GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 2 (323) Февраль 2022

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

No 2 (323) 2022

Published in cooperation with and under the patronage
of the Tbilisi State Medical University

Издается в сотрудничестве и под патронажем
Тбилисского государственного медицинского университета

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თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board 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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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

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Ежемесячный совместный грузино-американский научный электронно-печатный журнал
Общества Ограниченной Ответственности “Грузинская Деловая Пресса”.
Издается с 1994 г., распространяется в СНГ, ЕС и США

Website:
www.geomednews.com

Версия: печатная. **Цена:** свободная.
Условия подписки: подписка принимается на 6 и 12 месяцев.
По вопросам подписки обращаться по тел.: 293 66 78.
Контактный адрес: Грузия, 0177, Тбилиси, ул. Асатиани 7, IV этаж, комната 408
тел.: 995(32) 254 24 91, 5(55) 75 65 99
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GEORGIAN MEDICAL NEWS
Monthly Georgia-US joint scientific journal published both in electronic and paper formats by LLC Georgian Business Press. Published since 1994. Distributed in NIS, EU and USA.

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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).

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1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

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.

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10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

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ავტორთა საყურადღებოდ!

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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.

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5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

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:

FEATURES OF MORPHOLOGICAL RECONSTRUCTION OF PARADENTIUM ON THE BACKGROUND OF SIX-WEEK OPIOID ACTION WITH FURTHER WITHDRAWAL AND COMPLEX TREATMENT DURING FOUR WEEKS IN THE EXPERIMENT

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Opioid analgesics due to their strong analgesic effect are widely used in modern medical practice [7]. It is important, that the duration of opioid analgesic use should be as short as possible to avoid mental and physical addiction, as well as the development of drug tolerance and the risk of overdose. [5,7]. According to the professional medical literature, long-term use of opioids leads to evidential changes in the organism [12], where the pathology of the oral cavity, paradental tissues occupy a leading place in individuals, who abuse with narcotic substances [3]. Dental status in drug addicted people is overloaded by numerous pathological conditions of the tissues of the tooth and mucous membranes of the oral cavity, what complicates the differential diagnosis and treatment [3,4,15]. In addition, despite the improvement in dental health indexes in many countries, the prevalence of paradentitis remains extremely high, there is no standard treatment regimen today [2,14].

Taking into account the fact that the problem of drug addiction is constantly growing, in dentistry, data on the condition of the oral cavity organs, the structural components of the paradentium under the influence of opioid agents, both in clinical and morphological aspects, are extremely necessary. [13]. In this regard, the introduction of etiopathogenetic treatment of paradental diseases of various origins, including drug addiction is an urgent problem of today [3,4,6,8-10**]**. Paying attention that the issues of pathomorphogenesis and adequate treatment of dystrophic and inflammatory processes that develop in the paradentium under the action of opioid agents are still relevant, there is originated a necessity to develop in experiment an optimal scheme of pathogenetic complex treatment in such conditions.

The aim of the research is to study the features of microscopic reorganization of paradental tissues under six weeks of exposure to the opioid analgesic nalbuphine, its four-week withdrawal and medicinal correction using pentoxifylline and ceftriaxone in the experiment.

Material and methods. Research were performed on 22 nonlinear male rats, body weight 160–255 g, age 4.5–7 months. The first group were included intact rats (10). In the second group, animals (12) received intramuscular injections of nalbuphine during the first six weeks, followed by four weeks of drug withdrawal. The initial dose of the opioid analgesic nalbuphine during two weeks was 0.212 mg/kg; on 3-4th weeks the dose was increased to 0.225 mg/kg; along 5-6th weeks – 0.252 mg/kg. In order to correct the pathological changes that occur at the action of opioids in paradental tissues, on the background of the abolition of nalbuphine it was used antihypoxic drug pentoxifylline and the antibacterial drug ceftriaxone. Pentoxifylline was administered intramuscularly, daily from 7th to 10th week inclusively at a dosage of 2.86 mg. Ceftriaxone injections were performed during 11 days at the end of the experiment (9th-10th weeks) at a dose equivalent to rats, which was 2.86 mg for one rat weighting 200 g. The material was taken at the end of the tenth week of the experiment. Animals were kept in standard vivarium conditions and experiments were performed in accordance with international ethical principles approved by the General Assembly of the World Medical Association “About the Humane Treatment of Animals” (2000), and according to the decision of the Commission on Bioethics of Danylo Halytskyy Lviv National Medical University (protocol №5 of 24.05.2021). Before taking material, the animals were removed from the experiment using diethyl ether. Amputated upper and exarticulated lower jaws were used for histological examination. A complex decalcification of the obtained fragments of the upper and lower jaws was performed before making histological sections. Preparations for histological examination were prepared according to the generally accepted method using hematoxylin, eosin and azan dyes according to the Heidenhain method.

