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EFFECT OF CALCIUM HYDROXYAPATITE AND HYALURONIC ACID INJECTIONS ON INFLAMMATION MARKERS OF PERIODONT TISSUE

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The purpose of the study was to evaluate the anti-inflammatory properties of injections of calcium hydroxyapatite (CaNA) of different concentrations and hyaluronic acid on the condition of periodontal tissues in rats with experimental periodontitis. A subacute experiment was performed using a model of alimentary-induced periodontitis. Experimental studies have shown the ability of calcium hydroxyapatite in combination with hyaluronic acid to inhibit the activity of destructive enzymes and increase the activity of osteoblast markers in the bone tissue of the jaws of rats with periodontitis along with reducing markers of inflammation in the gums of animals with periodontitis. Injections of calcium hydroxyapatite with hyaluronic acid have a significant anti-inflammatory effect on the soft tissues of the periodontium, reducing the homogenates of the gums of rats with periodontitis malondialdehyde level by 24.6–40.3 %, acid phosphatase activity by 25.3–38.3 %, elastase activity by 23.5–29.8 %.

Key words: experimental periodontitis, rats', bone tissue, hyaluronic acid, calcium hydroxyapatite, periodontitis, subgingival injections.

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ВПЛИВ ІН'ЄКЦІЙ КАЛЬЦІЮ ГІДРОКСИАПАТИТУ ТА ГІАЛУРОНОВОЇ КИСЛОТИ НА МАРКЕРИ ЗАПАЛЕННЯ ТКАНИН ПАРОДОНТУ

Мета дослідження-оцінка протизапальних властивостей ін'єкцій препаратів кальцій гідроксиапатиту різної концентрації та гіалуронової кислоти на стан тканин пародонту у щурів з експериментальним пародонтитом. Підгострий експеримент проведено із застосуванням моделі аліментарно індукованого пародонтиту. Проведені експериментальні дослідження показали здатність препаратів гідроксиапатиту кальцію в поєднанні з гіалуроновою кислотою інгібувати активність деструктивних ферментів і збільшувати активність маркеру остеобластів в кістковій тканині щелепи щурів з пародонтитом поряд зі зниженням маркерів запалення в яснах тварин з пародонтитом. Ін'єкції препаратів кальцій гідроксиапатиту з гіалуроновою кислотою чинять виражену протизапальну дію на м'які тканини пародонту, знизивши в гомогенатах ясен щурів з пародонтитом рівень малонового діальдегіду на 24.6–40.3 %, активність кислої фосфатази – на 25.3–38.3 %, активність еластази – на 23.5–29.8 %.

Ключові слова: експериментальний пародонтит, щури, кісткова тканина, гіалуронова кислота, гідроксиапатит кальцію, періодонтит, під'ясневі ін'єкції.

The work is a fragment of the research project "Experimental research of the change in the tissues of the mice mouths under the influence of xenobiotics and hypoxia", state registration No. 108.21 0120U105477.

The mucous membrane of the mouth and lips is the subtlest indicator for assessing the pathological processes of the gastrointestinal tract, the immune status of the body, the general level of health, and the proliferation of cellular systems. Various studies prove the importance and relevance of finding solutions for the prevention and treatment of any disease that aggravates bone resorption and premature tooth loss. One of these diseases is periodontitis.

The problem of periodontal diseases is known for their widespread prevalence. Numerous studies in this area and the search for new methods of prevention and treatment of this pathology remain relevant. Calcium hydroxyapatite has been used in dentistry, both for topical application and for stimulation of bone regeneration in the surgical treatment of periodontal bone defects [6, 7, 9]. Many works are devoted to the healing and anti-inflammatory properties of hyaluronic acid drugs [4, 5, 10]. The combined use of these drugs in injectable form for osteoplastic purposes shows their advantage [8, 11].

