

edema, bleeding gums had remitted. Whereas under the influence of thymalin there was a regression of dental symptoms by 3.8 times, under the influence of parodontylin – by 7.2 times. Condition of periodontal tissues in animals improved more significantly on the 20th day of observation, the scale assessment of dental status indicated that in animals, treated with thymalin, it was 1.1, and by parodontylin – 0.3 points per animal. In studying the processes of lipid peroxidation in periodontal tissues, their significant reduction in rats with spontaneous periodontitis after administering parodontylin has been established. We also observed an increase in the activity of antioxidant enzymes. Hence, the activity of SOD was twice as high, catalase – by 1.95 times. Reactions of lipid peroxidation had the same dynamics in the blood of animals after administering periodontal polypeptides and thymalin, as in periodontal tissues. Significant decrease in the level of conjugated dienes, the concentration of the latter reaches the value of indices of intact animals was found. Similar results were obtained with regard to the level of TBA-active products, accumulation of MDA, spontaneous hemolysis of erythrocytes. Parodontylin reduced lipid peroxygenation of blood to a greater extent than thymalin. Also increased activity of SOD was observed. On the other hand, concentration of ceruloplasmin decreased by 25.4%.

Prospects for the further research. Administering periodontal polypeptides during spontaneous periodontitis leads to decrease in the responses of lipid peroxidation in periodontal tissues and blood. To a greater extent this effect is characteristic of parodontylin in comparison with thymalin.

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Key words polypeptides, periodontitis, antioxidant enzymes, parodontylin, thymalin

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SIGNIFICANCE OF GENE POLYMORPHISM IN THE DEVELOPMENT OF UTERUS LEIOMIOMA

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Uterine leiomyoma is a benign tumor of the myometrium and develops as a result of proliferation of muscle cells and connective tissue elements. When comparing the ultrastructure of collagen fibrils in the leiomyoma tissue and normal myometrium, it was found that leiomyoma contains collagen fibrils of an atypical structure and orientation compared to normal myometrium [1]. This indicates the leading role of matrix metalloproteinases in the pathogenesis of leiomyoma. Molecular genetic mechanisms of the effect of the altered hormonal background on the activity of the corresponding enzyme systems in the uterine tissue are poorly understood. More than 20 types of matrix metalloproteinases that carry out various stages of the degradation of collagen, elastin and other extracellular matrix proteins are known. Among them, matrix metalloproteinase-1 (MMP-1) plays a special role, which carries out the primary degradation of collagen molecules, after which they further decompose under the influence of other metalloproteinases [2]. Subsequent degradation of collagenolysis

products involves other MMPs, in particular stromelysin-1 (MMP-3). For the promoter region of MMP-1, 2 gene variants are known - the presence of 1G or 2G at position – 1607. MMP-3 carries out the subsequent destruction of collagen. For this gene, gene polymorphism at the position of the promoter-600 (5A/6A) is shown. Allele 5A is characterized by a higher level of transcription than allele 6A. The predominance of the 5A allele of the MMP-3 gene was found for women with metastatic breast cancer [3]. In addition, a number of studies have shown the importance of MTHFR (methylene tetrahydrofolate reductase) polymorphism, which catalyzes synthesis of 5-methyltetrahydrofolate, which is used in methylation processes. Option MTHFR C677T is accompanied by significantly reduced activity, which increases blood coagulation and cancer risks in women carriers of this gene [4]. The aim of this work was to determine the role of single nucleotide polymorphism of the genes of matrix metalloproteinases MMP-1, MMP-3 and MMP-9, as well as the MTHFR gene in the pathogenesis of uterine leiomyoma.

Materials and Methods. 58 patients, aged 27 to 60 years (mean age $47,2 \pm 0,6$), with verified diagnosis of uterine leiomyoma were included into the study. Morphological verification of the diagnosis in the operated patients was conducted. In order to study the molecular biological aspects of the pathogenesis of uterine fibroids, the promoter alleles of the MMP-1, MMP-3 and MMP-9 genes, as well as the MTHFR gene (C677T) were genotyped in the Laboratory of Pharmacogenetics and Genetic Safety of the National University of Pharmacy. Genomic DNA was isolated from the blood leukocytes of patients and donors after lysis, immobilization and DNA purification on a sorbent. The genotypes MMP-1 (1G/2G), MMP-3 (5A/6A), MMP-9 (C-1562T) and MTHFR (C677T) were determined using allele-specific polymerase chain reaction. Polymerase chain reaction primers were synthesized by Metabion (Germany).