Results and discussion. On histological examinations of paradental tissues of rats of the intact group it was noted that the epithelium of the gums is evenly structured, with signs of keratinization in the free part of the gingiva, the layers of cells are stratified. The integrity of the epithelial attachment was preserved in the area of the bottom of the gingival sulcus. The connective tissue of the mucous membrane of the gums and periodontium is formed by bundles of collagen fibers of different directions, vessels of the hemomicrocirculatory tract are with moderate blood supply (Fig. 1).

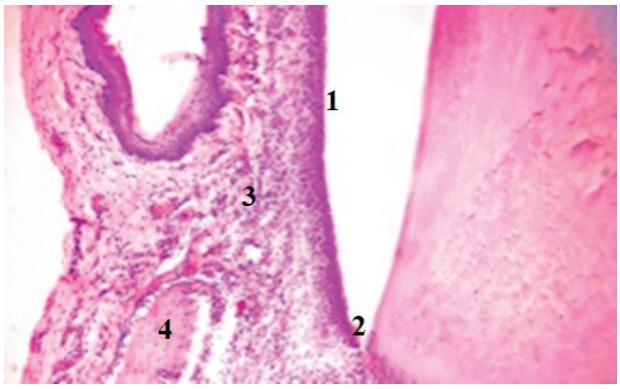
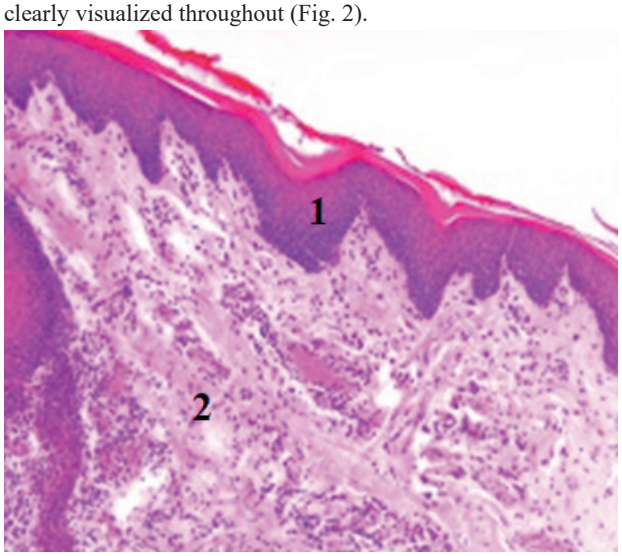


Fig. 1. Paradental tissues of intact rats. 1 - epithelium of the gingival sulcus, 2 - the bottom of the gingival sulcus 3 - connective tissue, 4 - bone tissue. Hematoxylin and eosin staining. Magnification x40

Histologic examination in rats of the second group showed that applied complex treatment with pentoxifylline and ceftriaxone under conditions of four-week withdrawal of the opioid analgesic nalbuphine, which was administered for six weeks at the beginning of the experiment, contributed to the positive dynamics of structural paradental tissue organization. However, complete recovery of the morphological rearrangement of the components of the paradentium in comparison with intact animals was not observed.

In the free and attached parts of the gums of white rats noted uneven thinning of the epithelial plate, with a slight violation of the stratification of cell layers. In some places, the phenomena of focal hyperkeratosis and desquamation were visualized (Fig. 2). This indicated the initial stages of adaptive restructuring of the epithe-

lial layer, which was a prerequisite for strengthening the potential abilities of the oral mucose membrane under conditions of complex drug correction. However, the thickening of the keratin layer at focal hyperkeratosis was accompanied by thinning of the granular one, sometimes prickle layer as well in comparison with intact animals, which was due to delayed exfoliation and was manifested by a decrease in the thickness of the epithelial plate. Intraepithelial infiltration was moderate, the contours of the basal membrane were clearly visualized throughout (Fig. 2).



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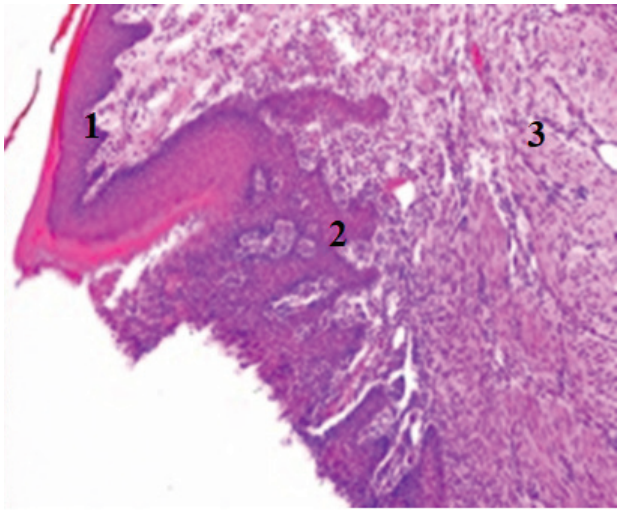


