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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

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7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

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In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

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1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

წარმოდგენილი გენეტიკური მექანიზმი, რომელიც პასუხისმგებელია კონსტიტუციური და ფაკულტატური ჰეტეროქრომატინის რემოდელირებაზე, ხაზს უსვამს დაავადებათა განვითარებაში გარეგანი და შინაგანი ფაქტორების მნიშვნელობას, და შეიძლება საფუძვლად დაედოს სიბერის პათოლოგიათა თერაპიული მკურნალობის სტრატეგიის შემუშავებას.

EPINEURIAL SUTURES, POLYETHYLENE GLYCOL HYDROGEL AND FIBRIN GLUE IN THE SCIATIC NERVE REPAIR IN RATS: FUNCTIONAL AND MORPHOLOGICAL ASSESSMENTS IN EXPERIMENT

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Mechanical damage to the peripheral nerve is a fairly common type of injury, which is characterized by a complex of long-term neurological disorders [2,4,10,11,19,28,33,38,41] and require significant financial costs [2,4,10,17,23,25,33,37,44]. Regeneration of the damaged nerve is a staged process and depends on a number of factors: the level and extent of damage, time from damage and microsurgical restoration, the method of microsurgery, revascularization [9]. The search for new and effective microsurgical techniques in the restoration of peripheral nerves is not complete.

The basic technical method of restoring the spatial integrity of the injured nerve is neuroraphy [14,16,31] – suturing the ends of the nerve "end-to-end" through epi- or perineurium with a biocompatible monofilament. The disadvantages of the method are time and financial cost, high manual qualification requirements for the surgeon, as well as the persistence of xenogenic suture material and incomplete spatial isolation of the injured area – additional triggers of local inflammatory reactions [3,13,29], which generally limit and slow down the regenerative growth of nerve fibers. All this motivates the development of sutureless sealed coaptation – adhesive, laser, photochemical [3,7,13-15,22,29,40,43,45,47], nanocomposite [18] or electrowelded [34].

The listed types of direct connection of nerve stumps, first of all, epineural suture (ES), are used in cases of easy, tension-free coaptation of nerve ends; otherwise recovery requires a graft [26]. The efficiency of regeneration and functional recovery is determined by the level of regeneration of nerve fibers through the sutured area, and if there are several such areas, as in the case of a graft, the number of regenerating nerve fibers in the distal nerve decreases. Grinsell D. and Keating C.P. note that at the level of one suture zone loses about 50% of nerve fibers, and after two suture areas - 75% [20].

The efficiency of functional recovery of the limb is influenced by both the level of nerve regeneration and the state of denervated muscles during reinnervation, such as malnutrition, fibrotic changes. The question arises of improving nerve regeneration by neuroraphy with innovative biodegradable polymers that would ensure the adhesion of the nerve ends and sufficient strength of this connection. The synthetic and biodegradable substances currently used in such way have partially realized this potential. Prospective data are available on the use of adhesives based on polyethylene glycol hydrogel (PEG) and fibrin glue (FG) [39]. The advantages of adhesives are ease of use, safety, less trauma to the nerve endings compared to ES, lower connective tissue density at the level of coaptation. However, there are concerns about the strength of connection of the nerve ends, so several ESs are still used to avoid "failure" of the suture [24]. Also, PEG and FG should not interfere with the regeneration of nerve fibers in the distal end of the nerve. Thus, FG is considered as an alternative to the microenvironment in conduits [12,32,35]. There is evidence for longer biodegradation of PEG in the damaged nerve and its better adhesion and strength compared to FG [30,42]. That is why a comparative analysis of the effectiveness of damaged nerve regeneration after different methods of neuroraphy is useful for neurosurgical practice.

The aim of the study was to evaluate the effectiveness of sciatic nerve regeneration after neuroraphy by ES, PEG and FG.

Material and methods. *The animal model.* The study was carried out with 30 white not purebred male rats (250±25 g, 5-6 months of age). Rats were randomly selected into the experimental groups:

Group № 1. Control – intact rats;

Group № 2. Shame-operated – a linear skin incision on the lateral surface of the femur was performed, the left sciatic nerve was isolated and mobilized. This was followed by layer-by-layer restoration of soft tissue integrity without nerve manipulation;

Group № 3. The complete transection (CT) of the sciatic nerve – the actions, as in the group № 2 with the additional complete transection of the sciatic nerve, the endings of the nerve were not connected, but remained freely in the wound. This was followed by layer-by-layer restoration of soft tissue integrity without nerve manipulation;

Group № 4. Epineural sutures (ES) – the actions, as in group № 2 with an additional complete transection of the sciatic nerve and its subsequent fixation end-to-end by epineurial neuroraphy with the atraumatic needle (4-6 epineurial sutures with a polyamide thread № 10/0);

Group № 5. Polyethylene glycol (PEG) – DuraSeal hydrogel – the actions as in group № 2 with an additional complete cross-section of the sciatic nerve and its subsequent fixation with use of hydrogel DuraSeal®, (Covidien LLC, USA) and 2 "fixating sutures".

Group № 6. Fibrin glue (FG) – Tisseel glue – the actions, as in group № 2 with an additional complete transection of the sciatic nerve and its subsequent fixation with Tisseel® fibrin glue and 2 "fixating sutures";

The surgery was performed under general anesthesia (xylazine 15 mg/kg and ketamine 70 mg/kg, intraperitoneally), according to the rules of asepsis and antiseptics. An access to the sciatic nerve in group 3 was performed as follows: an animal

was placed in a standard physiological position with its belly down, skin in the area of middle third of lateral surface of left thigh was shaved, treated with solution of povidone-iodine (Betadin, "EGIS", Hungary), dissected along the line of the most superficial location of the external femur surface, the area of attachment of both tendons of the biceps femoris to the femur was visualized, in this zone a linear section along the bone was performed; the muscle was allocated in the middle. The trunk of the sciatic nerve was visualized and opened at the interval from the exit from the pelvic cavity to the branching into the main branches. In animals of groups 3, 4, 5 and 6 at the middle of this site, the nerve was transected with microscissors.

