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WARFARIN THERAPEUTIC DOSE DEPENDENCE ON CYP2C9, CYP4F2, VKORC1 GENES POLYMORPHISMS IN PATIENTS WITH ATRIAL FIBRILLATION

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Introduction: Warfarin (WF) is a widely used drug to prevent thromboembolic events in patients with atrial fibrillation (AF). Its dose varies greatly due to a number of factors, including genetic features. The aim of the study was to establish relationship between CYP2C9, CYP4F2, VKORC1 genes polymorphisms and WF therapeutic dose in patients with AF.
Methods: A retrospective cohort study was conducted in 60 AF patients receiving WF who were observed at the specialized anticoagulant therapy monitoring office of the ZSMU University Clinic during one year. CYP2C9, CYP4F2, VKORC1 genes polymorphisms were studied by multiplex real time polymerase chain reaction.
Results: The mean CHA2DS2-VASC score was 3.43 ± 0.18, HAS-BLED score – 2.2 ± 0.13; the WF dose median was 5 mg (3.75; 6.25). It was found out that the VKORC1 mutant allele A presence increased the probability of WF dose less than median in 7.00 times (95% CI 1.982-24.716; $p < 0.05$), and the CYP4F2 mutant allele T increased the probability of WF dose more than median in 6.263 times (95% CI 1.583-24.780). Statistically significant effect of CYP2C9 gene polymorphism on WF dosing was not observed.
Conclusions: VKORC1 and CYP4F2 genes polymorphisms are associated with warfarin dose variation and should be taken into account in warfarin dosing.

Keywords: atrial fibrillation, warfarin, genes polymorphism, dosing