B

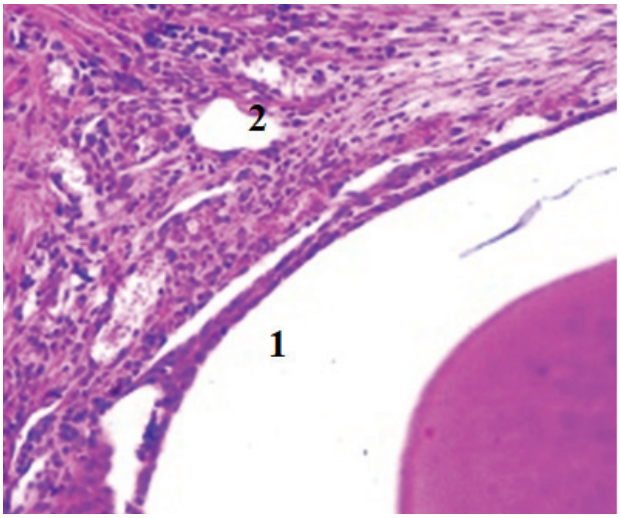
Fig. 2. Rat paradental tissues after ten weeks: six weeks of opioid use, four weeks after its withdrawal and correction with pentoxifylline and ceftriaxone.

A. 1 - thinning, desquamation of the epithelium, 2 - plethora, stasis of its lamina propria. Hematoxylin and eosin staining. Magnification x200

B. 1 - epithelium of the free part of the gums, 2 – reepithelialization in the area of the ulcer, 3 – moderate vascularization of its lamina propria. Hematoxylin and eosin staining. Magnification x100

Prolonged action of the opioid analgesic during six weeks in the initial stages of the experiment led to erosion and ulceration of the epithelial layer. However, our complex drug correction with the use of the antihypoxic drug pentoxifylline caused ulcer healing, which was manifested on histological preparations by areas of reepithelialization (Fig. 2). In the place of healing of ulcers the focal acanthosis was defined, which arose owing to the strengthened proliferation of a prickle and basal layers of an epithelial plate. However, on other areas the epithelial growths were mostly short, broad, with rounded tips. In addition, new ulcers or erosions were not detected in the epithelial plate of the free and attached parts of the gingiva.

In the upper and middle thirds of the gingival sulcus there was a slight thinning and exfoliation of the surface layer of the sulcular epithelium. In the lower third of the gingival sulcus were found signs of fragmentary damage of the epithelial attachment at the place of fixation to the enamel-cement border of the tooth, with small areas of erosion. However, signs of diffuse destruction of the connective part of epithelium of the gingiva and the formation of deep paradental pockets were not observed (Fig. 3). There were also no signs of pathological keratinization within the middle and lower thirds of the epithelium of the gingival sulcus.



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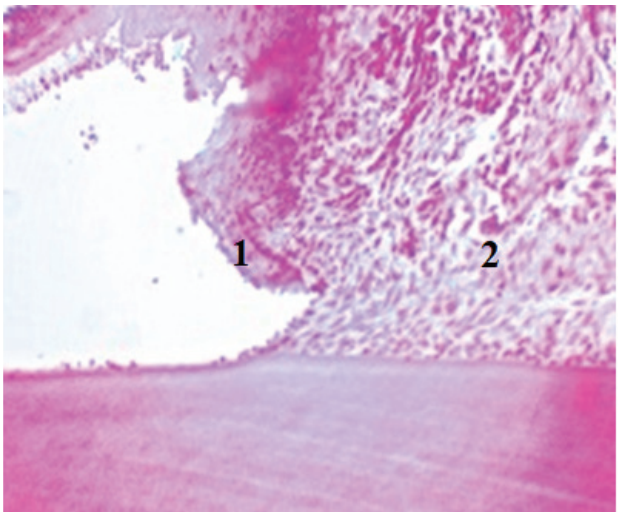


B

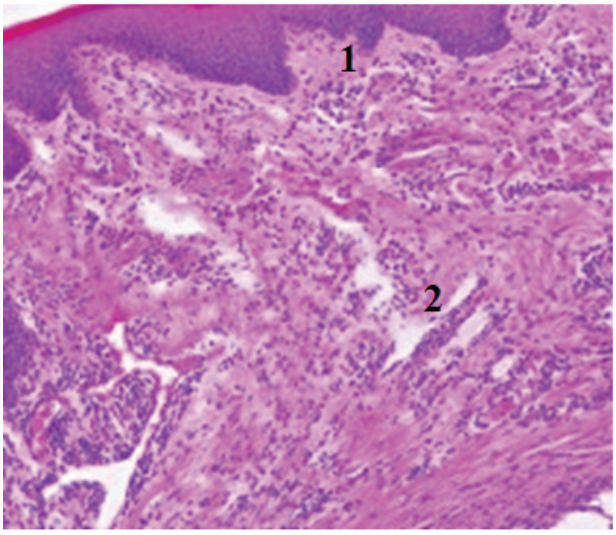
Fig. 3. Rat paradental tissues after ten weeks: six weeks of opioid use, four weeks after its cancellation and correction with pentoxifylline and ceftriaxone.