In Group 4 animals, traditional epineurial neurorrhaphia with sutures was performed (Fig. 1). The left sciatic nerve in the middle third of the hip was crossed with microscissors. Microsurgical suturing was carried out after sciatic nerve transection with monofilament atraumatic thread № 10.0 in the amount of 4-6 until the fascicles were matched satisfactorily.

In the animals of group 5 and 6 after isolation and nerve transection, two epineurial sutures were applied with an atraumatic thread № 10.0 at the distance of 180^0 from each other.

In the group of animals № 5 after two fixation sutures were made Tisseel fibrin adhesive solution was applied to the nerve ending connection site, using the Duo Syringe System. The junction of the endings of the crossed nerve were covered with a thin layer of fibrin adhesive solution.

In the 6th group of animals, after two fixation sutures were applied, a DuraSeal solution (5 ml Kit) was applied to the junction of the nerve endings. The system was prepared for the use according to instructions from the manufacturer. After the preparation of the system, gel was applied in a thin layer to the connected nerve site.

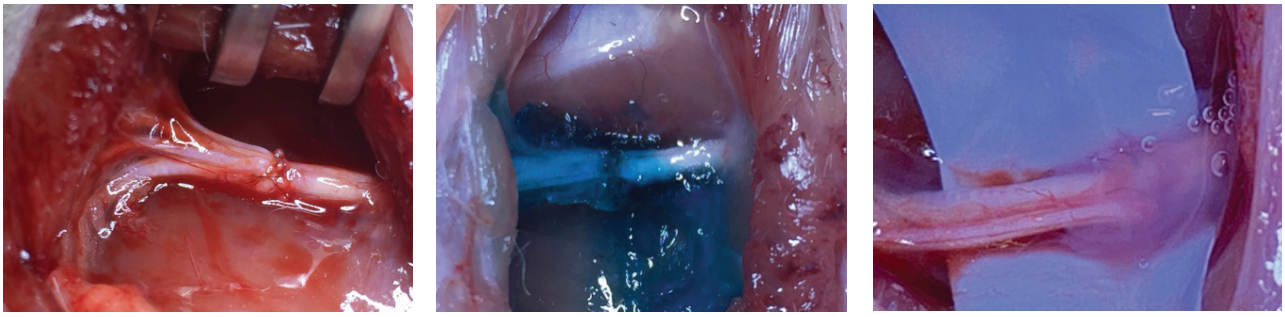
After the surgery and careful hemostasis in groups 2-6 layer-by-layer suturing of a postoperative wound was carried out with the certified atraumatic needle with a monofilament polyamide thread 4/0. In order to prevent infectious complications, benzyl penicillin solution in the dose of 1 mln u/1 kg body weight was administered to the posterior cervical site. For anti-inflammatory and anti-edema therapy, dexamethasone solution of 6 mg/kg body weight was administered intraperitoneally.

The Sciatic Functional Index (SFI). The SFI is aimed at quantitative assessment of the effects of the damaged sciatic nerve in rats. SFI quantifies functional deficits in animals by analyzing the trace change after injury. To do this, the limbs of rats were labeled with a dye (fucorcin) and rats were sent to the test track. Rat limb fingerprints were collected, the length between the limb fingers was measured and converted into quantitative values by the formula as described in the method [46].

Electroneuromyographic studies. Animals were anesthetized (intraperitoneal administration of a mixture of xylazine hydrochloride 15 mg/kg and ketamine hydrochloride 70 mg/kg) and fixed on the operating table belly down. A ground electrode (metallized tape soaked in 0.9% sodium chloride solution, 20 mm wide, 100 mm long) was fixed along the tail, and the sciatic nerve was isolated from the pelvic outlet till its branches, clearing the operating field with saline. The nerve was covered with a platinum hook-like bipolar electrode (monopolar diameter – 0.22 mm, distance between monopolars – 5,5 mm. The stimulating current was generated by a digital electroneuromyograph "Neuro-MVP-Micro" (LLC "NEUROSOFT", Russia), applied in pulse mode (pulse duration - 5 ms) with a frequency of 0.2 Hz (1 pulse for 5 sec) and a step of increasing the current at 1 mA. The excitation was recorded by the indicated electroneuromyograph using a concentric needle electrode (length - 25 mm, diameter - 0.3 mm, withdrawal area - 0.015 mm^2) at the motor point of the calf muscle. The distance between the stimulating and recording electrodes was ~ 25 mm. Analysis of neuromuscular function was assessed by ENMG parameters: M-response amplitude (AmV), latent M-response period (ms), excitation conduction velocity (mm/ms). For analysis only the parameters of the maximum M-response amplitude were used, which were obtained in most cases - at a stimulating current of 3 mA.

Histological and morphometric analysis. Distal sciatic nerve was fixed in 2.5% solution of glutaraldehyde in phosphate buffer with 1% osmium tetrachloride, dehydrated in increasing concentrations of ethanol and acetone. The tissue samples we embedded in the Epone-Araldite mixture. To get the ultrathin slices, we applied an ultratome (Reihart). The semi-thin sections were stained with toluidine blue, and then were stadied under a light microscope (Olympus BX 51) for histological and morphometrical examination. For morphometric examination, Carl Zeiss software (AxioVision SE64 Rel.4.9.1) and a camera attachment were used. Sciatic nerve samples for each rat were examined at high (×1000) magnification. The mean numerical density of the myelinated axons was estimated in photo (216×138 μm, average 0.03 mm^2), amount of sampling photo are 10-15 (2/3-3/4 of cros-section of nerve). The mean diameter (μm) of the myelinated axons was estimated by average of large and small diameters per individual fiber.

Data processing is carried out using the computer program of Origin v.9.0. The validity of the differences between the comparison groups was determined by Kruskal-Wallis H test. Differences between groups were considered statistically significant at $P<0.05$.



a b c

Fig. 1. Neuroraphy of the sciatic nerve of rats: a) sciatic nerve after ES; b) sciatic nerve after PEG (blue color); c) sciatic nerve after FG (white color)

All experimental procedures were conducted according of current standards of bioethics (EU Directive 2010/63/EU "on the protection of animals used for scientific purposes" (1986), European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes (1986), Law of Ukraine of February 21, 2006 No. 3447-IV "About protection of animals against ill treatment" (2006)). The protocol of the study was approved by the bioethical commission of Bogomolets National Medical University (protocol 113).