Results. Conducted analysis of the distribution of the studied gene variants showed a high frequency of occurrence of alternative alleles of the MMP-1, MMP-3, and MTHFR genes in patients. At the same time, the distribution of promoter alleles of the MMP-1 and MMP-3 genes almost corresponded to the classical Mendelian variant (50% of heterozygotes and 25% of homozygotes of both species). When analyzing the promoter polymorphism of the MTHFR gene in the sample, a tendency toward a predominance of carriers of the 677C allele was noted. An association was found between the allelic polymorphism 1G/2G of the MMP-1 gene, the development and growth rate of uterine leiomyoma. It was shown that the fast growth rate of fibroids correlates with a low frequency of occurrence in patients with the 1G/1G genotype of the MMP-1 gene. This dependence indicates the protective role of the less active 1G allele of the MMP-1 gene, which confirms the specific function of MMP-1 in the modification of the intercellular matrix in tumor growth zones. The risk of a benign tumor process in the myometrium in homozygotes for the 2G allele is 3 times higher than for homozygotes for the 1G allele.

Conclusion. It can be assumed that the overactive 2G allele, on the contrary, contributes to the onset and growth of leiomyoma. No association of the C-1562T polymorphism of the MMP-9 gene with development of leiomyoma was found.

Prospects for further research. Role of neoangiogenesis in the pathogenesis of fibroids is important [5]. Matrix metalloproteinases are involved in the degradation of the matrix during tissue growth, thereby forming a space for new capillaries to grow in the intercellular matrix, which provide nutrition to the neoplasms. Based on this, the use of angiogenesis inhibitors and matrix metalloproteinases is a promising method for treating fibroids.

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THE INFLUENCE OF IMMUNE ACTIVITY COMPOUNDS TO THE BLOOD SERUM CYTOTOXICITY AND THE LEPTIN LEVEL IN THE CONDITIONS OF HYPOESTROGENIA

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The estrogen activity decrease during the menopause causes changes in metabolic processes and is the principal pathogen factor of post-menopause metabolic syndrome (MS) development. In turn, MS is the risk factor of diabetes mellitus, cardiovascular, autoimmune and other chronic diseases with women at menopause [1]. The level of adipose tissue hormones, in particular, of leptin, correlates with the main components of MS, including obesity, insulin resistance, low intensity inflammation, enhancement of atherogenesis processes [2]. We showed the positive impact of immunotropic pharmacological compounds to the metabolic status with ovariectomized (OVE) rats with MS on the model of estrogen deficiency.

The purpose of the work was to study the changes of blood serum cytotoxicity and leptin concentration with the ovariectomized rats with MS and in the conditions of levamisole immune activity compounds application and its derivate PL-308.

Materials and Methods. The MS with OVE rats was modeled with the high carbohydrate diet (HCD) which was administrated 2 weeks after of surgery for 5 weeks. 5 groups of animals were created: 1st group – intact control; 2nd group – OVE rats ("OVE"); 3rd group – OVE rats which received 30 % sucrose solution and placebo ("OVE+HCD+placebo"); 4th group – OVE rats which were administrated with levamisole (L) through probe on the background of HCD in the dose 2.5 mg / kg of body weight ("OVE+HCD+L"); 5th group – OVE rats which were administrated with PL-308 on the background of HCD in the dose 4.0 mg / kg of body weight ("OVE+HCD+PL-308"). We evaluated the rat blood serum cytotoxicity (BSC) in the reaction of lymphocytolysis (G. Friemel, 1987), the leptin concentration was established by the method of enzyme immunoassay on the analyzer Stat Fax 2100 (USA) with the kit of «Diameb» (USA). The material treatment statistics is made with the calculation of arithmetic mean and its error. The evaluation of null hypotheses is made at the level of significance not more than 0.05.

Results. It is established that OVE is accompanied by the BSC increase almost threefold in the comparison with intact control (respectively 9.80 ± 0.80 % against 3.20 ± 0.60 %, $p \leq 0.05$). The presence of MS enhances significantly the BSC both compared to OVE control and intact rats (respectively 20.00 ± 1.40 % against 9.80 ± 0.80 %, i.e. 2 and 6 times, $p \leq 0.05$). It is known that the cytotoxic reactions can be mediated by cellular or antibody mechanisms, their increase is observed in various inflammatory, in particular, autoimmune processes. An increase in BSC under hypoestrogenia as such may indicate, in particular, the activation of the humoral immunity level and testify to the possibility of increasing the proinflammatory state and the level of autoantibodies in the early stages of estrogen deficiency. The combination of OVE and MS enhances the imbalance