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MORPHOMETRIC CHARACTERISTICS OF GINGIVAL COMPONENTS AT DIFFERENT TERMS OF EXPERIMENTAL OPIOID INFLUENCE

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ABSTRACT

The aim of the study was to investigate changes in morphometric parameters of the gingival epithelial thickness, connective tissue papillae height and lumen diameter of arterioles, capillaries and venules in the dynamics after two, four and six weeks of experimental opioid exposure. Studies were performed on outbred white male rats. In the experiment, animals were injected with increasing opioid analgesic nalbuphine for six weeks, which ranged from 0.212 to 0.252 mg / kg. For histological and morphometric studies, semi-thin sections of the upper and lower jaws of rats were used. It was found that with the introduction of the opioid analgesic nalbuphine in increasing doses, the difference in the components of the periodontium were statistically significant compared with similar values of intact animals, indicating reactive changes in the gingival mucosa during short-term opioid action. After six weeks of opioid exposure, morphometrically revealed a sharp change in the vector of dynamics, which was manifested by statistically significant changes in the values of the components of the gums compared with similar indicators of intact animals, indicating the development of inflammatory-dystrophic changes in periodontal tissues.

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An important factor in the development of diseases of the human body is drug abuse, which leads to complete disability, mental health disorders and high mortality [2, 9, 13]. Among the various types of drug addiction, opium addiction is considered the most malignant. The opioid epidemic has grown rapidly and became one of the most serious medical and social problems of our time [5, 6, 12]. In opioid-dependent individuals, significant changes are observed in the tissues and organs of the oral cavity, in which the prevalence of periodontitis is ten times higher than in those who do not use narcotic substances [1, 11]. At the same time, insufficient attention is paid to the study of inflammatory processes in the oral cavity and parodontium in drug addicted individuals, and also the mechanism of exposure of new narcotic substances has not been studied well [3, 14]. It should be noted that an important role in the pathomorphogenesis of periodontitis is played by the epithelium

condition of the mucous membrane of the gums and vascular disorders, which are one of the primary reasons of the inflammatory-dystrophic changes in the tissues and organs of the oral cavity [4, 7, 8]. However, in the medical literature there is no data on the development and peculiarities of the course of the pathological process in the mucous membrane and in the hemomicrocirculatory bed of the gingiva in the dynamics at different terms of the opioid analgesic.

The aim of the study the dynamics of changes in morphometric parameters in the thickness of the epithelium of the gums, the height of the connective tissue papillae and the diameter of the lumen of arterioles, capillaries and venules in dynamics in two, four and six weeks of action of the opioid analgesic in the experiment.

Materials and methods.

Studies were performed on 46 outbred white male rats, 4.5 – 6.0 months old. Group I - intact animals (10), group II – animals were administered daily opioid analgesic nalbuphine at increasing average therapeutic doses every 14 days, calculated for rats ranging from 0.212 mg/kg to 0,252 mg/kg for six weeks. Accordingly, rats were removed from the experiment after in two, four and six weeks. The containment and handling of the animals was carried out in accordance with the recommendations of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes". For histological and morphometric studies, semi-thin sections (5-7 μm) from the amputated upper and exarticular lower jaws of rats were used. Histological preparations were made according to the conventional method, preliminary decalcification of the hard tissues of the dental organ, using dyes hematoxylin and eosin, as well as azan by the method of Heidenhain. Morphometric examination and micrographs were performed using a MICROMed XS-4130 microscope. Further measurements were performed using ImageJ v.1.51 [10]. It was determined the average values of the thickness of the epithelium of the free gingival margin and of the gingival sulcus, the height of connective tissue papillae, as well as the diameter of the lumen of the components of the hemomicrocirculatory bed (HMCB) - arterioles, capillaries and venules of the superficial vascular bed of the mucous membrane of the gums. ANOVA analysis of variance with Tukey's test for post-hoc was used to determine the significance of the difference between three or more groups of animals. The difference was considered significant at a value of $p < 0.05$. All statistical calculations were performed using RStudio v software. 1.1.442 and R Commander v.2.4-4.

