GENETIC VARIANTS OF CYP2C9 AND VKORC1 IN PATIENTS WITH LVAD.

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Introduction: Warfarin mostly used as oral anticoagulant in many pathological conditions such as deep vein thrombosis, heart valve prosthetics, blood vessels stenting and especially Left Ventricular Assist Device (LVAD). Key enzyme of the warfarin biotransformation is CYP2C9, from cytochrome P450 system, and target for the action of warfarin is vitamin K epoxide reductase complex subunit 1. Therefore, allelic variants of the CYP2C9 and VKORC1 genes are most important in the dosage of warfarin. It should be noted that the genetic component of warfarin metabolism various in different ethnic groups. The aim of our work was to study CYP2C9 and VKORC1 polymorphisms in Kazakh patients with implanted LVADs.

Materials and methods: Patient recruitment was carried out in the National Research Cardiac Surgery Center, Astana. We include in study patients with LVAD who signed confirmed informed consent. Venous bloods of 100 patients (93 males, 7 females) were collected. Genomic DNA was isolated with Wizard® Genomic DNA Purification Kit (Promega), CYP2C9 (rs1799853, rs1057910, rs28371686) and VKORC1 (rs8050894, rs9934438, rs9923231) genotypes were determined by allelic discrimination using TaqMan assays on Fast Real-Time PCR System (Applied Biosystems).

Results: Among our patients with LVAD were found different allelic variants of VKORC1 gene. Only 12% (12/100) had a wild-type allele of three polymorphisms, 37 patients had a homozygous variant with 3 polymorphisms (rs8050894, rs9934438, rs9923231) and 2 polymorphisms (rs9934438, rs9923231) - 20% (20/100) and 17% (17/100) respectively. Other remaining patients had different heterozygous combinations of VKORC1 polymorphisms. The genotyping results of CYP2C9 showed prevalence in patient's wild-type of allelic variant for all polymorphisms. Variants of heterozygous allele were determined in 8% (8/100) for 1 polymorphism (rs1799853) and in 7% (7/100) for another polymorphism (rs1057910).

Conclusion: Thus, in patients with LVAD were identified various genetic variants in VKORC1 and CYP2C9. Patients with homo- and heterozygous mutant allelic variants need to reduce the dose of warfarin to achieve a target INR in comparison patients with wild type.