A. 1 – exfoliation of the sulcular epithelium, 2 – moderate edema of the lamina propria. Hematoxylin and eosin staining. Magnification x200

B. 1 - focal disorganization of epithelial attachment, 2 – marginal periodontium. Hematoxylin and eosin staining. Magnification x400

In the connective tissue of the gingival mucosa was determined a slight swelling of the intercellular substance and moderate perivascular infiltration. The structure of the bundles of collagen fibers of lamina propria was partially restored, only in some places observed their disorganization (Fig. 2, 4). In large areas, the connective tissue papillae were mostly short and smooth, with rounded tips.

In a hemomicrocirculatory channel of lamina propria of a mucous membrane of gingiva a weakly positive dynamics was observed, however, the expressed signs of hypervascularization on histologic preparations were not visually noted also. Hemomicrovessels were mostly moderately blood-filled, single small focal hemorrhages of diapedetic nature were visualized. However, in some places the phenomena of angiogenesis which were shown by formation of capillary buds in the thickness of layers of lamina propria of a mucous membrane of gingiva were noted also (Fig. 4).



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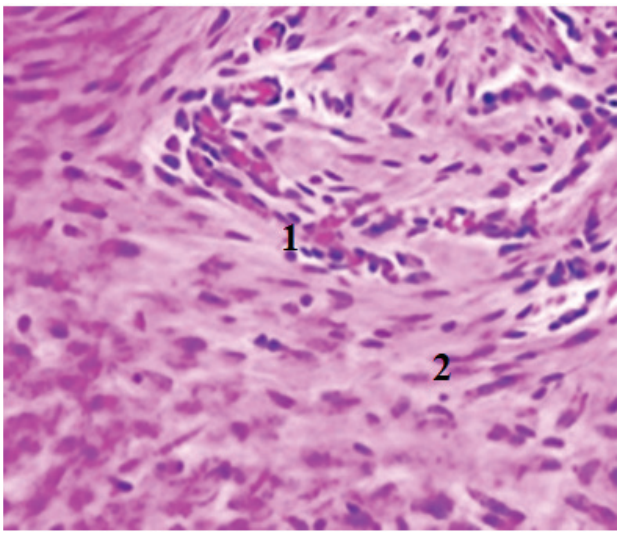


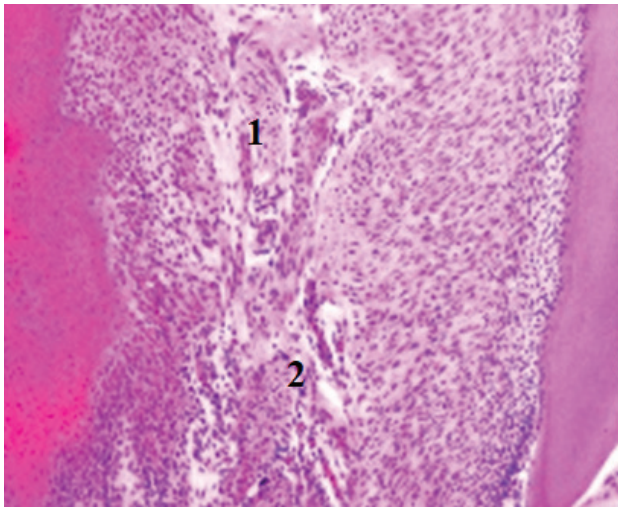
B

Fig. 4. Rat paradental tissues after ten weeks: six weeks of opioid use, four weeks after its cancellation and correction with pentoxifylline and ceftriaxone.

A. 1 – connective tissue papillae, 2 - edema, infiltration of the lamina propria. Hematoxylin and eosin staining. Magnification x200

B. 1 – angiogenesis in lamina propria; 2 – moderate infiltration of connective tissue. Hematoxylin and eosin staining. Magnification x400

In the fibrous connective tissue of the marginal and apical periodontium signs of pronounced disorganization of the intercellular substance and collagen fibers were not observed. Fibers of circular ligaments were partially fragmented; the intercellular substance of the marginal periodontium was moderately swollen. However, no diffuse destruction of the circular ligament was observed (Fig. 3). Within the apical periodontium there were phenomena of mucoid edema, which were manifested by minor destructive changes in collagen fibers and intercellular substance (Fig. 5).



