Algorithm of personalised diagnostics and treatment in secondary prevention of ischemic stroke

ABSTRACT

Cerebrovascular diseases are the second most common cause of mortality and a significant cause of morbidity. Ischaemic stroke accounts for 88% of cases, with 35% of ischemic stroke being due to cardioembolism in atrial fibrillation, where anticoagulation therapy is indicated. Direct anticoagulants (DOACs) are preferred in secondary prevention. Approximately 5-10% of patients per year will fail treatment and develop recurrent stroke; conversely, approximately 2-4% will experience major bleeding during treatment. According to recommendations, there is no need to monitor DOAC levels unless complications occur. In this thesis, the role of genetic polymorphisms in relation to dabigatran and apixaban, and more precisely to drug levels, which influence the safety and efficacy of therapy, is analysed. For dabigatran, the polymorphisms of *CES1* and *ABCB1* genes were studied, for apixaban the polymorphisms of *ABCB1*, *CYP3A5*, *ABCG2* and *SULT1A1* were studied. Our study found a statistically significant effect of the *CES1* SNP rs2244613 on lower dabigatran levels, without a higher risk of ischemic events. In our cohort the presence of the *ABCB1* rs4148738 SNP significantly increased the risk of bleeding complications. For apixaban, the *ABCG2* SNP rs2231142 correlated with lower drug levels. For warfarin, VKORC1 and CYP2C9 polymorphisms are crucial for dose prediction, based on which a new dosing algorithm has been developed. This paper proposes incorporating genetic data into clinical decision-making to improve the safety and efficacy of stroke therapy.

KEYWORDS: anticoagulants, apixaban, dabigatran, hemorrhagic complications, ischemic stroke, personalised medicine, pharmacogenetics, plasmatic concentrations, warfarin