MOLECULAR GENETIC MECHANISMS OF DEVELOPMENT OF CHRONIC VENOUS INSUFFICIENCY

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The actuality. Chronic venous insufficiency (CVI) is an important medical problem in developed countries. Increased venous pressure in varicose veins (VV) may contribute to the overexpression of certain matrix metalloproteinases (MMPs) that affect the endothelium, smooth muscle and extracellular matrix proteins of the vein wall. Gelatinases, which include MMP-2 (gelatinase A) and MMP-9 (gelatinase B), are responsible for the degradation of the extracellular matrix (ECM) in the vein wall under both physiological and pathological conditions

The aim of the research. Since the mechanisms leading to the formation of CVI are still not fully understood, the purpose of our study was to evaluate the role of polymorphisms of the MMP-9 (Gln279Arg) and VEGF (C936T) genes in the formation of chronic venous insufficiency of the veins of the lower extremities.

The material and methods of the research. We examined 98 patients aged 20 to 78 years with chronic venous insufficiency, including, in accordance with the CEAP classification, 45 patients were with moderate severity of CVI (class C3-C4) and 53 patients with severe CVI (class C5-C6), who were hospitalized in the Department of Cardiovascular Surgery of the clinics of the Andijan State Medical Institute.

The research results and their discussion

Analysis of the Gln279Arg polymorphism in the MMP9 gene did not reveal deviations in the distributions of genotypes from those expected under Hardy-Weinberg equilibrium (HWE) ($\chi2=1.89$, $p=0.168$ in the main group; $\chi2=1.72$, $p=0.183$ in the control group).

The presence of the Gln/Gln genotype of the Gln279Arg polymorphism in the MMP9 gene, on the contrary, has a protective function in preventing the development of severe forms of CVI (OR = 0.7; 95% CI = 0.35 - 1.38; p = 0.3).

When analyzing the C936T polymorphism in the VEGFA gene, no deviations in the distributions of genotypes from those expected under Hardy-Weinberg equilibrium (HWE) were detected ($\chi2=1.43$, $p=0.225$ in the main group; $\chi2=1.91$, $p=0.166$ in the control group).

The distribution frequency of C/C, C/T, and T/T genotypes was 66%, 28.3%, and 5.7%, respectively, in the main group and 77%, 19.5%, and 3.4%, in the control group. As can be seen from our data, the combination of the C/T and T/T genotypes of the C936T polymorphism in the VEGFA gene indicates a higher risk of developing severe forms of chronic venous insufficiency (CEAP C5-C6) (OR = 1.6 and 1.7; 95% CI=0.73 - 3.6 and 0.33 - 8.51). The presence of the C/C genotype of the Gln279Arg polymorphism in the MMP9 gene, on the contrary, has a protective function in preventing the development of severe forms of CVI (OR = 0.6; 95% CI = 0.27 - 1.23).

Changes in MMP and VEGF activity were observed in many diseases of the circulatory system. The development of CVI is associated with a decrease in wall thickness, changes in hemodynamics, the flow of inflammatory cytokines, changes in the ECM and increased production of reactive oxygen species (ROS) that affect the activity of MMPs VEGFA increases the permeability of existing blood vessels, helping to maintain inflammation by allowing white blood cells to migrate to their destination. Thus, the results obtained in the course of the study reliably indicate the presence of an association between the carriage of the Arg allele and the Gln/Arg and Arg/Arg genotypes of the Gln279Arg polymorphism in the MMP9 gene, as well as the carriage of the T allele and the C/T and T/T genotypes of the C936T polymorphism in the MMP9 gene., gene VEGFA with the risk of developing complicated forms of chronic venous insufficiency.

Conclusions and implications. Our study revealed a significant role of the MMP 9 (Gln279Arg) and VEGFA (C936T) gene polymorphisms in CVI formation. The results of this study confirm that the expression of MMP-9 and VEGF genes is altered in patients with CVI. Overexpression of these genes can contribute to the spread of the inflammatory process and indicates intensive remodeling of the extracellular tissue in the wall of the varicose vein. The conducted study shows the relationship between CVI and polymorphisms of the VEGF and MMP-9 genes.