Results and discussion. We analyzed the functional state of the limb of rats during the experiment with the use of SFI (Fig. 2). At 2 weeks after neuroraphy, a statistically significant higher SFI was found in the group with ES and PEG (P <0.05). At 3 and 4 weeks, SFI increased in all three groups (P <0.05). At 4 weeks, SFI values in the FG group were significantly lower compared to ES and PEG.

The results of electroneuromyography are shown in Fig. 3 and Table 1. It was was found significantly smaller amplitude of the M-response of the skeletal muscles of the shin in all three groups with neuroraphy. The amplitude of the M-response in the group with FG was smaller compared to the ES-group (P <0,05); there was no statistically significant difference between the ES and PEG groups. In the ES-group, the latency period of registration of the M-response was significantly longer (0.85 ± 0.05 ms vs 0.62 ± 0.04 in shame-operated rats). The latency period in the PEG- and FG-group approached to the control values (within the statistical error of control- to ES-group). The recorded excitation conduction velocity was significantly lower in the ES-group compared to control and Sham-operated rats by 25.1% and 31.1% (P <0.05) respectively. The excitation conduction velocity in the PEG- and FG-group is within the statistical error of the control and ES-group. The tendency in increase of the M-response in the PEG- and FG-group (except the amplitude in the FG-group) may indicate a more efficient reinnervation of skeletal muscles by regenerated nerve fibers from the damaged sciatic nerve. Statistically lower M-response rates in the ES-group indicate delayed (extended, prolonged) muscle reinnervation after neuroraphy compared to PEG- and FG-group.

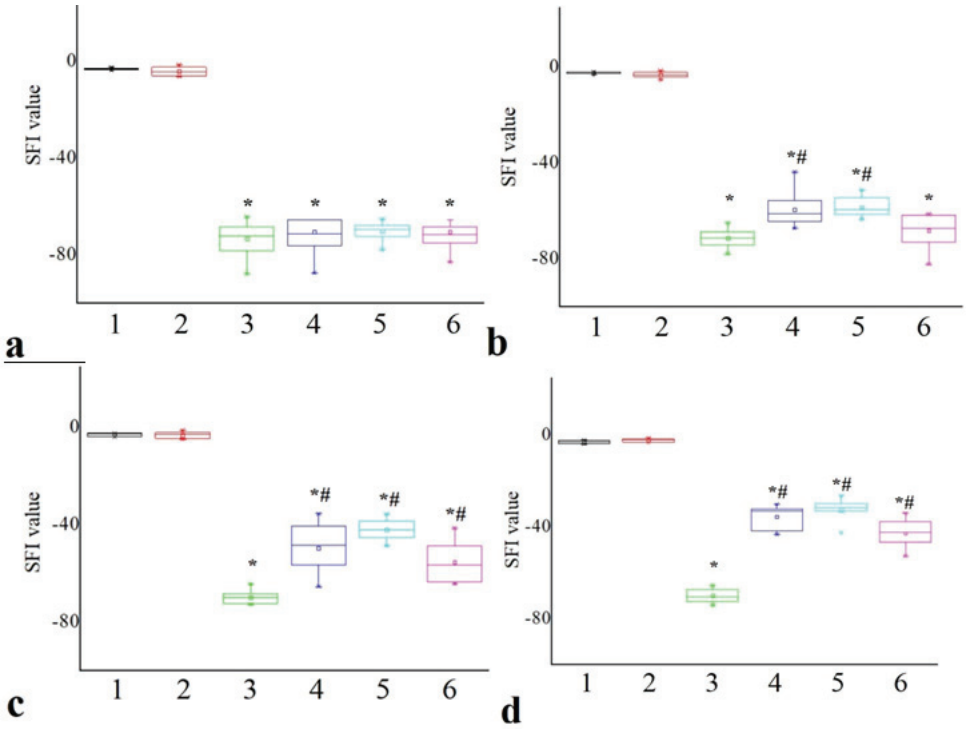


*Fig. 2. Charts of changes in SFI in rats after ES, PEG and FG (Mean±SD): a – 1 week; b – 2 weeks; c – 3 weeks; d – 4 weeks; on the abscissa: 1 – control; 2 – shame-operated group; 3 – neurotomy; 4 – ES; 5 – PEG; 6 – FG; * P < 0.05 in comparison with the control and shame-operated group; # P < 0.05 in comparison with the neurotomy*

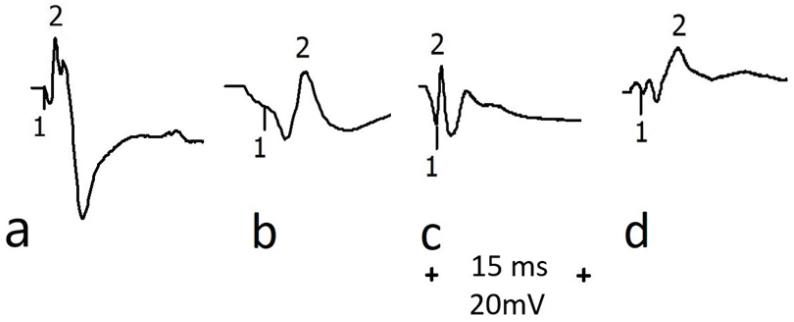


Fig. 3. Myograms recorded in rats on the 30-th day after neuroraphy: a – shame-operated group; b – ES; c – PEG; d – FG; 1 - primary-positive peak; 2 - positive peak

Table 1. Parameters of electroneuromyography in rats after sciatic nerve neuroraphy on the 30-th day (Mean±SEM)

Group	Amplitude of negative-positive peak, mV	Latency period, ms	Excitation conduction velocity, mm/ms
Control	19.3±0.95	0.68±0.02	40,9±1,61
Shame-operated	19.1±1.78	0.62±0.04	44,4±3,42
ES	6.67±1.19*	0.85±0.05@	30,6±1,40*
PEG	7.28±0.75*	0.76±0.06	37,9±2,94
FG	5.1±0.29*#	0.76±0.02	33,9±1,09

** - P<0.05 compared to the the control and shame-operated group;*
@ - P<0.05 compared to the the control and shame-operated group; # - P<0.05 compared to the the PEG

