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## THE EFFECT OF A COMPLEX OF POLYUNSATURATED FATTY ACIDS WITH $\alpha$ -TOCOPHEROL ON THE STATE OF PERIODONTAL BONE TISSUE IN EXPERIMENTAL CHOLESTEROL ATHEROSCLEROSIS IN RABBITS

### **Abstract.**

*In experimental cholesterol atherosclerosis, the general mechanisms of free radical damage to the liver and bone tissue of rabbits were revealed. The complex of polyunsaturated fatty acids (PUFA) with  $\alpha$ -tocopherol showed angioprotective, antioxidant properties and protection of the bone structures of the periodontium from lipid peroxidation. Angioprotective properties were observed in the complex of PUFA with  $\alpha$ -tocopherol. The complex has shown protection of periodontal bone structures from free radical lipid oxidation and antioxidant properties.*

**Keywords:** *experimental cholesterol atherosclerosis, lipid peroxidation (LPO), polyunsaturated fatty acids (PUFA),  $\alpha$ -tocopherol, periodontal bone tissue, rabbits.*

Recently, in addition to the well-known theory of the accumulation of cholesterol in the zones of atherosclerotic lesions of the vessel wall [1], a theory was put forward, according to which the basis of the pathogenesis of atherosclerosis are transport disorders, intracellular deficiency and subsequent disorders of polyene fatty acid metabolism [2]. Essential polyunsaturated fatty acids (PUFA)  $\omega$ -6 and  $\omega$ -3 enter the mammalian body only with food, since their cells do not contain enzymes that catalyze the introduction of double bonds into the fatty acid chain beyond the 9th carbon atom.

It is known that endothelial cells, fibroblasts and some blood cells synthesize biologically active substances from essential PUFAs – prostaglandins (PG) (prostacyclin), thromboxanes (TX) and leukotrienes. Bone cells also have the ability to synthesize these highly active compounds from endogenous and exogenous PUFAs. With the help of the enzyme cyclooxygenase, the resulting PGs regulate the metabolism of bone cells - osteoblasts and osteoclasts [3].

Under the influence of the enzyme lipoxygenase during the metabolism of PUFAs, their hydroxylated derivatives, leukotrienes, are formed. The effects of these compounds are the migration of leukocytes, changes in vascular permeability, etc. During the development of periodontitis, substances are determined that activate the elements of the osteoclastic system - microbiological agents, inflammatory cells (monocytes, polymorphonuclear leukocytes, lymphocytes) and their products (PG, heparin) [4]. A direct connection between periodontal disease and atherosclerosis has not been identified at present, however, in severe forms of

periodontitis related to chronic infections, a cascade of immunological reactions can contribute to atherosclerotic changes in the vascular wall. At the same time, atherosclerosis, like periodontitis, is more common in people of mature and old age.

The aim of this study was to study the state of lipid peroxidation in the bone tissue of the periodontium in experimental atherosclerosis in rabbits and the effect of the PUFA complex with  $\alpha$ -tocopherol on these processes.

### Materials and methods

In the experiment, 29 outbred rabbits were used, distributed in the following series: group 1 - intact (5 rabbits), 2 - control (8 rabbits) with cholesterol atherosclerosis (CA). The model of atherosclerosis in rabbits was reproduced according to N.N. Anichkov-S.S. Khalatov by daily oral administration of 20% cholesterol solution in coconut oil for 20 days; Group 3 - 7 rabbits received a complex containing a concentrate of polyunsaturated fatty acids  $\omega$ -3: 30% eicosapentaenoic and 40% docosahexaenoic acids) produced by VNIRO (RF) with  $\alpha$ -tocopherol acetate (23.6 mg per 1 g of concentrate) at a dose of 0.5 mg / kg body weight of rabbits. The PUFA complex was injected daily against the background of experimental atherosclerosis for 20 days. At the end of the experiment on day 21, blood was taken from the marginal ear vein of rabbits for biochemical studies. Then the animals were killed and the area of the aorta lesion was determined in experimental atherosclerosis and the effect of the complex on it by the method of direct planimetry.

The objects of biochemical studies were blood serum, liver, bone of the alveolar bone and femur of rabbits. The level of lipid peroxidation (LPO) was assessed by the content of acyl hydroperoxides (AGP) [5] of the total fraction of lipoproteins in the blood serum; to determine the level of diene conjugates (DC) [6] in bone tissue and the kinetics of MDA [7] accumulation in the liver. The components of the physiological antioxidant system (FAS) were determined by the activity of glutathione reductase (GR) [8], as well as by the content of

thiols [9] in the bone tissue of rabbits. The data obtained were processed statistically using the Student's t-test.

#### Research results and discussion

In rabbits with experimental cholesterol atherosclerosis, peroxidation syndrome developed - a more than 10-fold increase in the content of acylhydroperoxides of the total lipoprotein fraction in the blood serum was revealed (Table 1). The accumulation of MDA was accelerated in the liver of rabbits after 1-hour incubation of its homogenate as compared with the intact group (Table 1).

Table 1

#### Influence of PUFA complex with $\alpha$ -tocopherol on lipid peroxidation parameters in blood and liver of rabbits with experimental cholesterol atherosclerosis (M $\pm$ m; p; p<sub>1</sub>)

The studied indicators	Groups		
	Intact	Control (CA)	Complex
	blood		
AGP content (units ext / ml)	0,29 $\pm$ 0,09	3,06 $\pm$ 0,53 p<0,001	1,97 $\pm$ 0,09 p <sub>1</sub> =0,06
	liver		
Kinetics of MDA accumulation (U / g tissue) 0 hour incubation	2,00 $\pm$ 0,29	2,28 $\pm$ 0,35	2,91 $\pm$ 0,18
1 hour incubation	2,60 $\pm$ 0,15	3,26 $\pm$ 0,27 p=0,07	3,53 $\pm$ 0,60

Note. In Tables 1 and 2, the reliability index p is calculated in comparison with the intact group; p<sub>1</sub> - compared with the control.

