EVALUATION OF POLYMORPHISM OF MTHFR AND F5 GENES IN PATIENTS WITH IMPLANTED LEFT VENTRICULAR ASSIST DEVICES (LVAD)

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Chronic heart failure (CHF) is a global phenomenon, and the overall incidence and prevalence of the condition are steadily increasing. Medical therapies have proven efficacious, but only a small number of pharmacological options are in development. The main strategic direction in the effective treatment of severe forms of CHF to date is surgical treatment, implantation of left ventricular assist devices (LVAD) and heart transplantation. The field of mechanical circulatory support has seen immense growth since the early 2000s, and LVADs have transitioned over the past decade from large, pulsatile devices to smaller, more-compact, continuous-flow devices. Carrying out constant antiaggregant and anticoagulant therapy is associated with a risk of bleeding and thrombosis in the post-operative period. It is necessary to conduct complex genetic, pharmacogenetic and functional studies, including the use of modern molecular technologies to predict the clinical course and outcomes of this category of patients.

Aim of study is to study the polymorphisms of the MTHFR and F5 genes in patients with implanted LVADs for the further prediction of thrombosis development.

Material and methods. The study included patients with CHF who were implanted with LVAD on the basis of the National Scientific Cardiosurgical Center (n = 52), Astana. The control group consisted of practically healthy persons, without cardiovascular pathology, comparable in sex, age (n = 95). Genomic DNA was isolated from the blood using commercial kits. To study polymorphisms rs1801133 rs1801131 of the MTHFR gene and rs6025 gene F5, a real-time polymerase chain reaction method with allelic discrimination with TaqMan probes was used.

Results. The C677T MTHFR C/C, C/T, T/T genotypes occurred at a frequency of 44.2%, 42.3%, 13.5%, respectively, in patients with LVAD, and 57.9%, 30.5%, 11, 6%, respectively, in the control group. The genotypes A1298C MTHFR were distributed as follows: A/A, A/C, C/C - 53.8%, 38.5%, 7.7%, respectively, in the group of patients with LVAD and 30.5%, 63.1% , 6.3%, respectively, in the control group. Individuals with the 677TT genotype had a 1.3 fold higher risk of developing thrombosis (OR = 1.71, 95% CI = 1.21-2.43, p <0.01 codominant model), whereas individuals with the 677CT or TT genotype had a 1.2 fold increased risk (OR = 1.55, 95 % CI = 1.11-2.16, p <0.01). The allele frequency of T MTHFRC677T was 25.2% in patients with LVAD and 30.2% in the control group. Individuals with genotypes of 1298AC + CC had a 1.2 fold decrease in the risk of thrombosis (OR = 0.68, 95% CI = 0.49-0.95, p <0.05), which may indicate a protective role of this polymorphism. The allele frequency with MTHFR A1298C was 33.7% in the group of patients and 27.3% in the control group. The distribution of the r56025 genotypes of the F5 gene did not reveal mutant variants among the examined groups, the wild type of CC was found in 98.1% of the study group and 99.5% in the control group.