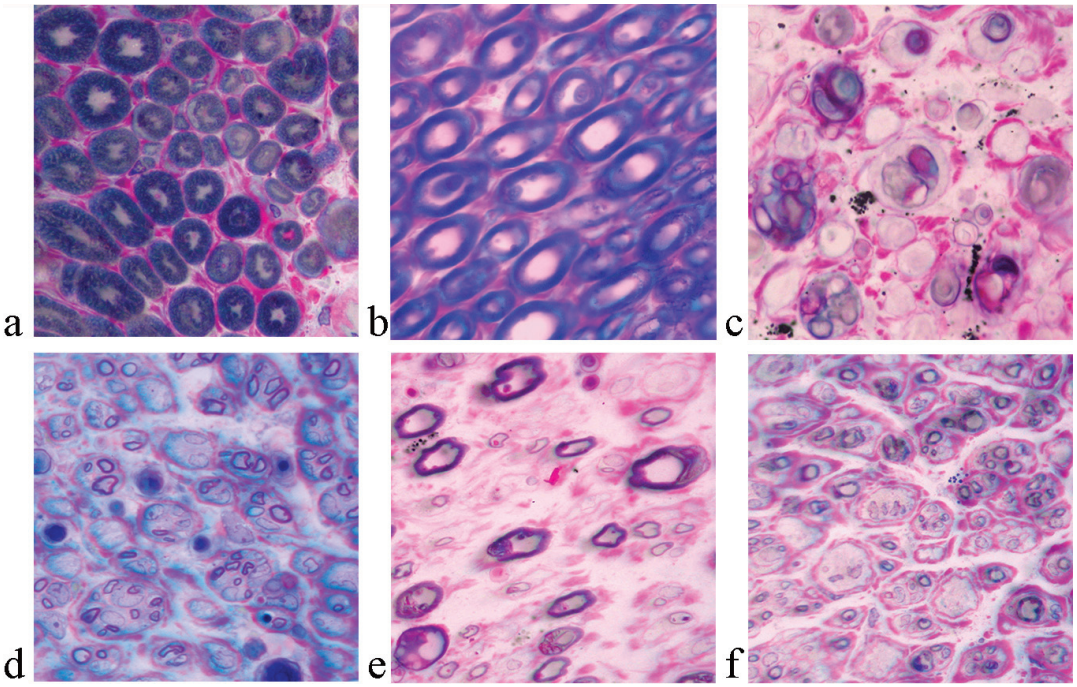


Fig. 4. Transverse section of a rat sciatic nerve stained by M.A. Hayat method: a – control; b – shame-operated group; c – neurotomy; d – ES; e – PEG; f – FG. Magnification ×1000

On the 30th day after neuroraphy, an analysis of the regeneration of myelin nerve fibers in the distal segment of the sciatic nerve was performed. Fig. 4 illustrates transverse half-thin sections of the sciatic nerves of the comparison groups. After complete neurotomy without neuroraphy, spontaneous regeneration was absent, so in the atrophically altered distal segment of the nerve the data were not analyzed (in table 2 presented as not analyzed, NA). According to the results of research in all cases after neuroraphy there was a regeneration of nerve fibers through the area of the nerve coaptation. Some tendencies between comparison groups were revealed. Thus, in PEG-group regeneration of «thick» myelin nerve fibers took place (number of nerve fibers by 25.9%, P <0.05; fiber diameter by 36.9%, P <0.05), and in FG-group regeneration of «thin» nerve fibers took place to a greater extent (number of nerve fibers by 38.3%, P <0.05). Morphometric analysis (Table 2) showed a significantly greater number of myelin nerve fibers in the distal nerve end in the PEG- and FG-group vs ES-group, and PEG promoted the regeneration of larger fibers (with a thicker myelin sheath). This indicates an acceleration of remyelination of axial cylinders on the 30th day after neuroraphy with the use of PEG.

Table 2. Morphometric data of myelin nerve fibers in the distal segment of the sciatic nerve on the 30th day (Mean±SEM)

Group	Number of myelinated nerve fibers, in test-zone	Diameter of myelinated nerve fibers, µm
Control	200.0±13.1	15.28±0.36
Shame-operated	197.4±10.7	15.81±0.35
CT	NA	NA
ES	38.5±2.4*	4.82±0.05*
PEG	48.5±2.7*^	8.58±0.18*^
FG	56.8±4.3*^	5.23±0.06*

** - P<0.05 compared to the control and shame-operated group; ^ - P<0.05 compared to the ES;*
NA – not analyzed (regeneration is absent)

This article aims to investigate the effectiveness of sciatic nerve regeneration in neuroraphy with use of epineural suture and connection with use of adhesives. There are concerns that PEG and FG are not strong enough to connect the nerve endings. This is confirmed by experimental data of some authors. Thus, the recovery of the nerve after the application of FG by the level of strength was equal to the recovery with the use of sutures only after 2-4 weeks [42]. Due to concerns about the strength of coaptation of the nerve ends, several sutures are still used, which increases the strength of the adhesive connection and reduces nerve injury due to fewer sutures.

Therefore, its use in clinical practice is limited only as an additional method in microsurgical suture reconstruction. In our own experiments, we followed the same algorithm. We first formed 2 fixating sutures and then applied PEG or FG, while the "classic" version of neuroraphy was the application of 4-6 epineural sutures. Analysis of the effectiveness of the recovery process included evaluation and comparison of functional and morphological data. The summarizing analysis indicates that PEG was significantly better at promoting functional recovery, both in terms of SFI (acceleration of limb locomotor function) and in terms of skeletal muscle M-response (latency response period and excitation conduction velocity). Compared with ES and PEG, the use of FG had less significant parameters compared to PEG. The study of cross sections of the sciatic nerve allowed to detect and quantify the regeneration rate of myelin nerve fibers, which explains the results of the M-response. Statistical analysis indicates a positive effect of PEG and FG on nerve regeneration, although significantly greater remyelination (analysis based on fiber diameter) was confirmed only in the group with PEG, which explains the faster functional recovery of the limb.