Results and discussion.

Morphometric indicators after two weeks of opioid action were characterized by different dynamics (Fig. 1). The thickness of the epithelium of the free gingival margin increased to an average of $157,67 \pm 20,97 \mu\text{m}$ (the difference is statistically significant when compared with the indicator of the intact group, $p = 0,003$), as did the index of the thickness of the sulcular epithelium – $74,43 \pm 12,44 \mu\text{m}$, although this increase was not statistically confirmed compared to the intact group ($p = 0,51$). And the papillae height decreased to $56,20 \pm 4,67 \mu\text{m}$ (significant difference, $p = 0,012$).

The diameter indicators of the hemomicrocirculatory bed components in this term also had different dynamics. Thus, the diameter of the arterioles decreased to $9,71 \pm 1,05 \mu\text{m}$. And capillaries and venules increased in diameter compared to intact group indicators to averages of $5,65 \pm 0,68 \mu\text{m}$ and $18,27 \pm 2,65 \mu\text{m}$, respectively. All indicators had statistical significance of changes compared to the corresponding values of indicators of the intact group ($p < 0,0001$) (Fig. 2).

Thus, after two weeks of the experiment it was morphometrically found that the mean values of the components of the gingival mucosa were statistically different from those of animals of the intact group, except for an insignificant increase in the thickness of the epithelium of the gingival sulcus. and venules), which was due to the action of opioid analgesics in the early stages.

Morphometric indices after four weeks maintained the dynamics of the previous period. Thus, the values of the thickness of the epithelium of the free gingival margin and the sulcular epithelium reached the maximum of $165,74 \pm 27,52$ and $79,98 \pm 13,02 \mu\text{m}$, respectively. This increase was confirmed statistically when compared with the intact group ($p < 0,001$), and the sulcular epithelium – when compared with the previous term ($p = 0,013$). The papillae height also repeated the dynamics of the previous term and decreased sharply ($47,48 \pm 4,88 \mu\text{m}$). Such a sharp decrease in this indicator was statistically significant both when compared with the value of the intact group ($p < 0,001$), a decrease of the average value on $11,87 \mu\text{m}$ and when compared with the previous term ($p < 0,001$, a decrease of the average value on $8,72 \mu\text{m}$) (Fig. 1).

The indicators of the lumen diameter of the hemomicrocirculatory bed components in this subgroup did not have pronounced dynamics compared with the previous term, however, they had differences compared to the intact group. In particular, the diameter of the arterioles came close to the meaning of the intact group and was $10,42 \pm 1,41 \mu\text{m}$, remaining significantly smaller than the intact animal index ($p < 0,0001$). And the diameters of capillaries and venules remained at the level of indicators of the previous term and were $5,76 \pm 0,76 \mu\text{m}$ and $18,90 \pm 2,73 \mu\text{m}$, respectively, however, also had a statistical significance of changes compared with the corresponding values of indicators of the intact group, $p < 0,0001$ (Fig. 2).

Thus, after four weeks of opioid analgesic, differences in morphometric parameters of the gums were found, which were reflected in a significant increase in the average values of epithelial plate thickness, a significant decrease in connective tissue papillae, and a statistically confirmed decrease in the diameter of the lumen and arterioles. due to the action of nalbuphine in the subacute period of opioid exposure.

