deficiency anemia (31.3%), among which mild anemia prevails (96.9%).

2. The main nutritional risk factors of IDS are poor nutrition and unhealthy diet associated with inadequate intake of food containing heme iron (the average daily consumption of meat and meat products is even 15.3% below the minimum physiological level, of fish – 50.8%) and increased consumption of food containing significant amounts of demineralizing factors (tea, coffee, etc.).

3. Correlation analysis of data on the consumption of certain food products showed that a statistically significant positive impact on the performance of red blood cells and iron metabolism (the major indicators of iron deficiency) had such food products as meat, sausages, liver, fish, to a lesser extent – fruits and berries. Tea and coffee had a negative impact on key indicators of red blood cells. No statistically significant effect of bread, bakery and cereal products at the rates of an adequate iron supply of the respondents were found. Therefore, in order to prevent IDS of nutritional origin in risk groups at individually regulated and organized diet it is recommended to increase consumption of food products which are sources of heme iron (meat, liver, fish), and to reduce excessive consumption of tea, coffee that can be made at the approach of diet to the proposed preventive food packages and menus.

4. A daily food package and diet were proposed which

are designed for primary and secondary prevention of alimentary conditioned IDS in women.

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SUMMARY

DRUG-FREE MODALITIES OF IRON DEFICIENCY CONDITIONS IN UKRAINE

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The article is devoted to studying the impact of nutritional factors on the occurrence and progression of iron deficiency states (IDS) in young women and developing the main alimentary methods of their prevention. The revealed IDS prevalence among women aged from 16 to 29 years without non-alimentary reasons for the occurrence of iron deficiency is 41.6%, among which latent iron deficiency – 10.3%, clear iron deficiency (anemia) – 31.3%. It was found out that the strongest positive impact on the performance of red blood cells and iron metabolism produce had such food products as meat, sausages (the con-

tent of meat protein is not less than 15%), liver, fish and fruits. Tea, coffee, milk, eggs adversely affect the main indicators of the IDS. No statistically significant effect of bread, bakery and cereal products at the rates of an adequate iron supply of the respondents were revealed. A scientific rationale for a daily food package and diet designed for primary and secondary prevention of alimentary conditioned IDS in women is given.

Keywords: iron deficiency, iron, young women, diet, food, alimentary prevention.

РЕЗЮМЕ

НЕМЕДИКАМЕНТОЗНАЯ КОРРЕКЦИЯ ЖЕЛЕЗОДЕФИЦИТНЫХ СОСТОЯНИЙ В УКРАИНЕ

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Целью исследования явилось изучение влияния алиментарных факторов на возникновение и развитие железодефицитных состояний (ЖДС) у молодых женщин и разработка мероприятий их алиментарной профилактики.

Изучена распространенность ЖДС среди женщины в возрасте от 16 до 29 лет, которые не имели неалиментарных причин для возникновения железодефицита. Выявлена распространенность ЖДС у данного контингента на уровне 41,6%, в том числе латентный железодефицит (ЛЖД) констатировали у 10,3% обследованных, а явный дефицит железа (анемия) – у 31,3%.

Установлено, что наибольшее положительное влия-

ние на показатели красной крови и обмен железа имеют такие продукты как мясо, мясная колбаса (не менее 15% мясного белка), печень, рыба, фрукты. Чай, кофе, молоко, яйца негативно влияют на основные показатели дефицита железа. Статистически значимого влияния овощей, хлебобулочных и крупяных изделий на показатели обеспеченности организма респондентов железом не выявлено.

Научно обоснован продуктовый набор пищевых продуктов и рацион питания для молодых женщин с целью первичной и вторичной профилактики ЖДС алиментарного происхождения.

რეზიუმე

რკინადეფიციტური მდგომარეობების არამედიკამენტური კორექცია უკრაინაში

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კვლევა ეძღვნება ალიმენტური ფაქტორების გავლენის შეფასებას რკინადეფიციტური მდ-

გომარეობის აღმოცენებასა და განვითარებაში ახალგაზრდა ქალებში და ღონისძიებების შე-

მუშავეებს მათ ალიმენტური პროფილაქტიკისათვის. შესწავლილია რკინადეფიციტური მდგომარეობა 16-29 წლის ასაკის ქალებში, რომელთაც არ ჰქონდათ არაალიმენტური მიზეზები რკინის დეფიციტის განვითარებისათვის. ასეთი ტიპის კონტინგენტში რკინადეფიციტური მდგომარეობების გავრცელება გამოვლინდა 41,6%-ის ფარგლებში, მათ შორის ლატენტური რკინადეფიციტი დაუდგინდა გამოკვლეულთა 10,3%-ს, რკინის გამოხატული დეფიციტი კი - 31,3%-ს. დადგენილია, რომ ყველაზე მეტად