The purpose of the study was to evaluate the anti-inflammatory properties of calcium hydroxyapatite drugs of various concentrations, without the addition of hyaluronic acid and with the addition of crosslinked and uncrosslinked hyaluronic acid, after single subgingival injections on the condition of the periodontal tissues of rats with experimental periodontitis.

Materials and methods. The study was carried out on 78 Wistar rats of herd breeding, females aged 6-7 months with an average weight of 285±34 g. The animals were divided into 5 groups:

1. Intact;
2. Periodontitis (P);

3. Periodontitis with subgingival injections of calcium hydroxyapatite at a concentration of 55.7 % (P+Ca);

4. Periodontitis with subgingival injections with a mixture of "calcium hydroxyapatite with crosslinked hyaluronic acid", where the concentration of calcium hydroxyapatite was 55.7 % (P+Ca+HA stab.);

5. Periodontitis with subgingival injections with a mixture of "calcium hydroxyapatite + uncrosslinked hyaluronic acid", where the concentration of calcium hydroxyapatite was 27.85 % (P+Ca+HA unstab.).

The experimental pathology of periodontitis was reproduced by adding peroxidized sunflower oil to the feed at the rate of 1 ml per 1 animal per day [3]. On the 21st day of periodontitis modeling, a single injection of drugs was carried out into the gums of the lower molars of rats at a dose of 0.1 ml. The following drugs were used in the work: for group 3 "Calcium hydroxyapatite" Crystalys (Luminera, Israel), for group 4 "Hydroxyapatite calcium and crosslinked hyaluronic acid" HArmonyCa (Luminera, Israel) and for group 5 "Hydroxyapatite calcium and uncrosslinked hyaluronic acid" Crystalys and Luminera Hydryal 2 % in a 1:1 ratio (Luminera, Israel).

The rats were taken out of the experiment under thiopental anesthesia by bloodletting from the heart 2 weeks, 4 weeks and 6 weeks after injections of the drugs. In homogenates of bone tissue (75 mg/ml 0.1 N citrate buffer pH 6.1), the activity of elastase was determined by hydrolysis of N-t-BOC-L-alanin-p-nitrophenyl ester, alkaline (ALP) and acid phosphatases (AP) by para-nitrophenyl phosphate hydrolysis at pH 10.1 and 4.8 [3], respectively. In gingival homogenates (20 mg/ml 0.05 M Tris-HCl buffer pH 7.5), inflammation markers were determined: the content of malondialdehyde with thiobarbituric acid (MDA), the activity of elastase and acid phosphatase [3]. The statistical processing of the obtained results was carried out according to the Student-Fisher method [1]. The null hypothesis was accepted at p=0.05.

Results of the study and their discussion. The study of enzymes in the jaws of animals revealed abnormalities in the bone tissue of rats with periodontitis. As can be seen from the data presented in Table 1, an alimentary excess of peroxides leads to a decrease in the activity of alkaline phosphatase in the jaws of rats with periodontitis by 1.7 times ($p<0.001$), which indicates inhibition of the intensity of bone mineralization.

At subsequent stages of the study, the activity of the bone resorption marker was low and corresponded to the values in intact animals ($p>0.1$ and $p1<0.01–0.05$) (table 1).

Table 1

Influence of calcium and hyaluronic acid drugs on the activity of alkaline phosphatase, acid phosphatase and elastase in the bone tissue of the lower jaw of rats with experimental periodontitis