The data obtained by us confirm the experimental results of other authors [39, 40, 42], expend and clarify them. There are several views on the effect of PEG and FG on nerve regeneration: the direct effect of PEG and FG, the strength of the nerve connection, the state of the paraneural environment. Previously, it was hypothesized that PEG as a chemical fusogen could cause cell membranes to fuse (as used in vitro to fuse cells, create a hybrid cell line), in this case – a crossed axon, if PEG was applied in a short time period, and even were obtained some results [6]. But the analysis of the hypothesis, the evidential part of the results did not stand up to criticism, primarily due to the axial cylinders of the distal segment, which were "lost", are subjects to Waller's degeneration, which eliminates any possibility of axon fusion [8].

Although some authors still consider these theoretical issues [36]. Ovoids of degeneration we still have registered on the 30th day and the time of their elimination in the nerve is a separate factor that affects the recovery, because they are the products of destruction of damaged nerve fibers, which delay the tempo of regeneration. We did not analyze the elimination of ovoids, because we believe that the relative level of regeneration of nerve fibers is the main indicator of the effectiveness of recovery. According to this algorithm, the use of PEG gave better results than FG.

The direct action of FG is controversial. Thus, fibrin can inhibit cell migration and germination of nerve fibers [1], and at the same time can be used as an element of the extracellular matrix for adhesion and elongation of axons [27]. Another factor is the strength of the connection between the nerve endings. In a study [30], nerve ruptures at the level of coaptation were greater (more frequent) after nerve repair via FG, but not after sutures and PEG. Therefore, own experimental data and data of other authors [24, 30, 36] indicate better efficiency of PEG application in comparison with FG based on parameters of regeneration of nerve fibers, functional parameters or biomechanical characteristics. Although Koulaxouzidis G et al. [27] did not note differences in coaptation and nerve rupture between ES and FG. In this case, FG equally covers the nerve for up to 6 weeks [5], while in our own studies we did not register FG at the 4th week. We also hypothesize that PEG creates a temporary limiting biodegradable barrier around the damaged nerve from the paraneural environment, preventing scar formation after injury. The results of Isaacs J. et al. partially confirm this: the thickness of the perineural scarring tissue in the longitudinal projection of the nerves at the coaptation level was smaller after PEG vs FG [24]. In the same context, FG forms a fibrin capsule around the conduits, stimulates the infiltration of scar tissue, which prevents nerve regeneration, and promotes nerve regeneration in non-porous conduits [5]. Therefore, PEG in the form of a hydrogel is a more promising tool in microsurgical repair of damaged nerves as an adhesive, which promotes faster nerve regeneration, reinnervation of denervated muscles and functional recovery of the limb.

REFERENCES

1. Akassoglou K., Akpinar P., Murray S., Strickland S. Fibrin is a regulator of Schwann cell migration after sciatic nerve injury in mice. // Neurosci Lett, 2003,338(3),185-188.
2. Antoniadis G., Kretschmer T., Pedro M.T., Konig R.W., Heinen C.P.G., Richter H.P. Iatrogenic nerve injuries prevalence, diagnosis and treatment. // Deutsches Arzteblatt International, 2014,111(16),273-9.
3. Barton M.J., Morley J.W., Stoodley M.A., Lauto A., Mahns D.A. Nerve repair: toward a sutureless approach. // Neurosurgical Review, 2014,37(4),585-95.
4. Bekelis K., Missios S., Spinner R.J. Falls and peripheral nerve injuries: anage-dependent relationship. // J Neurosurg, 2015,123(5),1223-9.
5. Bhatnagar D., Bushman J.S., Murthy N.S., Merolli A., Kaplan H.M., Kohn J. Fibrin glue as a stabilization strategy in peripheral nerve repair when using porous nerve guidance conduits. // J Mater Sci Mater Med, 2017,28(5),79.
6. Bittner G.D., Ballinger M.L., Raymond M.A. Reconnection of severed nerve axons with polyethylene glycol. // Brain Res, 1986,367(1-2),351-5.
7. Bloom J.D., Bleier B.S., Goldstein S.A., Carniol P.J., Palmer J.N., Cohen N.A. Laser facial nerve welding in a rabbit model. // Archives of Facial Plastic Surgery, 2012,14(1),52-8.
8. Brent Neumann, Casey Linton, Rosina Giordano-Santini, Massimo A. Hilliard. Axonal fusion: an alternative and efficient mechanism of nerve repair. // Progress in Neurobiology, 2019,173,88-101.
9. Caillaud M., Richard L., Vallat J.M., Desmoulière A., Billet F. Peripheral nerve regeneration and intraneural revascularization. // Neural Regen Res, 2019,14(1),24-33.
10. Castillo-Galvan M.L., Martinez-Ruiz F.M., de la Garza-Castro O., Elizondo-Omana R.E., Guzman-Lopez S. Study of peripheral nerve injury in patients attended by traumatism. // Gaceta Medica De Mexico, 2014,150(6),527-32.
11. Dalamagkas K., Tsintou M., Seifalian A. Advances in peripheral nervous system regenerative therapeutic strategies: a biomaterials approach. // Materials Science & Engineering C-Materials for Biological Applications, 2016,65,425-32.
12. di Summa P.G., Kalbermatten D.F., Pralong E., Raffoul W., Kingham P.J., Terenghi G. Long-term in vivo regeneration of peripheral nerves through bioengineered nerve grafts. // Neuroscience, 2011,181,278-91.