გამოხატული დადებითი გავლენა წითელი სისხლის შემადგენლობაზე და რკინის ცვლაზე აქვს ისეთ პროდუქტებს, როგორცაა ხორცი, ძეხვი (ხორცის ცილის არანაკლებ 15%-იანი შემცველობით), ღვიძლი, თევზი, ხილი, ხოლო ჩაი, ყავა, რძე, კვერცხი უარყოფითად მოქმედებს რკინის დეფიციტის ძირითად მანქვენებლებზე. ბოსტნეულის, პურ-ფუნთუშეულის და მარცვლოვანი პროდუქტების სტატისტიკურად სარწმუნო გავლენა რესპოდენტების ორგანიზმის რკინით მარაგებაზე არ გამოვლინდა.

NITRIC OXIDE SYNTHESIS INTENSITY ASSESSMENT BY THE CONTENT OF ITS TERMINAL STABLE METABOLITES IN THE BLOOD OF RATS UNDER FLUORIDE INTOXICATION

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The degree of pathogenic effects in the development of stress-reaction is largely determined by the state of stress-limiting systems, in particular, the system of nitrogen oxide (NO). It has been proven that NO-dependent regulation of the central parts of the stress reaction is ensured by the fact that the pituitary gains a widely represented NO-ergic innervation from the hypothalamus [14, 18, 25]. The observed property NO of modulating the release of major stress hormones of the pituitary suggests an important role of NO in regulating its functioning and preventing excessive activation of the central link of the stress-system. There is evidence in the literature that NO can block the peripheral release of stress hormones and protect cells and organs from stress-related injuries [2, 12, 17, 28]. In particular, low concentrations of NO suppress the release of catecholamines from the adrenal glands and sympathetic nerve endings, resulting in the restriction of stress response [3, 11, 20, 22].

The final stable metabolites of NO include nitrite and nitrate anions (NO₂, NO₃), defining whose concentrations serve as an indirect method for assessing the intensity of NO synthesis [4, 8, 13, 26]. The concentration of NO is the main factor in its numerical bio-effects (regulatory, protective, damaging). At low concentrations of NO, direct effects aimed at maintaining homeostasis prevail, for example, vascular, respiratory and nervous systems, prevail; at high concentrations of NO – the indirect effects predominate, primarily due to the formation of peroxynitrite. It is known that when the velocity of free radical reactions increases in the body, NO can react with a superoxide anion radical to form peroxynitrite – a highly reactive compound with destructive properties in relation to proteins and lipids [5, 6, 21].

The aim of the research is to evaluate the intensity of nitric oxide synthesis in the experiment by the content of its terminal stable metabolites in the blood of rats exposed to sodium fluoride.

Material and methods. The studies were conducted on adult Wistar rats weighing 180-220 g, which were kept under steady state vivarium at constant temperature and natural light in plastic cages on a balanced diet. Rats were subjected to oral exposure by means of a probe with aqueous solutions of sodium fluoride (SF) daily for 60 days at a dose of 1/10, 1/100 and 1/1000 DL50, respectively, of 20 mg/kg, 2 mg/kg and 0.2 mg/kg body weight (average lethal dose of SF for rats, obtained orally, is 200 mg/kg). Animals of the control group were given appropriate amounts of drinking water. The study was conducted at 10, 20, 30, 50 and 60 days after the start of the experiment. Each group included 10 animals. Animals were euthanized by decapitation with a guillotine knife, pre-anesthetizing with sodium thiopental in a dose of 50 mg/kg of mass.

The content of nitrite and nitrate anions in blood plasma was determined spectrophotometrically at 540 nm by color reaction with Grissan reagent [7, 15, 23]. Before the analysis, precipitation of proteins 0.5 M KOH and 5% ZnSO₄ was carried out. Since diazotization reaction is specific to nitrites only, for the determination of nitrates, their previous recovery was carried out.

Statistical analysis of the results was performed using Statistica 6.1 (StatSoft, Inc., USA). The comparison of two normal distributions was carried out using Student's t-test. If at least one of the distributions was not normal, Mann-Whitney Ranking criterion was used to compare independent samples. The critical level of significance was considered p<0.05.