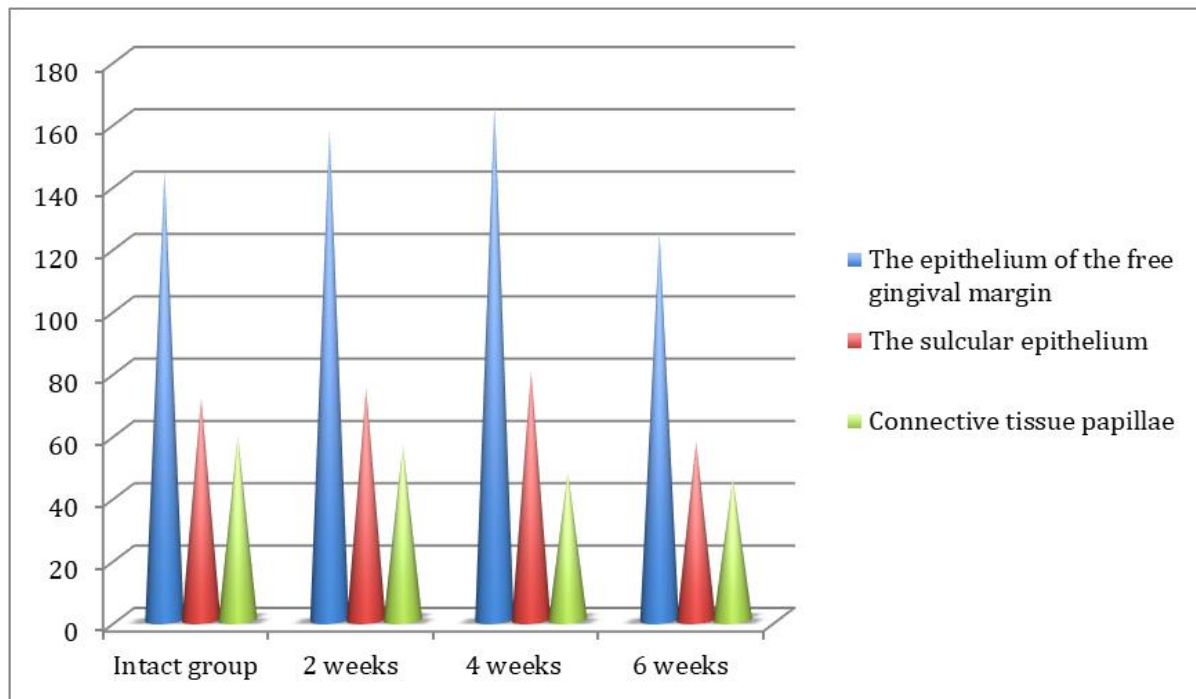


Fig. 1. Dynamics of morphometric indices of the thickness of the epithelium of the gingival and the height of the connective tissue papillae of rats during the six weeks of opioid action.

Most morphometric indicators after six weeks of opioid exposure were characterized by a sharp change in the dynamics vector (Fig. 1). The average thickness of the epithelium of the free gingival margin decreased compared to the previous term – $124,70 \pm 27,02 \mu\text{m}$. Such dynamics are statistically significant when compared with the intact group and the previous study period ($p < 0,001$). A similar trend was observed with the indicator of the thickness of the sulcular epithelium - a sharp decrease on $22,74 \mu\text{m}$ compared with the previous term till $57,24 \pm 12,79 \mu\text{m}$, which was confirmed statistically when compared with intact animals ($p < 0,001$), and with a previous term ($p < 0,001$). But the average value of the connective tissue papillae height retained the previous tendency to decrease - its index in this term decreased on $1,82 \mu\text{m}$ and was $45,66 \pm 7,83 \mu\text{m}$ (the difference compared to intact animals is statistically significant, $p < 0,001$).

The diameters of the hemomicrocirculatory bed components during this term had small dynamics. The diameter of the arterioles increased on $2,88 \mu\text{m}$ compared to the indicator of the previous term and was $13,30 \pm 2,36 \mu\text{m}$, this increase was statistically significant both in comparison with the indicator of the intact group ($p < 0,0001$) and when compared with indicator of the previous term ($p < 0,0001$). The capillary diameter also increased slightly to $6,13 \pm 0,80 \mu\text{m}$, this increase was statistically significant both in comparison with the intact animal index ($p < 0,0001$) and when compared with the previous term indicator ($p < 0,0001$). Venules diameters remained almost at the level of the

previous term, their average value was $19,11 \pm 2,71 \mu\text{m}$, however, had statistical significance of changes compared with the corresponding indicators of the intact group, $p < 0.0001$ (Fig. 2).