Group	Time after injection	Biomarkers		
		Alkaline phosphatase	Acid Phosphatase	Elastase
		μkat/kg	μkat/kg	μkat/kg
Intact	2 weeks	117.6±4.67	2.89±0.51	15.26±1.09
	4 weeks	117.3±3.33	2.91 ±0.52	15.32±1.11
	6 weeks	117.6±4.67	2.89±0.51	15.26±1.09
P	2 weeks	70.12±5.45*	4.05±0.31*	24.98±1.36*
	4 weeks	77.80±4.40*	4.45±0.07*	28.83±1.89*
	6 weeks	80.35± 3.57*	4.50±0.40*	26.96±2.96*
P+Ca	2 weeks	65.62±4.75*	3.79±0.13	18.91±2.82#
	4 weeks	66.53±7.15*	3.49±0.21	27.20±2.89*
	6 weeks	80.76±4.64*	3.37±0.53	20.03±1.82*#
P+Ca+HA stab.	2 weeks	80.67±3.82*	2.29±0.29#	17.13±0.70#
	4 weeks	80.71±4.89*	3.10±0.28#	20.98±3.12
	6 weeks	100.27±6.29*#	3.04±0.25#	16.92±1.11#
P+Ca+ HA unstab.	2 weeks	75.39±5.02*	3.67±0.07	16.98±2.12#
	4 weeks	75.61±8.68*	3.71±0.10	23.28±1.31*#
	6 weeks	95.90±12.19#	3.12±0.22#	18.55±1.67#

Note. * – reliability of differences to the indicator in the intact group; # – reliability of differences to the indicator in the "periodontitis" group. The injection of calcium hydroxyapatite (55.7%) into the gums of rats of the 3rd group did not have a significant effect on the alkaline phosphatase activity, which remained at a low level ($p<0.001$-0.002 and $p_1>0.1$) at all stages of the study.

Calcium injections (55.7 %) in combination with crosslinked hyaluronic acid in the 4th group contributed to an increase in the activity of bone alkaline phosphatase only at the last term after 6 weeks ($p1<0.05$ and $p>0.05$).

The injection of calcium hydroxyapatite (55.7 %) into the gums of rats of the 3rd group did not have a significant effect on the alkaline phosphatase activity, which remained at a low level ($p<0.001–0.002$ and $p1>0.1$) at all stages of the study.

The use of a calcium composition (27.85 %) with uncrosslinked hyaluronic acid also stimulated the alkaline phosphatase activity in the bone tissue of the jaws of rats of the 5th group ($p<0.001–0.05$ and $p_1>0.1$) only after 6 weeks. The results obtained indicate that the use of injections of calcium hydroxyapatite in a concentration even by 2 times lower than in the 4th group, in combination with uncrosslinked hyaluronic acid, can prevent a decrease in the activity of bone alkaline phosphatase during periodontitis.

Modeling of periodontitis caused an increase in the activity of acid phosphatase (AC) in the jaws of rats, which indicates active resorption of bone tissue, since this enzyme is considered to be a marker of osteoclast activity. The increase in acid phosphatase was 40.1 % after 5 weeks of pathology modeling ($p<0.01$). 54.0 % ($p<0.05$) after 7 weeks and 55.7 % ($p<0.05$) after 9 weeks of pathology modeling.

Injection of calcium hydroxyapatite (55.7 %) did not significantly affect the activity of bone acid phosphatase in rats with periodontitis at the first stage ($p>0.05$ and $p1>0.1$). In 4 and 6 weeks after injections, the inhibitory effect of hydroxyapatite on the activity of acid phosphatase in the jaws of rats with periodontitis was established. The level of this indicator corresponded to normal values ($p>0.1$).

Injections of calcium (55.7 %) in combination with crosslinked hyaluronic acid had a more pronounced inhibitory effect on the activity of acid phosphatase, and hence on the resorption of bone tissue in the jaws of rats with periodontitis. The acid phosphatase activity in the jaws of the 4th group of rats decreased to normal 2 weeks after injections ($p>0.1$ and $p1<0.01$).

The composition of calcium (27.85 %) with uncrosslinked hyaluronic acid, only at the last stage, 6 weeks after its injection, reduced the activity of acid phosphatase in the jaws of rats to a level. occupying intermediate values between the norm and periodontitis ($p>0.05$).

