SECTION 13.
PHARMACY AND PHARMACOTHERAPY

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PHARMACOGENOMICS APPROACH TO WARFARIN THERAPY

Among oral anticoagulant medications, warfarin has been widely prescribed to prevent and treat thromboembolic events like valvular heart disease, stroke, venous thromboembolism, and atrial fibrillation. However, inter-individual genetic variability may affect pharmacokinetic (PK) and pharmacodynamic (PD) processes of warfarin, resulting in variation in drug response. Results of the several investigations have explored the role of pharmacogenetics in determining the dose, risk of the clinical complications and obtaining the optimal warfarin therapeutic outcomes. S- and R-enantiomer warfarin are differently involved in Warfarin-mediated inhibition of vitamin K epoxide reductase complex 1 (VKORC1), which is encoded by the VKORC1 gene and known to be related to PD of the drug [1, 4]. Moreover, VKORC1 polymorphisms are likely associated with warfarin dose requirements and drug sensitivity [2]. Additionaly, R and S isomers of warfarin are involved in PK of the drug. S-warfarin is mainly metabolized by CYP2C9 enzyme, and individuals carrying the CYP2C9*2 and *3 allele genotypes are known as poor metabolizers (individuals with reduced catalytic property), therefore require lower warfarin doses [1, 3]. Vuorinen and colleagues examined the relation between VKORC1 and CYP2C9 variants and the incidence of adverse drug reactions in warfarin-treated patients in a real-world setting and obtained interesting results. They conducted a cohort study comprising 2508 participants with cardiovascular disease (who at least once purchased warfarin). Responders were classified in genetically normal, and sensitive or highly sensitive ones. Results revealed, that sensitive and highly sensitive responders had more international normalised ratio (INR) tests above 3 (high value), testifying that participants of this group required a lower daily dose of warfarin. Moreover, no significant differences were observed in the incidence of hemorrhage outcomes between two groups, and the incidence of thromboembolic events was higher in sensitive or highly sensitive group [4]. However, evidences of the benefits of genotype-guided approach to determine the dose of the warfarin and its association with clinical adverse events remains controversial.

References:

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