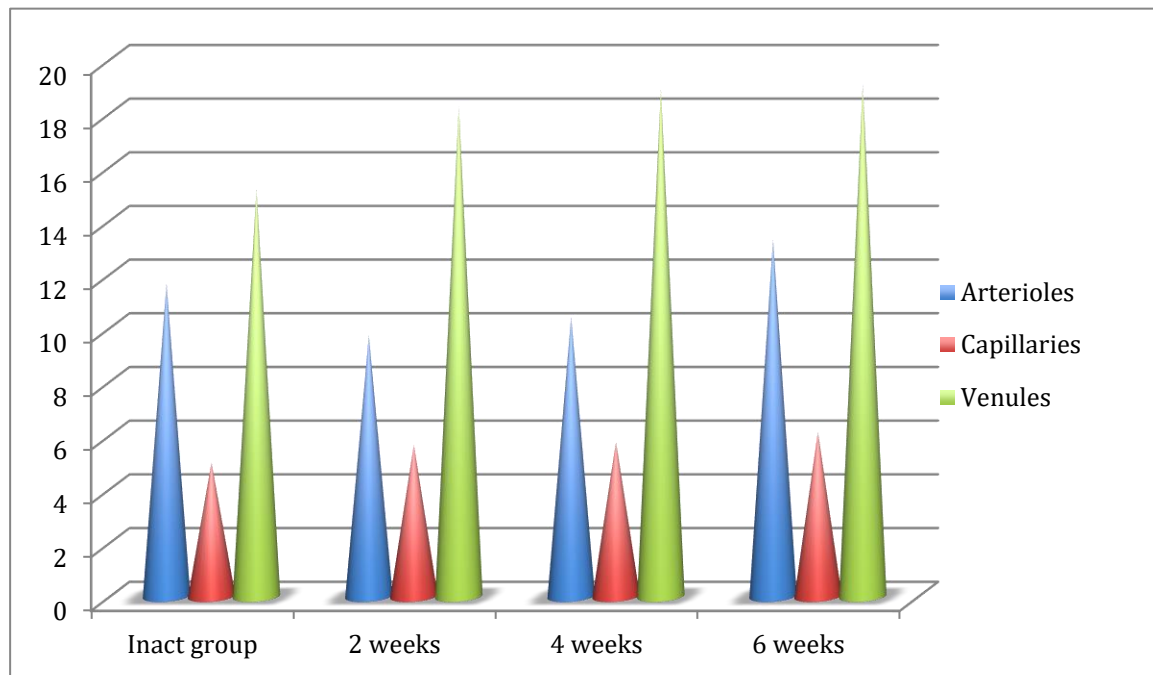


Fig. 2. Dynamics of morphometric indices of the lumen diameter of the rats gingival hemomicrovessels during six weeks of opioid action.

Thus, at the end of the sixth week of opioid exposure, a significant decrease in the average values of the thickness of the gum epithelium, a statistically significant decrease in papillary height and a significant increase in the diameter of the lumen of hemomicrovascular compared with similar indicators of intact animals.

Conclusions.

1. Morphometrically, it was found that after two weeks of opioid action, the difference in the components of the periodontium was statistically significant compared with similar values of intact animals, indicating reactive changes in the gingival mucosa due to imbalance between the links of the preparation.

2. Opioid administration for four weeks resulted in metric changes in the components of the gums of animals, which showed statistically significant differences from the corresponding indicators of the intact group of animals, due to the progression of reactive changes and the development of acute inflammation in periodontal tissues.

3. After six weeks of opioid action, morphometrically, a sharp change in the vector of dynamics was observed, which was manifested by statistically significant changes in the values of gum components compared to similar indicators of intact animals, indicating a rapidly progressing course and transition to inflammatory-dystrophic process.

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