The results of a study of the activity of bone elastase in the jaws of rats with periodontitis have shown an interest. It is known that this enzyme takes part in the hydrolysis of the protein part of the bone tissue. After 5 weeks of consumption of peroxidized oil by rats, elastase activity in the jaw bone tissue increased by 63.7 % ($p<0.002$), by 88.9 % ($p<0.001$) after 7 weeks, and by 76.7 % ($p<0.001$) after 9 weeks of pathology modeling.

Injection of calcium hydroxyapatite (55.7 %) in group 3 rats prevented an increase in elastase activity in the bone tissue of rats with periodontitis only 2 weeks after injections ($p>0.1$ and $p1>0.1$). At subsequent terms of the study, the activity of elastase in the bone tissue of rats of this group was high ($p_1>0.05–0.1$), which indicates the low ability of calcium hydroxyapatite without hyaluronic acid to inhibit the destruction of bone tissue.

Elastase activity in the bone tissue of rats of the 4th group, who received injections of calcium hydroxyapatite (55.7 %) in combination with crosslinked hyaluronic acid, was low and corresponded to the level in intact animals at all stages of the analysis ($p>0.05$-0.1 and $p1<0.001–0.01$).

Calcium hydroxyapatite (27.85 %) with uncrosslinked hyaluronic acid also had an inhibitory effect on collagen destruction in the jaws of rats with periodontitis. since the elastase activity in the 5th group did not exceed the normal values ($p>0.05–0.1$) and was lower than in periodontitis ($p1<0.01–0.05$). It is important to emphasize that the calcium concentration in this group is by 2 times lower than in the 3rd and 4th groups, which indicates a more pronounced ability of the calcium composition with hyaluronic acid to inhibit the destruction of bone tissue collagen induced by lipid peroxides.

In the gums of rats with periodontitis, the markers of inflammation – MDA level, acid phosphatase and elastase activity – were determined. As can be seen from table 2, the modeling of periodontitis causes the accumulation of the secondary product of lipid peroxidation, malondialdehyde, in the gums of rats of the 2nd group. Its content increased after 5 weeks by 54.8 % ($p<0.02$), after 7 weeks by 82.2 % ($p<0.001$) and after 9 weeks by 74.1 % ($p<0.001$). This indicates the intensification of peroxide processes in the gum tissue. The injection of calcium hydroxyapatite into rats of the 3rd group did not significantly affect the MDA level in the rat gum after 2 weeks ($p1>0.2$). After 4 weeks, a decrease in this indicator by 1.4 times ($p1<0.001$) was recorded, and after 6 weeks, a more significant (by 1.6 times) decrease in the MDA level ($p>0.6$ and $p1<0.001$).

After 6 weeks, the MDA level was high (table 2), which indicates a fast, but not prolonged antioxidant effect of this composition ($p<0.01$ and $p1<0.002$).

The concentration of MDA in the gums of animals of the 4th group decreased significantly 4 weeks after injection ($p1<0.002$) and to the normal level at the last period of the study ($p>0.7$ and $p1<0.001$).

The composition of calcium hydroxyapatite with uncrosslinked hyaluronic acid reduced the MDA level to the greatest extent in the 1st observation period ($p1<0.05$) and turned out to be the most effective,

but in the next period, no differences in the MDA level in the gums of rats of 3rd, 4th and 5th group were detected. Studies have shown an intensification of lipid peroxidation in the gums of rats consuming long-term peroxidized oil, as well as the ability of calcium hydroxyapatite drugs, more prominent in combination with hyaluronic acid, prevent the accumulation of a toxic product of MDA in the gums of rats, induced by an alimentary excess of lipid peroxides.

