

comparison group ( $p < 0.001$ ). Content of acute phase reactant and FG coagulation factor in the blood after the treatment in both groups was not statistically different from the baseline data. Level of expression of mRNA gene of I $\kappa$ B $\alpha$  in mononuclear cells was significantly decreased in the study group and amounted to  $-0.496$  ( $-0.591 - +0.665$ ) ( $p = 0.048$ ), whereas in the comparison group it increased ( $0.424$  ( $-0.589 - +1.817$ )), but it was not statistically reliable ( $p = 0.296$ ).

**Conclusion.** In patients with stable coronary heart disease concurrent with NAFLD, activation of low-intensity CSI has been detected. The use of combination of betaine, arginine and quercetin in the comprehensive therapy of patients contributes to lowering the level of CSI by inhibiting the signal transduction via the NF- $\kappa$ B pathway, which may be due to the anti-inflammatory properties of these components of integrated therapy with an effect on certain targets of the pro-inflammatory cascade.

**Prospects for further research.** The obtained results substantiate the importance of identifying the low intensity CSI markers for assessing the course and progression of CHD concurrent with NAFLD. Detection of anti-inflammatory effect rendered by the combination of betaine, arginine and quercetin in these patients demonstrates the need for further studies of the molecular mechanisms of action and clinical efficacy of these components of integrated therapy with the aim of developing new therapeutic approaches.

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**Key words:** coronary heart disease, non-alcoholic fatty liver disease, chronic systemic inflammation, quercetin, betargin.

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## SHARED GENETIC FACTORS OF CONNECTIVE TISSUE-RELATED DISORDERS IN WOMEN

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Pelvic organ prolapse (POP) is one of the most common pelvic floor disorders among pre- and postmenopausal women. POP is an isolated or combined descent or dropping down of pelvic organs as a result of weakening of the muscular-ligamentous apparatus. It is assumed that POP may result from age and/or trauma related connective tissue disturbances [1]. Hereditary features of the connective tissue structure may influence

POP and other connective tissue-related phenotypes [2, 3]. Stress urinary incontinence (SUI) and chronic venous insufficiency of the lower limbs (CVI) often mentioned as comorbidities with POP [4]. The disease connections on molecular level may be partially based on shared genetic susceptibility. Study was performed to determine whether genetic variants in the genes involved in the organization of elastic fibers (*FBLN5*, *LOXL1*, *ELN* and *FBN1*) are associated with multiple forms of connective tissue pathology (POP, SUI, CVI).

**Materials and Methods.** Tagged SNP approach to increase the genetic coverage of the investigated genes (Haploview 4.2 software) was used. Total DNA was extracted from venous blood. The genotyping of 19 selected SNPs (*FBLN5*: rs2430339, rs12586948, rs2284337, rs2498841, rs2018736, rs12589592, rs2430369, rs2245701, rs2474028, rs929608, rs2430347, rs2284338, rs2267989; *LOXL1*: rs2165241, rs2304719, rs893821, rs2415231; *FBN1*: rs6493328 and *ELN*: rs10949834) was performed using an allele specific tetra-primer PCR. The study sample set included patients (n=234) diagnosed with POP; controls (n=323) were women without POP and no prior history of prolapse surgery. The average age of the participants was 57.59±10.88 and 56.76±12.90 years, respectively. For the study sample, there were also data on the presence/absence of a history of SUI and CVI. These diseases were significantly more frequent in the group of women with POP. For the statistical analysis, the initial sample consisting of groups with POP and without this pathology was re-formed to obtain: 1) the case group with SUI (n=64) and the control group without SUI (n=477); 2) the case group with CVI (n=91) and the control group without CVI (n=452). Multiple logistic regression was applied to evaluate the associations between SNPs and POP, SUI, and CVI.