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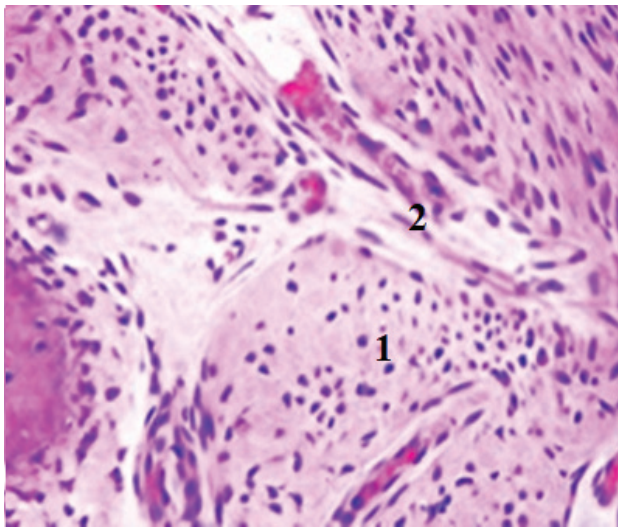

B

Fig. 5. Rat paradental tissues after ten weeks: six weeks of opioid use, four weeks after its withdrawal and correction with pentoxifylline and ceftriaxone.

A. 1 – mucoid edema in the periodontium, 2 – small diapedetic hemorrhages in the periodontium. Hematoxylin and eosin staining. Magnification x100

B. 1 – mucoid edema, 2 – blood-filled vessels in the periodontium. Hematoxylin and eosin staining. Magnification x400

In small areas areas detachments of collagen fibers of the periodontium from the periosteum of the alveolar process there were visualized. Dense formed and soft unformed connective tissue of the periodontium was moderately infiltrated, where it was dominated by fibroblasts and fibrocytes. In the marginal and apical parts of the

periodontium, moderately blood-filled vessels were noted, as well as small focal hemorrhages of diapedesic nature.

However, the manifestations of impaired hemorheological properties and permeability of vascular walls were not systemic. The use of medicinal correction contributed to the partial normalization of microcirculation. This was manifested by a decrease in signs of stasis in the lumen of blood vessels, aggregation of erythrocytes and their adhesion, which generally contributed to the reduction of swelling processes in the periodontium (Fig. 5). At the microstructural level, dense periodontal fusion with periosteum and tooth root cementum was detected.

As a result of our research, it was found that the positive effect of the combined action of the medicines used in the experiment led to a significant improvement in the morphological organization of paradental tissues during long-term opioid action. At the same time, there is evidence that as a universal non-specific criterion that occurs in paradentitis and determines the direction of treatment, is the structural and functional state of paradental tissues, including gingival mucosa, which is associated with hemomicrocirculatory disorders that can lead to tissue hypoxia and energy deficit [1]. Thus, in patients with generalized paradentitis with the use of thiotriazoline, which has anti-ischemic and antioxidant effects, there was observed a decrease in the edema process, the appearance of epithelial cell regeneration and the restoration of microcirculation [2].

In the complex therapy of drug addicted persons, including those with opioid addiction, researchers point to the feasibility of using medicines with antioxidant and anti-inflammatory properties, which contributes to the positive dynamics in the structural rebuilding of paradental tissues [4,16]. In particular, such medicinal properties are inherent for the pentoxifylline drug [11]. On the background of drug addiction, including opioid abuse, along with the use of traditional anti-inflammatory therapy, it is advisable to use antibacterial drugs that have a direct impact on the development and progression of the inflammatory process [6 8,9]. Thus, the use of pentoxifylline and ceftriaxone on the background of four-week withdrawal of opioid, which was administered to rats during six weeks, allowed to achieve the desired therapeutic effect on the morphological rearrangement of the components of the paradentium in the experiment.

Conclusions. The use of pentoxifylline and ceftriaxone after the period of 4-weeks withdrawal of opioid, which was administered during 6 weeks at the beginning of the experiment, prevented the rapid progression of inflammatory-dystrophic process and caused a protective effect on paradental tissues. Reepithelialization in the area of ulcers healing was noted in the epithelial plate of the gums, and signs of focal hyperkeratosis and acanthosis were visualized, which was a prerequisite for strengthening the potential of the oral mucosa under conditions of complex medical correction.

The structure of the bundles of collagen fibers of the lamina propria of the gingival mucosa was partially restored, the phenomena of angiogenesis were noted, which indicated the activation of reparative processes in the connective tissue of the paradentium. Signs of mucoid edema were observed in the periodontium, indicating superficial connective tissue damage, as well as reduction of stasis and erythrocyte aggregation in the lumen of blood vessels, which improved microcirculation and gradually restored the structural organization of paradental tissues.