Table 2

Influence of calcium and hyaluronic acid drugs on the concentration of malondialdehyde (MDA), activity of acid phosphatase (AP) and elastase in the gums of rats with peroxide periodontitis

Group	Time after injection	Biomarkers		
		Malondialdehyde	Acid Phosphatase	Elastase
		mmol/kg	μkat/kg	μkat/kg
Intact	2 weeks	22.22±2.01	20.03±1.64	53.33±2.05
	4 weeks	22.33±2.13	20.09±1.55	53.42±2.12
	6 weeks	22.17±2.11	20.12±1.58	53.19±1.98
P	2 weeks	34.40±3.12*	24.92±1.62*	73.00±5.37*
	4 weeks	40.49±2.35*	25.89±1.28*	77.00±1.51*
	6 weeks	38.68±1.88*	30.00±2.19*	75.67±1.46*
P+Ca	2 weeks	30.34±0.63*#	19.52±1.16#	87.44±5.19*#
	4 weeks	29.05±1.22*#	19.34±1.24#	81.22±2.59*#
	6 weeks	23.93±2.23#	20.01±0.60#	57.89±3.62#
P+Ca+HA stab.	2 weeks	28.74±0.88*#	19.01±1.50#	89.67±6.24*#
	4 weeks	29.07±1.64*#	18.16±1.30#	72.22±5.60*#
	6 weeks	23.08±1.48#	18.50±1.62#	54.00±2.23#
P+Ca+ HA unstab.	2 weeks	27.14±1.27*#	22.79±2.01	94.44±3.53*#
	4 weeks	29.23±1.05*#	22.04±1.59	69.13±4.53*#
	6 weeks	29.17±1.43*#	22.42±1.56	53.11±3.71#

Note. * – reliability of differences to the indicator in the intact group; # – reliability of differences to the indicator in the "periodontitis" group.

Acid phosphatase (AP) is a marker of increased membrane permeability. It is known that the development of inflammation is accompanied by a sharp increase in the activity of this enzyme in tissues, so, acid phosphatase activity is considered to be a marker of inflammation [3]. An alimentary excess of lipid peroxides led to a significant increase in the activity of acid phosphatase in the gingival tissue of rats of the 2nd group. So, after 5 weeks of modeling periodontitis in the gums of animals, an increase in acid phosphatase activity was noted by 24.4 % ($p<0.05$), after 7 – by 29.3 % ($p<0.01$), and after 9 weeks - by 49.8% ($p<0.002$). The obtained results indicate the development of inflammation in the gums of animals under the influence of long-term consumption of lipid peroxides with food.

Injection of calcium hydroxyapatite to animals with periodontitis decreased after 2 weeks the acid phosphatse activity in the gums to normal ($p> 0.8$ and $p1 <0.01$). Subsequently, the activity of acid phosphatse in the gums of rats of the 3rd group remained low ($p>0.7–0.8$ and $p1<0.001–0.002$).

Lower values of this marker of inflammation were registered in the gums of rats of the 4th group, which were injected with calcium hydroxyapatite in combination with crosslinked hyaluronic acid. The acid phosphatase activity in the gums of rats of this group 4 weeks after injection was 29.9 % lower than in animals of the 2nd group ($p>0.4$ and $p1<0.001$) and 38.3 % lower after 6 weeks ($p>0.5$ and $p1<0.001$).

The use of calcium hydroxyapatite in combination with uncrosslinked hyaluronic acid in rats of the 5th group caused a significant decrease in acid phosphatase activity in the gums of animals at the last observation period, 6 weeks after the injection of the drug composition ($p>0.3$ and $p1<0.01$).

According to the acid phosphatase analysis, the most effective composition was calcium hydroxyapatite with stabilized hyaluronic acid.

Modeling of periodontitis led to an increase in elastase activity in rat gums by 36.9 % ($p<0.02$) after 5 weeks. by 44.4 % ($p<0.001$) after 7 weeks and by 41.9 % ($p<0.001$) after 9 weeks of pathology modeling. as evidenced by the results, presented in table. 2.