**Results.** All SNPs were in Hardy–Weinberg equilibrium in the cases and in the controls. Significant associations of SNPs rs2284337, rs2018736, rs12589592, rs2474028 (*FBLN5*) and rs2304719 (*LOXL1*) with POP; rs2498841 and rs2284338 (*FBLN5*) with SUI; rs2430339, rs2498841, rs2430369 (*FBLN5*), rs2304719 (*LOXL1*) and rs6493328 (*FBN1*) with CVI were found. The top association signals were found for *FBLN5* rs12589592-A ( $P=0.0012$ , OR=0.40, 95% CI: 0.23-0.71) in POP group, *FBLN5* rs2498841-T ( $P=0.037$ , OR=3.45, 95% CI: 1.16-10.26) in SUI group and *FBN1* rs6493328-A ( $P=0.0015$ , OR=0.16, 95% CI: 0.04-0.69) in CVI group. After the correction for multiple comparisons (FDR, the number of comparisons was 19), the association of rs2018736 ( $P=0.033$ ), rs12589592 ( $P=0.029$ ), and rs2474028 ( $P=0.029$ ) of *FBLN5* gene with POP, as well as of *FBLN5* rs2498841 ( $P=0.047$ ) and *FBN1* rs6493328 ( $P=0.021$ ) with CVI, was confirmed. We identified *FBLN5* haplotype rs12586948(A)-rs2284337(A)-rs2430347(A)-rs2430369(C), associated with a high risk for each of the studied diseases ( $P=0.035$ , OR=1.51, 95% CI:1.03–2.21 for POP;  $P=0.022$ , OR=1.81, 95% CI:1.09–2.99 for SUI;  $P=0.048$ , OR=1.61, 95% CI:1.00–2.58 for CVI). For SUI and POP, a common risk haplotype rs12586948(A)-rs2284337(A)-rs2430347(A)-rs2498841(G)-rs2018736(C)-rs2430369(C)-rs2245701(G) with a frequency of 2.28% (SUI) and 2.21% (POP) was identified ( $P=0.022$ , OR=3.25, 95% CI: 1.19–8.86 and  $P=0.025$ , OR=2.96, 95% CI: 1.15–7.61, respectively). Each of these alleles groups as well as *LOXL1* haplotype rs2165241(C)-rs2304719(T)-rs2415231(C), correlated with an increase of the number of co-occurring connective tissue pathologies (POP, SUI and CVI).

**Conclusions.** Thus, comorbidity of connective tissue diseases (POP, SUI and CVI) can be genetically determined, in particular, in the presence of the common risk haplotypes of the *FBLN5* and *LOXL1* genes. Further study of the shared genetic factors will make it possible to develop complex diagnostic criteria of these diseases.

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**Key words:** *pelvic organ prolapse, stress urinary incontinence, chronic venous insufficiency of the lower limbs, comorbidity, genetic factors*

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## LABORATORY ASSESSMENT OF THE EFFICIENCY OF ORTHOPEDIC TREATMENT OF EXTENSIVE DENTAL DEFECTS

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The survival of a dental implant is influenced by many factors, including: somatic (heredity, age, degree of osteoporosis, immunity, diseases of internal organs) and local factors (degree of trauma from the intervention, biomechanical characteristics of the implant-jaw system, periimplantity, etc.) [3]. The dental implant material plays an equally important role in the evolution of the “titanium surface-bone” coupling: the condition of the surface, the area of contact with bone, its strength and density, and the time spent on different stages of orthopedic treatment. For example, plastic deformation of an implant or its fracture is possible with insufficient strength of titanium used in the manufacture of an implant [1].

There is a need to search for safe high-strength materials for health. Previous data had shown that Nanotechnologies and nanomaterials remains promising. Use of dental implants from nanostructured titanium has been reflected in few published works on experimental animals [2]. There are no clinical studies in this direction, which explains the relevance of our research. Objective of the study was to increase the clinical effectiveness of dental implantation in the treatment of patients with extensive dentition defects due to non-separable dental implants with immediate load of nanostructured titanium.

**Materials and Methods.** 57 people with dentition defects were examined and underwent orthopedic treatment. Given the characteristics of prosthetics, patients were divided into two groups. In group 1 (n=30) with single-stage dental implantation with immediate load, collapsible screw titanium implants from conventional alloy BT-6 were used. Group 2 (n=27) underwent a one-stage dental implantation with immediate loading with non-separable conical-shaped dental implants made of nanostructured titanium of the Nano-Grade 4 brand with a grain size of 50-150 nm (grains of other titanium alloys, including the Grade 4 brand, about 1000 nm in size). Nanostructured titanium “Nano-Grade 4” is very durable in comparison with titanium alloys, which makes it possible to use it in non-removable orthopedic treatment. The age of 2 clinical groups varied from 37 to 72 years. The average age of 1 group was  $54,7 \pm 1,1$  years, 2 groups –  $53,2 \pm 1,4$  years. The structure of dentition defects according to Kennedy was represented by lateral defects included (group 1 – 83,3%, group 2 – 8,5%), there were few unilateral and bilateral terminal defects. The levels of C-reactive protein (C-RP) and tumor necrosis factor-alpha (TNF- $\alpha$ ) were determined on days 1, 7, 14, 30 and 90 in the oral and peri-implantation fluid. The study of the content of C-RB was performed using a latex diagnosticum to detect the C-reactive protein “CRP - latex test”, and TNF- $\alpha$  - using an enzyme immunoassay.

**Results.** Initially, level of C-RP in the oral fluid in group 1 was  $6,3 \pm 0,4$  mg/l, in group 2 –  $6,5 \pm 0,5$  mg/l. Concentration of TNF- $\alpha$  in the oral fluid in group 1 was  $36,7 \pm 2,2$  pg/ml, in group 2 –  $35,1 \pm 3,1$  pg/ml. In 1, 7, and 14 days after surgery, level of C-RP and TNF- $\alpha$  in the