13. Eren A., Atalar H., Seymen C.M., Pinarli F.A., Kaplanoglu G.T., Turanli S. Sutureless approach with vein grafts and mesenchymal stem cells in primary nerve repair: functional and immunohistological results. // Microsurgery, 2018;38(7):780-9.
14. Fairbairn N.G., Meppelink A.M., Ng-Glazier J., Randolph M.A., Winograd J.M. Augmenting peripheral nerve regeneration using stem cells: a review of current opinion. // World Journal of Stem Cell, 2015,7(1),11-26.
15. Fairbairn N.G., Ng-Glazier J., Meppelink A.M., Randolph M.A., Valerio I.L., Fleming M.E., et al. Light-activated sealing of acellular nerve allografts following nerve gap injury. // Journal of Reconstructive Microsurgery, 2016,32(6),421-30.
16. Forli A., Bouyer M., Aribert M., Curvale C., Delord M., Corcella D., et al. Upper limb nerve transfers: a review. // Hand Surgery & Rehabilitation, 2017,36(3),151-72.
17. Foster C.H., Karsy M., Jensen M.R., Guan J., Eli I., Mahan M.A. Trends and cost-analysis of lower extremity nerve injury using the national inpatient sample. // Neurosurgery, 2019,85(2),250-6.
18. Frost S.J., Mawad D., Hook J., Lauto A. Micro- and nanostructured biomaterials for sutureless tissue repair. // Advanced Healthcare Materials, 2016,5(4),401-14.
19. Gordon T., Eva P., Borschel G.H. Delayed peripheral nerve repair: methods, including surgical 'cross-bridging' to promote nerve regeneration./ Neural Regen Res, 2015,10(10),1540-4.
20. Grinsell D., Keating C.P. Peripheral nerve reconstruction after injury: a review of clinical and experimental therapies. // Biomed Res. Int., 2014, 2014.
21. Hayat M.A. Principles and techniques of electron microscopy: biological applications. // Cambridge University Press, 2000,543.
22. Henderson P.W. Immediate and complete restoration of peripheral nerve function after injury is attainable by a combination of surgical and chemical interventions. // Medical Hypotheses, 2018,113,65-7.
23. Immerman I., Price A.E., Alfonso I., Grossman J.A.I. Lower extremity nerve trauma. // Bulletin of the Hospital for Joint Disease, 2014,72(1),43-52.
24. Isaacs J., Klumb I., McDaniel C. Preliminary investigation of a polyethylene glycol hydrogel "nerve glue". // J Brachial Plex Peripher Nerve Inj., 2009,4,16.
25. Khalifeh J.M., Dibble C.F., Dy C.J., Ray W.Z. Cost-effectiveness analysis of combined dual motor nerve transfers versus alternative surgical and nonsurgical management strategies to restore shoulder function following upper brachial plexus injury. // Neurosurgery, 2019,84(2),362-77.
26. Kornfeld T., Vogt P.M., Radtke C. Nerve grafting for peripheral nerve injuries with extended defect sizes. // Wien Med Wochenschr., 2019,169(9-10),240-51.
27. Koulaxouzidis G., Reim G., Witzel C. Fibrin glue repair leads to enhanced axonal elongation during early peripheral nerve regeneration in an in vivo mouse model. // Neural Regen Res., 2015,10(7),1166-71.
28. Kouyoumdjian J.A. Peripheral nerve injuries: a retrospective survey of 456 cases. // Muscle Nerve, 2006,34(6),785-8.
29. Li R.J., Liu Z.G., Pan Y.M., Chen L., Zhang Z.X., Lu L.J. Peripheral nerve injuries treatment: a systematic review. // Cell Biochemistry and Biophysics, 2014,68(3),449-54.
30. Lin K., Yang D., Chu I. et al. DuraSeal as a ligature in the anastomosis of rat sciatic nerve gap injury. // Journal of Surgical Research, 2010,161(1), 101–110.
31. Liu G-y, Jin Y., Zhang Q., Li R. Peripheral nerve repair: a hot spot analysis on treatment methods from 2010 to 2014. // Neural Regeneration Research, 2015,10(6),996-1002.
32. Longo M.V., Marques de Faria J.C., Isaac C., Nepomuceno A.C., Teixeira N.H., Gemperli R. Comparisons of the results of peripheral nerve defect repair with fibrin conduit and autologous nerve graft: an experimental study in rats. // Microsurgery, 2016,36(1),59-65.
33. Missios S., Bekelis K., Spinner R.J. Traumatic peripheral nerve injuries in children: epidemiology and socioeconomics. // Journal of Neurosurgery-Pediatrics, 2014,14(6),688-94.
34. Molotkovets V.Y., Medvediev V.V., Korsak A.V., Chaikovsky Yu.B., Tsymbaliuk V.I. Restoration of the integrity of a transected peripheral nerve with the use of an electric welding technology. // Neurophysiology, 2020,52,31–42.
35. Pabari A., Yang S.Y., Mosahebi A., Seifalian A.M. Recent advances in artificial nerve conduit design: strategies for the delivery of luminal fillers. // J Control Release, 2011,156(1),2–10.
36. Paskal A.M., Paskal W., Pietruski P., Wlodarski P.K. Polyethylene glycol: the future of posttraumatic nerve repair? Systemic review. // Int J Mol Sci, 2019,20(6),1478.
37. Rosberg H.E., Carlsson K.S., Hojgard S., Lindgren B., Lundborg G., Dahlin L.B. Injury to the human median and ulnar nerves in the forearm - analysis of costs for treatment and rehabilitation of 69 patients in Southern Sweden. // Journal of Hand Surgery-British and European Volume, 2005,30B(1),35-9.
38. Scholz T., Krichevsky A., Sumarto A., Jaffurs D., Wirth G.A., Paydar K., et al. Peripheral nerve injuries: an international survey of current treatments and future perspectives. // Journal of Reconstructive Microsurgery, 2009,25(6),339-44.
39. Sexton K.W., Pollins A.C., Cardwell N.L., et al. Hydrophilic polymers enhance early functional outcomes after nerve autografting. // J Surg Res., 2012,177(2),392-400.
40. Soucy J.R., Sani E.S., Lara R.P., Diaz D., Dias F., Weiss A.S., et al. Photocrosslinkable gelatin/tropoelastin hydrogel adhesives for peripheral nerve repair. // Tissue Engineering Part A, 2018,24(17-18),1393-405.
41. Taylor C.A., Braza D., Rice J.B., Dillingham T. The incidence of peripheral nerve injury in extremity trauma. // Am J Phys Med Rehabil., 2008,87(5),381-5.
42. Tse R., Ko J.H. Nerve glue for upper extremity reconstruction. // Hand Clinics, 2012,28(4),529–540.
43. Turner N.J., Johnson S.A., Foster L.J.R., Badylak S.F. Sutureless nerve repair with ECM bioscaffolds and laser-activated chitosan adhesive. // Journal of Biomedical Materials Research Part B-Applied Biomaterials, 2018,106(5),1698-711.
44. Wali A.R., Park C.C., Brown J.M., Mandeville R. Analyzing cost-effectiveness of ulnar and median nerve transfers to regain forearm flexion. // Neurosurgical Focus, 2017,42(3).
45. Wang C., Oh S., Lee H.A., Kang J., Jeong K-J., Kang S.W., et al. In vivo feasibility test using transparent carbon nanotube-coated polydimethylsiloxane sheet at brain tissue and sciatic nerve. // Journal of Biomedical Materials Research Part A, 2017,105(6),1736-45.
46. Wang T., Ito A., Aoyama T., Nakahara R., Nakahata A., Ji X., Zhang J., Kawai H., Kuroki H. Functional evaluation outcomes correlate with histomorphometric changes in the rat sciatic nerve crush injury model: a comparison between sciatic functional index and kinematic analysis. // PLoS One, 2018,13(12),e0208985.
47. Wang W.J., Degrugillier L., Tremp M., Prautsch K., Sottaz L., Schaefer D.J., et al. Nerve repair with fibrin nerve conduit and modified suture placement. // Anatomical Record-Advances in Integrative Anatomy and Evolutionary Biology, 2018,301(10),1690-6.

