IMPACT OF CYP2C9 AND VKORC1 GENES POLYMORPHISM TO THE THERAPEUTIC DOSE OF WARFARIN IN PATIENTS WITH ATRIAL FIBRILLATION

D.Akpanova[1], S.Berkinbayev[1], D.Ospanova2, A.Musagaliyeva[1]

[1]Scientific Research Institute of Cardiology and Internal Disease (Astana, Kazakhstan)

Kazakh Medical University of Continuing Education (Almaty, Kazakhstan)

mekebekovs@inbox.ru

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Introduction. For many years warfarin was the drug of choice for the prevention of thromboembolic complications in patients with AF. But warfarin therapy has some difficulties, including a narrow therapeutic window and the need for continuous laboratory monitoring. In the last decade, many scientific studies have been devoted to the impact of the genetic characteristics of the patient, in particular, CYP2C9 and VKORC1 gene polymorphism, on warfarin therapy.

Methods. We examined 50 patients with AF of Kazakh nationality who underwent genetic testing to study the relationship between gene polymorphisms and the therapeutic dose of warfarin.

Results. Among the studied patients the most common genotype of the CYP2C9*2 gene was the "wild" CC genotype - 74% (n = 37) and 26% (n = 13) of patients had heterozygous CT genotype. Also 92% of the patients were carriers of the "wild" AA genotype of CYP2C9*3 gene. For patients with the CC genotype of the CYP2C9*2 gene the daily dose of warfarin was 3.88 ± 0.3 mg, and for patients with CT genotype- 3,22 ± 0,5 mg (p = 1.02). The dose of warfarin for carriers of the "wild" AA genotype of CYP2C9*3 gene was 3.79 ± 0.27 mg, and for carriers of the heterozygous AC variant- 3.59 ± 0.35 mg (p = 0.74). So, there was no statistically significant difference in the average therapeutic dose of warfarin in patients with different genotypes of CYP2C9*2 and CYP2C9*3. Among the studied patients the most common genotype of the VKORC1C1173T gene was heterozygous CT genotype- 56%, the TT genotype was in 38% of patients and wild genotype (CC) 6% of patients. When analyzing the dose of warfarin, depending on the polymorphism of the gene VKORC1C1173T, it was established that in the carriers of the "wild" CC genotype the dose of warfarin was 6.25 ± 1.56 mg, which is almost 2 times higher than in homozygous carriers of the mutant allele TT- 2.99 ± 0.29 mg (p <0.05).

Conclusions. The patients of Kazakh nationality with the mutant allele of the VKORC1C1173T gene needs in lower therapeutic doses of warfarin.