REFERENCES

1. Бабай О.М. Методика та досвід оцінки ефективності лікування пацієнтів з генералізованим пародонтитом за даними ультраструктурного аналізу епітелію ясен. // Український журнал екстремальної медицини ім.Г.О.Можаєва. 2016; 2(17): 5–10.
2. Бучковська А.Ю., Наконечна ОВ., Петришин О.А., Струс Х.І. Ультраструктурне дослідження слизової оболонки ясен при генералізованому пародонтиті. // Світ медицини та біології. 2018; 4(66): 145–148.
3. Зубачик В.М., Федун І.Р. Біохімічні показники ротової рідини у наркозалежних хворих на хронічний генералізований пародонтит. // Клінічна стоматологія. 2017; 2: 9–14.
4. Паталаха О. В., Лоскутова І. В. Комплексне лікування генералізованого пародонтиту в наркозалежних хворих на токсичний гепатит. // Вісник наукових досліджень. 2018; 2: 103–109. doi.org/10.11603/2415-8798.2018.2.9089.
5. Barnett M.L., Olenski A.L., Jena A.B. Opioid-prescribing patterns of emergency physicians and risk of long-term use. // N Engl J Med. 2017; 376(7): 663–673. DOI: 10.1056 / NEJMsa1610524.
6. Buttar R, Aleksejuniene J, Coil J. Antibiotic and opioid analgesic prescribing patterns of dentists in Vancouver and endodontic specialists in British Columbia. // J Can Dent Assoc. 2017;83:
7. Dalal S., Bruera E. Pain Management for Patients With Advanced Cancer in the Opioid Epidemic Era. // American Society of Clinical Oncology Educational Book. 2019; 39: 24–35. doi: 10.1200/EDBK_100020.
8. Dana R., Azarpazhooh A., Laghapour N., Suda K.J., Okunseri C. Role of dentists in prescribing opioid analgesics and antibiotics: an overview. // Dent Clin North Am. 2018; 62: 279–294. doi: 10.1016/j.cden.2017.11.007.
9. D`Couto H., Robbins G., Ard K., Wakeman S., Alves J., Nelson S. Outcomes of outpatient antibiotic treatment of injection drug users discharged to home with central venous access. // Open Forum Infectious Diseases. 2016; 3(1): 1334. doi:10.1093/ofid/ofy056
10. Fik V.B., Paltov Ye.V., Kryvko Yu.Ya. Ultrastructural condition of rats periodontal tissue in opioid influence during two weeks and after its four-week withdrawal on correction. // Reports of morphology. 2019; 2(25): 49–55. DOI: 10.31393/morphology-journal-2019-25(2)-06.
11. McCarty M.F., O'Keefe J.H., DiNicolantonio J.J. Pentoxifylline for vascular health: a brief review of the literature. // Open Heart. 2016; 3:e000365. doi: 10.1136/openhrt-2015-000365.
12. Paltov E. V., Kovalyshyn O. A., Fik V. B. et al. Pathomorphological changes in rats` retinal layers at the end of the twelth week of experimental opioid influence.// International Academy Journal Web of Scholar. 2019; 4(34):19–22. DOI: https://doi.org/10.31435/rsglobal_wos/30042019/6444
13. Pang J., Tringale K.R., Moss W.J., May M.E., Furnish T. et al. Chronic Opioid Use Following Surgery for Oral Cavity Cancer. Otolaryngol. //Head Neck Surg. 2017; 143(12): 1187–1194.
14. Preshaw P. M. Detection and diagnosis of periodontal conditions amenable to prevention. // BMC Oral Health. 2015; 15(1): 1-5. DOI: https://doi.org/10.1186/1472-6831-15-S1-S5.
15. Teoh L. Opioid prescribing in dentistry – is there a problem? // Aust Prescr. 2020; 43:144–145. DOI: 10.18773/austprescr.2020.056.
16. Zhao-Fleming, H., Hand A., Zhang K. Effect of non-steroidal anti-inflammatory drugs on post-surgical complications against the backdrop of the opioid crisis. // Burns Trauma. 2018; 6(1): 25. doi: 10.1186/s41038-018-0128-x.

SUMMARY

FEATURES OF MORPHOLOGICAL RECONSTRUCTION OF PARADENTIUM ON THE BACKGROUND OF SIX-WEEK OPIOID ACTION WITH FURTHER WITHDRAWAL AND COMPLEX TREATMENT DURING FOUR WEEKS IN THE EXPERIMENT