SUMMARY

EPINEURIAL SUTURES, POLYETHYLENE GLYCOL HYDROGEL AND FIBRIN GLUE IN THE SCIATIC NERVE REPAIR IN RATS: FUNCTIONAL AND MORPHOLOGICAL ASSESSMENTS IN EXPERIMENT

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Mechanical damage to the peripheral nerve is a fairly common type of injury, which is characterized by a complex of long-term neurological disorders and require significant financial costs. The aim of this work is to evaluate the efficiency of sciatic nerve (SN) regeneration after neuroraphy using epineural suture (ES), polyethylene glycol hydrogel (PEG), and fibrin glue (FG). The studies were carried out on 30 white outbred male rats, which were divided into six experimental groups: Group №1: intact rats; Group №2: Sham operated; Group №3: complete transection of the SN; Group №4: nerve repair with ES; Group №5: nerve repair with PEG; Group №6: nerve repair with FG. Functional recovery was assessed at 1, 2, 3, 4 postoperative weeks using a walking-track analysis with subsequent determination of the sciatic nerve functional index (SFI). At 4 weeks, electroneuromyography, histological and morphometric analyzes were performed. The combined analysis indicated that PEG significantly improved functional recovery, both in the SFI index and in the skeletal muscle M-response. Compared to ES and PEG, the use of FG was reflected in a lower significance of the indicators compared to PEG. Statistical analysis indicates a positive effect of PEG and FG on nerve regeneration, although significantly greater remyelination (analysis based on fiber diameter) was confirmed only in the PEG group, which explains the faster functional recovery of the limb. PEG in the form of a hydrogel is a more promising agent in microsurgical restoration of damaged nerves as an adhesive, it promotes rapid nerve regeneration, denervated muscle re-innervation and functional limb recovery.

Keywords: sciatic nerve, repair, epineural sutures, polyethylene glycol hydrogel, fibrin glue, functional outcome.

РЕЗЮМЕ

ЭПИНЕВРАЛЬНЫЙ ШОВ, ПОЛИЭТИЛЕНГЛИКОЛЬ ГИДРОГЕЛЬ И ФИБРИНОВЫЙ КЛЕЙ В ВОССТАНОВЛЕНИИ СЕДАЛИЩНОГО НЕРВА: ФУНКЦИОНАЛЬНАЯ И МОРФОЛОГИЧЕСКАЯ ОЦЕНКА В ЭКСПЕРИМЕНТЕ

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Механическое повреждение периферического нерва - весьма частый вид травмы, который характеризуется комплексом длительных неврологических расстройств и обусловливает значительные финансовые затраты.

Цель исследования - оценка эффективности регенерации седалищного нерва после нейрорафии с помощью эпиневрального шва, полиэтилен гликоля гидрогеля и фибринового клея. Исследования проводились на 30 белых беспородных самцах крыс, которые разделены на шесть экспериментальных групп: группа №1 - интактные крысы; группа №2 - ложно-оперированные; группа №3 - полное пересечение седалищного нерва (СН); шруппа №4 - соединение концов СН с помощью эпиневрального шва (ЭШ); группа №5 - соединение концов СН с помощью полиэтилен гликоля гидрогеля (ПГГ); группа №6 - соединение концов СН с помощью фибринового клея (ФК). Функциональное восстановление оценивалось в конце I, II, III, IV недели после операции с помощью тест-ходов на дорожке с последующим определением функционального индекса седалищного нерва (ИСН). На IV неделе проводили электронейромиографию, гистологический и морфометрический анализы. Обобщающий анализ указывает, что ПГГ достоверно лучше способствовал функциональному восстановлению, как по ИСН, так и М-ответу скелетных мышц. В сравнении с ЭШ и ПГГ, применение ФК отразилось в меньшей значимости показателей относительно ПГГ. Статистический анализ указывает на положительное действие ПГГ и ФК на регенерацию нерва, хотя достоверно большая ремиелинизация (анализ на основе диаметра волокон) подтверждена только в группе с ПГГ, что объясняет более быстрое функциональное восстановление конечности. ПГГ в форме гидрогеля является более перспективным средством в микрохирургическом восстановлении поврежденных нервов в качестве клея, способствует быстрой регенерации нерва, реинервации денервированных мышц и функциональному восстановлению конечности.

რეზიუმე

ეპინევრული ნაკერი, პოლიეთილენგლიკოლ-ჰიდროგელი და ფიბრინული წებო საჯდომი ნერვის აღდგენაში: ფუნქციური და მორფოლოგიური შეფასება ექსპერიმენტში

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პერიფერიული ნერვის მექანიკური დაზიანება ტრავმის საკმაოდ ხშირი სახეა, რომელიც ხანგრძლივი ნევროლოგიური დარღვევებით ხასიათდება და მნიშვნელოვან ფინანსურ დანახარჯს განაპირობებს.