Studies have shown that bone tissue was more resistant to the activation of LPO processes than soft tissues. The content of diene conjugates as a result of modeling atherosclerosis did not significantly increase in the bone tissue of rabbits (mostly in the femur) (Table 2).

Table 2

#### The effect of PUFA preparations on the content of diene conjugates and FAS components in the bone tissue of rabbits with cholesterol atherosclerosis (M $\pm$ m; p; p<sub>1</sub>)

Experience Series	Diene conjugates (ext. Units / g)	Glutathione reductase activity (nmol / s g)	content	
			SH-groups (mol / g <sub>0</sub> )	SS-groups (mol / g)
alveolar bone				
Intact	0,11 $\pm$ 0,0010	0,73 $\pm$ 0,078	0,10 $\pm$ 0,02	0,59 $\pm$ 0,080
Control (HA)	0,11 $\pm$ 0,0070	0,32 $\pm$ 0,018 p=0,05	0,53 $\pm$ 0,09 p=0,001	0,45 $\pm$ 0,090
HA + complex	0,084 $\pm$ 0,013 p <sub>1</sub> =0,08	0,44 $\pm$ 0,048 p <sub>1</sub> =0,05	2,50 $\pm$ 0,62 p <sub>1</sub> <0,001	0,030 $\pm$ 0,010 p <sub>1</sub> <0,001
femur				
Intact	0,12 $\pm$ 0,0080	0,48 $\pm$ 0,011	0,11 $\pm$ 0,02	0,010 $\pm$ 0,0010
Control (HA)	0,15 $\pm$ 0,023	0,17 $\pm$ 0,073 p=0,01	1,45 $\pm$ 0,17 p<0,001	0,00 p<0,001
HA + complex	0,041 $\pm$ 0,0070 p <sub>1</sub> <0,001	0,22 $\pm$ 0,068	4,25 $\pm$ 0,74 p <sub>1</sub> <0,001	0,010 $\pm$ 0,0030 p <sub>1</sub> =0,01

When modeling cholesterol atherosclerosis, the activity of glutathione reductase decreased in the bone of the alveolar bone by 2.3 times (p = 0.05) and 2.8 times (p = 0.01) in the femur (Table 2). The levels of sulfhydryl protein groups (SH-groups) in the bone of the alveolar bone and femur were significantly increased compared to the intact group (Table 2).

Against the background of experimental atherosclerosis, the complex of PUFAs with  $\alpha$ -tocopherol showed an angioprotective effect. It significantly reduced (6.7 times; p < 0.001) the area of atherosclerotic changes in the aorta of rabbits: 11%  $\pm$  8 versus 74%  $\pm$  11 in the control group (CA).

The complex reduced the content of AGP in the blood serum of rabbits by 1.6 times and did not significantly change the kinetics of MDA accumulation in the liver (Table 1). In the bone of the alveolar bone, a significant increase in the activity of glutathione reductase was observed.

Under the influence of the complex in the bone of the alveolar bone and in the femur of rabbits, the content of sulfhydryl groups of proteins significantly increased (4.7 and 2.9 times, respectively). At the same time, in these objects of study, the level of disulfide compounds (SS-groups) significantly decreased (Table 2).

### Conclusion

Thus, we have demonstrated the general mechanisms of free radical damage to the liver and bone tissue of experimental animals under the influence of reproduced atherosclerosis. In addition, in the bone of the alveolar process and the femur of rabbits, LPO activation and a decrease in the functioning of the FAS components were revealed as a result of this action.

The complex of PUFA with  $\alpha$ -tocopherol showed an angioprotective effect. It has a protective effect in the bone tissue of the periodontium against free radical lipid oxidation and has antioxidant properties.

The data obtained indicate that atherosclerosis of the arteries contributes to the disruption of the antioxidant systems of the periodontal bone tissue. It can be assumed that the development of periodontitis with a known risk factor - atherosclerosis, to a certain extent, is caused by peroxide mechanisms.

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## EFFECT OF A COMPLEX CONTAINING 1- $\alpha$ HYDROXYCHOLI-CCALCIFEROL, ANTIOXIDANTS AND CALCIUM PHOSPHATE IN AN ANTIOXIDANT-FREE DIET AND ADDITIONAL LOCAL EXPOSURE

### Abstract.

*In experiments on 53 white rats, the protective properties of a complex containing 1 $\alpha$ OHD<sub>3</sub>, antioxidants and calcium phosphate were studied. Modeling of periodontal pathology was carried out under conditions of a common risk factor for the development of periodontitis - peroxidation syndrome and a local factor - dental plaque.*

**Keywords:** modeling, antioxidant-free diet, dental plaque, complex, 1 $\alpha$ -hydroxycholecalciferol, antioxidants.

The general risk factors for the development of periodontitis are currently recognized as neuropsychiatric stress, physical inactivity, unbalanced nutrition, including chronic insufficiency of antioxidants due to the significant role of free radical oxidation of lipids

and biopolymers of periodontal membranes in periodontitis [1,2]. Along with the general, periodontitis-specific risk factors are known, which include dental plaque.

The aim of this study was to study the combination of antioxidants with the hormonal form of vitamin D<sub>3</sub>

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