It is important to note that 2 weeks after injections of all drugs, the activity of elastase in the gum tissues increased more significantly than in the gums of animals of the 2nd group, which had periodontitis ($p1<0.01–0.05$). Since other markers of inflammation (MDA level and acid phosphatase activity) in the gums of rats of groups 3-5 at this time of observation either did not change or decreased, it can be assumed that such an increase in elastase activity may be associated not with an inflammatory response, but with an active rearrangement of elastic fibers of the gum tissue, caused by the injection of drugs. Evidence of this was the analysis data at the next stage, 4 weeks after the injection. The degree of elastase activity in the

gums of animals of 3-5 groups did not exceed the value of this indicator in the gums of rats of the 2nd group (p1>0.2–0.4).

In a systematic review, Salwowska N. et al., (2016) it is shown that additional therapy with hyaluronic acid provides a longer therapeutic effect compared to the use of glucocorticosteroids and non-steroidal anti-inflammatory drugs in chronic inflammatory diseases of the joints, skin and mucous membranes [10]. We have not compared the anti-inflammatory activity of hyaluronic acid with other classes of anti-inflammatory drugs, but the experimental results are encouraging.

6 weeks after injections of calcium hydroxyapatite or its combination with hyaluronic acid, a decrease in elastase activity in the gums of all experimental groups of rats (p1<0.001) to normal values (p>0.3–0.8) was recorded. The obtained results, along with the normalization of the MDA content and acid phosphatase activity in the gums of rats with periodontitis, testify the absence of inflammation in the soft tissues of the periodontium during periodontitis, and hence to the anti-inflammatory efficacy of the drugs.

Analyzing the obtained results, we can conclude that the most pronounced inhibitory effect on the enhanced bone resorption of the jaws of rats with peroxide periodontitis was exerted by calcium hydroxyapatite at a concentration of 55.7 % with crosslinked hyaluronic acid. After injection with this drug, it was possible to completely suppress the activity of destructive enzymes in the bone, as well as to normalize the processes of bone mineralization by increasing the activity of alkaline phosphatase.

Unexpectedly, the calcium drugs turned out to be effective at a concentration of 27.85 %, which is by 2 times lower than the others, but in combination with 2 % uncrosslinked hyaluronic acid. Apparently, the inhibition of the activity of destructive enzymes of acid phosphatase and, to a greater extent, elastase of the jaw bone tissue occurs under the influence of the injection of unstabilized hyaluronic acid [2]. This composition has a maximum effect from 2 to 4 weeks, but after 6 weeks the effectiveness decreases, which indicates the possibility of course administrations of drugs with a lower concentration of calcium hydroxyapatite. These data correlate with the results obtained earlier by other researchers [8, 9, 11].

Analysis of markers of inflammation in the gums of rats with periodontitis established the activation of lipid peroxidation by an increase in the MDA level, an increase in the permeability of lysosomal membranes according to the activity of acid phosphatase and an increase in the destruction of elastic fibers of the soft tissues of the periodontium according to an increase in the activity of elastase. The injection of calcium hydroxyapatite, as well as its combinations with crosslinked and uncrosslinked hyaluronic acid after 6 weeks, contributed to the normalization of all the studied parameters, and therefore showed anti-inflammatory efficacy. The most prominent anti-inflammatory effect can be noted for injections of calcium hydroxyapatite with hyaluronic acid.

Conclusions

1. Nutritional intake of peroxidized sunflower oil led to the activation of resorption in the jaws of rats: an increase in the activity of destructive enzymes (acid phosphatase and elastase) and a decrease in the activity of alkaline phosphatase involved in mineralization.

2. Injections of all drugs with calcium hydroxyapatite increased the calcium content in bone tissue by 45.1-84.0%.

3. Injection of calcium hydroxyapatite drugs with hyaluronic acid promoted inhibition of acid phosphatase (by 25.1–32.4 %) and elastase (by 25.7–37.2 %), as well as an increase in the activity of alkaline phosphatase in animal bone tissue (by 19.4–24.8 %). Alkaline phosphatase activity in rats injected with calcium hydroxyapatite alone remained low, as in periodontitis.

4. The drugs of calcium hydroxyapatite in a concentration of 27.85 %, which is by 2 times lower than the others, but in combination with 2% uncrosslinked hyaluronic acid increased the calcium content to almost normal.