კვლევის მიზანს წარმოადგენდა საჯდომი ნერვის რეგენერაციის ეფექტურობის შეფასება ნეირორაფიის შემდეგ ეპინევრული ნაკერის, პოლიეთილენგლიკოლ-ჰიდროგელის და ფიბრინული წებოს გამოყენების პირობებში. კვლევა ჩატარდა 30 თეთრ უჯიშო მამრ ვირთაგვაზე, რომლებიც დაიყო ექვს ექსპერიმენტულ ჯგუფად: ჯგუფი I – ინტაქტური ვირთაგვები; ჯგუფი II – ცრუ-ნაოპერაციებთა ჯგუფი; III – საჯდომი ნერვის სრული გადაკვეთა; ჯგუფი IV – საჯდომი ნერვის ბოლოების დაკავშირება ეპინევრული ნაკერით; ჯგუფი V – საჯდომი ნერვის ბოლოების დაკავშირება პოლიეთილენგლიკოლ-ჰიდროგელით; ჯგუფი VI – საჯდომი ნერვის ბოლოების დაკავშირება ფიბრინული წებოთი.

ფუნქციური აღდგენა ფასდებოდა ოპერაციიდან I, II, III და IV კვირის ბოლოს სიარულის ტესტის

საშუალებით, საჯდომი ნერვის ფუნქციური ინდექსის შემდგომი განსაზღვრით. IV კვირას ტარდებოდა ელექტრონეირომიოგრაფია, ჰისტოლოგიური და მორფომეტრიული ანალიზები.

შედეგების განზოგადება მიუთითებს, რომ პოლიეთილენგლიკოლ-ჰიდროგელი მეტად უწყობს ხელს ფუნქციურ აღდგენას როგორც საჯდომი ნერვის ფუნქციური ინდექსის, ასევე, ჩონჩხის კუნთების მიოგრაფიული პასუხის მიხედვით. ეპინევრულ ნაკერთან და პოლიეთილენგლიკოლ-ჰიდროგელთან შედარებით, ფიბრინული წებოს გამოყენებამ განაპირობა მაჩვენებლების ნაკლები სიდიდე პოლიეთილენგლიკოლ-ჰიდროგელთან მიმართებით.

სტატისტიკური ანალიზი მიუთითებს პოლიეთილენგლიკოლ-ჰიდროგელის და ფიბრინული წებოს დადებით გავლენაზე ნერვის რეგენერაციაზე, თუმცა, სარწმუნოდ უფრო მაღალი რემიელინიზაცია (ბოჭკოთა დიამეტრის ანალიზის მიხედვით) დადასტურდა მხოლოდ პოლიეთილენგლიკოლ-ჰიდროგელის ჯგუფში, რითაც აიხსნება კიდურის უფრო სწრაფი ფუნქციური აღდგენა. დაზიანებული ნერვების მიკროქირურგიული აღდგენისას პოლიეთილენგლიკოლი ჰიდროგელის სახით წარმოადგენს უფრო პერსპექტულ საშუალებას, როგორც წებო, უწყობს რა ხელს ნერვის სწრაფ რეგენერაციას, დენერვირებული კუნთების რეინერვაციას და კიდურის ფუნქციურ აღდგენას.

PECULIARITIES OF ACTIVATION OF COMPENSATORY-ADAPTIVE PROCESSES IN ADULT RAT LIVER CAUSED BY UNILATERAL NEPHRECTOMY

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At the modern stage, the study of the mechanisms of compensatory-adaptive processes of separate as well as inter organs, has acquired special importance. The urgency of the problem is further enhanced by its social nature. Deep study of these mechanisms allows for the rational employment of such people after treatment. In this sense, special attention is given to organs such as the heart,liver and kidneys. Recently, two types of responses after acute organ failure have appeared to be shared in the liver, heart, and kidney: (i) surviving differentiated parenchymal cells undergo cell hypertrophy via polyploidization; and (ii) a population of progenitors, mostly identified as resident, more immature diploid parenchymal cells, self-renew and differentiate to replace lost cells [12]. Complex metabolic transformations, as well as detoxification and filtration processes, as it is known, maintain the body's homeostasis [5]. A pathological condition that develops during liver damage and revealed in impaired kidney function, including acute renal failure, has been known for about 100 years as hepatorenal syndrome. Despite numerous treatments, a significant reduction in mortality has not been achieved to date [3,13,15-17].

Particular importance today is also attached to the study of compensatory mechanisms induced in response to increased functional load on the liver after various renal pathologies or resections. Latent hepatopathy caused by increased functional load on the liver in response to renal resection is revealed in experimental animals and patients. Thus, any changes in the functioning of these organs, including those caused by surgery, increase the risk of severe complications and inevitably lead to systemic disorders. Based the above, the urgency of the problem of inter organ compensatory mechanisms and the expediency of intensive research in this direction is clear [4].

Recent studies have found relatively little information that compensatory and adaptive growth of liver is not always accompanied by strictly regulated sequential regeneration processes such as proliferation, hypertrophy, and polyploidy. For example, it has been shown that 4 days after the common bile duct ligation, ploidy of destructive liver parenchyma cells is increased [7]. Increasing of the degree of polyploidy was found under radiation and oxidative stress [10]. It has been established that, in the case of alimentary dyslipidemia, the mechanism of regeneration depends on the duration of use of the hepatogenic ration and the degree of damage [1]. Clinical trials have shown that after unilateral nephrectomy for any reason, patients need constant follow-up, since the changes that develop over the years in the remaining kidney primarily affect liver function [14]. For example, after unilateral nephrectomy decrease in urine output and glomerular filtration, which leads to the so-called latent hepatopathy is occur [2]. At the same time, it is not yet known, for example, which mechanism of adaptive growth is used by the liver in response to dysfunction resulting from unilateral nephrectomy.

Evaluation of changes in hepatocyte ploidy of white adult rats at different time from unilateral nephrectomy is the aim of the work.

Material and methods. *Experimental Animals and Model.*

Experiments were carried out on adult white rats(130-150 g). All laboratory animals have been housed in cages at room temperature (25°C), with free access to standard food and water chow and subjected to a 12 h light/dark cycle. Unilateral nephrectomy (resection of the right kidney) was performed under ether anesthesia.

Experimental groups

The animals were divided into 2 groups: 1. Control group - intact rats that underwent false surgery; 2. Experimental group - animals that underwent unilateral nephrectomy. liver and renal tissue (study material) was taken at 24 h, 48 h, 72 h, after Unilateral nephrectomy.

1 mg/kg of colchicine (Sigma, USA) was injected into the animals of both the control and the test groups for determination of the colchicine mitotic index per 1000 cells (‰).