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This study aimed to research the features of microscopic reorganization of paradental tissues under six-week exposure to the opioid analgesic nalbuphine, and under the conditions of its four-week withdrawal and medicinal correction with pentoxifylline and ceftriaxone in the experiment. The study was performed on 22 male rats, weighing 160-255 g, aged 4.5-7 months. Animals were administered nalbuphine for 6 weeks, with a gradual increase in dose (0.212-0.252 mg/kg). after period of four-week withdrawal of nalbuphine, a medicinal correction was performed using pentoxifylline and ceftriaxone (2.86 mg). The complex treatment made after 4-week period of opioid withdrawal, which was administered to animals during 6 weeks, led to the healing of ulcers, which showed signs of reepithelialization. The structure of collagen fibers of the lamina propria of the gingival mucosa was partially restored, the signs of angiogenesis were determined. Signs of mucoid edema and reduction of hypervascularization, stasis, erythrocyte aggregation in the lumen of blood vessels were observed in the periodontium, what helped to improve microcirculation and restoration of the structural organization of the paradentium. The use of pentoxifylline and ceftriaxone after period of 4-weeks withdrawal of opioid, which was administered for 6 weeks at the beginning of the experiment, prevented the rapid progression of inflammatory-dystrophic process and caused a protective effect on paradental tissues.

Key words: opioid analgesic, white rats, paradental tissues, histological research, complex treatment.

РЕЗЮМЕ

ОСОБЕННОСТИ МОРФОЛОГИЧЕСКОЙ ПЕРЕСТРОЙКИ ПАРОДОНТА НА ФОНЕ ШЕСТИНЕДЕЛЬНОГО ДЕЙСТВИЯ ОПИОИДА С ПОСЛЕДУЮЩЕЙ ОТМЕНОЙ И КОМПЛЕКСНЫМ ЛЕЧЕНИЕМ НА ПРОТЯЖЕНИИ ЧЕТЫРЕХ НЕДЕЛЬ В ЭКСПЕРИМЕНТЕ

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Целью исследования явилось определить особенности микроскопической реорганизации пародонта при шестинедельном воздействии опиоидного анальгетика налбуфин и после четырехнедельной его отмены медикаментозной коррекции пентоксифиллином и цефтриаксоном в эксперименте.

Исследование проведено на 22 нелинейных крысах-самцах, массой 160-255 г, 4,5-7 месяцев. Животным вводили налбуфин в течение 6 недель с постепенным увеличением дозы (0,21-0,252 мг/кг). На фоне четырехнедельной отмены налбуфина проводили медикаментозную коррекцию пентоксифиллином и цефтриаксоном (2,86 мг). Проведенное комплексное лечение на фоне 4-недельной отмены опиоида, который вводили животным в течение 6 недель, обусловило заживление язв, что проявилось в реэпителизации слизистой оболочки десен. Структура коллагеновых волокон собственной пластинки слизистой оболочки десен частично восстанавилась, наблюдались признаки ангиогенеза. В периодонте визуализировались признаки мукоидного отека и уменьшения гиперваскуляризации, стаза, агрегации эритроцитов в просвете сосудов, что способствовало улучшению микроциркуляции и восстановлению структурной организации пародонта. Применение пентоксифиллина и цефтриаксона на фоне 4-недельной отмены опиоида, который вводили в течение 6 недель в начале эксперимента, предотвращает быстрое прогрессирование воспалительно-дистрофического процесса и оказывает протекторное действие на ткани пародонта.

რეზიუმე

პაროდონტის მორფოლოგიური ცვლილებების თავისებურებები ოპიოიდის ექვსკვირიანი მოქმედების ფონზე შემდგომი მოხსნით და ოთხკვირიანი კომპლექსური მკურნალობისას ექსპერიმენტში

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კვლევის მიზანს წარმოადგენდა პაროდონტის მიკროსკოპიული რეორგანიზების თავისებურებების განსაზღვრა ოპიოიდური ანალგეზიური საშუალების - ნალბუფინის ექვსკვირიანი მოქმედების ფონზე და მისი ოთხკვირიანი მოხსნის შემდეგ, ასევე, მედიკამენტური კორექციისას პენტოქსიფილინით და ცეფტრიაქსონით ექსპერიმენტში.

კვლევა ჩატარდა 160-255 გ მასის და 4,5-7 თვის ასაკის 22 არახაზოვან მამრ ვირთაგვებზე. ცხოველების ორგანიზმში 6 კვირის განმავლობაში შეჰყავდათ ნალბუფინი, დოზის თანდათანობითი გაზრდით (0,21-0,252 მგ/კგ). ნალბუფინის ოთხკვირიანი მოხსნის ფონზე ტარდებოდა მედიკამენტური კორექცია პენტოქსიფილინით და ცეფტრიაქსონით (2,86 მგ). კომპლექსური მკურნალობის ჩატარებამ ოპიოიდის ოთხკვირიანი მოხსნის ფონზე, რომელიც ორგანიზმში შეჰყავდათ 6 კვირის განმავლობაში, განაპირობა წყლულების შეხორცება, რაც გამოიხატა ღრძილების ლორწოვანი გარსის რეეპითელიზაციაში. ღრძილების ლორწოვანი გარსის კოლაგენური ბოჭკოების სტრუქტურა ნაწილობრივ აღდგა, გამოიხატა ანგიოგენეზის ნიშნები. პერიოდონტში აღიყნიშნა მუკოიდური შეშუპების და ჰიპერვასკულარიზაციის, სტაზის, სისხლძარღვის სანათურში ერითროციტების აგრეგაციის ნიშნების შემცირება, რამაც ხელი შეუწყო მიკროცირკულაციის გაუმჯობესებას და პაროდონტის სტრუქტურულ აღდგენას. პენტოქსიფილინის და ცეფტრიაქსონის