5. Injections of calcium hydroxyapatite drugs with hyaluronic acid had a pronounced anti-inflammatory effect on the soft tissues of the periodontium, reducing the level of MDA in homogenates of the gums of rats with periodontitis by 24.6–40.3%. acid phosphatase activity - by 25.3–38.3 %, elastase activity – by 23.5–29.8 %.

Perspectives for further research may be associated with the study of the clinical use of calcium hydroxyapatite drugs with hyaluronic acid for the prevention and treatment of periodontitis.

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MORPHOLOGICAL AND FUNCTIONAL CHANGES OF THE HEPATIC VASCULAR BED UNDER THE CONDITIONS OF MODELING ALCOHOLIC HEPATITIS

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The experiments were performed on 30 white adult outbred male rats weighing 180–220 g. Animals were divided into 2 groups: I – □□tr□1 (□=6); □□ – animals with simulated alcoholic hepatitis (n=24). We studied the total NO synthase activity, peroxynitrite, nitrites and nitrosothiols concentrations in rat liver homogenate. We also studied morphometric parameters of hemomicrocirculatory tract of the rat liver. On the 7th day of modeling of alcoholic hepatitis interparticle arteries and veins and lobular arterioles narrow. The central vein dilates. The sinusoidal capillaries around the hepatic triad and central vein dilate. Alcoholic hepatitis increases the total activity of NO synthases, the concentration of peroxynitrites and nitrosothiols, but reduces the concentration of nitrites in the liver of rats on day 7 of the experiment. Nitric oxide and its metabolites play an important role in the regulation of the resistant part of the hemomicrocirculatory tract of the rat liver in the first three days of the experiment. Further redistribution of nitric oxide cycle metabolites leads to an increase in the concentration of peroxynitrite, which is a factor of secondary alteration.

Keywords: liver, alcoholic hepatitis, rats.

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МОРФО-ФУНКЦІОНАЛЬНІ ЗМІНИ СУДИННОГО РУСЛА ПЕЧІНКИ ЗА УМОВ МОДЕЛЮВАННЯ АЛКОГОЛЬНОГО ГЕПАТИТУ

Експерименти виконані на 30 білих статевозрілих безпородних щурах-самцях, вагою 180-220 г. Тварини були розділені на 2 групи: I – контрольна (n=6); II група – тварини, яким моделювали алкогольний гепатит (n=24).

В гомогенаті печінки щурів визначали активність загальної NO-синтази, концентрації пероксинітриту, нітритів та нітрозотіолів. Також визначали морфометричні параметри гемомікроциркуляторного русла печінки щурів. На 7 добу моделювання алкогольного гепатиту міжчасточкові артерії і вени, часточкові артеріоли звужуються. Центральна вена розширюється. Синусоїдні капіляри навколо печінкової тріади і центральної вени розширяються. Алкогольний гепатит збільшує загальну активність NO-синтаз, концентрацію пероксинітритів та нітрозотіолів, проте знижує концентрацію нітритів у печінці щурів на 7 добу експерименту. Оксид азоту і його метаболіти грають важливу роль в регуляції резистентної ланки гемомікроциркуляторного русла печінки щурів перші три доби експерименту, подальший перерозподіл метаболітів циклу оксиду азоту призводить до збільшення концентрації пероксинітриту, який виступає фактором вторинної альтерації.

Ключові слова: печінка, алкогольний гепатит, щури.

Depending on age, alcohol abuse is the fifth risk factor for premature death and disability worldwide. Alcohol is a leading risk factor for mortality and overall disease complications in the 15-59 age group [1]. According to WHO statistics, alcohol causes about 2.5 million deaths annually [2]. Alcohol consumption is a major etiological factor in the pathogenesis of chronic liver diseases such as fatty liver disease, alcoholic hepatitis, liver fibrosis or cirrhosis and hepatocellular carcinoma [3].