გამოყენება ოპიოიდის ოთხკვირიანი მოხსნის შემდეგ, რომელიც 6 კვირის განმავლობაში შეჰყავდათ ექსპერიმენტის დასაწყისში, განსაზღვრავს ანთებით-დისტროფიული პროცესის სწრაფი პროგრესირების თავიდან აცილებას და ახდენს დამცველობით მოქმედებას პაროდონტის ქსოვილებზე.

GENDER RELATED DIFFERENCES IN SEX HORMONE-MEDIATED ANXIOLYTIC EFFECTS OF ELECTROMAGNETIC STIMULATION DURING IMMOBILIZATION STRESS

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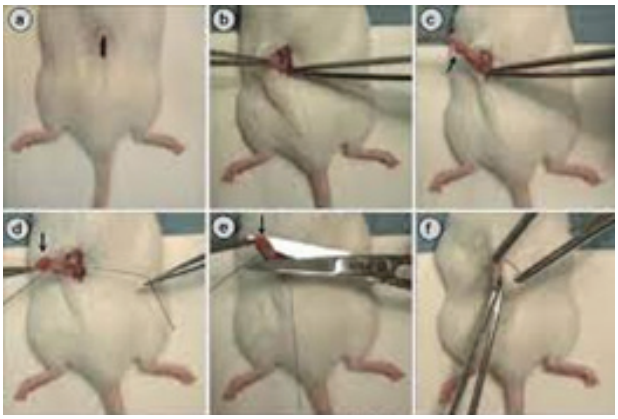
Many physiological systems help the body to cope with stress or to adapt. Proper activation of these systems is crucial not only for an adequate response to a threat but also for return the body to biological equilibrium after the stressor has been eliminated. Consequently, many pathological conditions are characterized by an inadequate or inappropriate response to stress[3,4]**.** The effects of stress rapidly activate the hypothalamic-pituitary-adrenal (HPA) axis, causing physiological changes through the secretion of glucocorticoids [3,6]. Changes occur in the brain and throughout the body. In response to HPA-mediated stress, activation of corticotrophin-releasing hormone (CRH) neurons in the paraventricular nucleus of the hypothalamus (PVH), stimulates the secretion of adrenocorticotropic hormone (ACTH) into the pituitary gland. The ACTH in turn, elevates the glucocorticoid synthesis and its release from the adrenal cortex. Corticosterone levels are significantly increased in females compared to males against the background of stressful effects. Besides the release of ACTH is regulated by sex hormones — both estradiol and testosterone [9-11,13]. Thus the activation of the HPA axis depends on both sex hormones and corticosterone. In male castrated rats, the corticosterone content increases dramatically after stress. Corticosterone content decreases in the presence of androgen supplementation. A different picture is found in female rats. After ovariectomy, the corticosterone content decreases after exposure to the stressors and increases after estradiol administration [12]. Estradiol disrupts GR-mediated negative feedback on the HPA axis and interferes with GR expression and binding in the pituitary and hippocampus [10,17].

EMS is noninvasive method for treatment of many neurodegenerative disorders [1,2,8]. The EMF is biologically active and penetrates into the living tissue without any impediments. It is unclear how the low-frequency EMS mediate effects on living organism. The main goal was to study EMS effects on immobilizing stress- induced behavior depending on sex hormone.

Material and methods. Experiments were conducting on intact and gonadectomized rats both gender (n=32, 4–6 months old, 190-220 g). The rats were group-housed (5 per cage) in standard box cages on a 12-hour light-dark cycle. Food and water were available ad libitum. Rats were randomly divided into two groups: gonadectomized females (n=8) and males (n=8) and intact control females (n=8) and males (n=8). Six rats from each group were immobilized. Effects of EMS were studied in all group of rats.

For the development of moderate stress, the immobilization stress was chosen. Immobilization procedure was carry out in plexiglass box**,** equipped with a moving partition, with which was restrain the animal. This model allow to adjust the duration of stress factor taking into account the specifics of the experiment. In our case, chronic stress by a 10-day immobilization of 2 hours a day were chosen. For repetitive EMS, the following parameters were used: 15000 Hz frequency, 1,5 m/Tesla, during 20 min, 10 days.

Gonadectomy - Surgery was performed under ether anesthesia, using standard procedures [14] (Pic.)



Pic. Steps of gonadectomy procedures in male (a) and female (b) rats. (Aymen Idris figures)