PK/PD OF WARFARIN ASSOCIATED WITH GENETIC POLYMORPHISMS OF VKORC1 AND CYP2C9 IN INDONESIAN PATIENTS.

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ABSTRACT

Warfarin is an oral anticoagulant for treatment and prevention the thromboembolic disorder. VKORC1 and CYP2C9 are known as key enzymes that contribute to warfarin dose requirement. To decide appropriate dose of warfarin, we determined genotype variations of VKORC1 and CYP2C9 in Indonesian population and evaluated the association between genotype variations and warfarin response in Indonesian patients receiving very low-dose warfarin. Genotyping of gene variants in VKORC1 and CYP2C9 have carried out by PCR-RFLP in 206 Indonesian subjects. Concentrations of R-warfarin and S-warfarin in plasma and PT-INR were used as a pharmacokinetic and pharmacodynamic indices, respectively. The frequencies of mutant alleles of VKORC1-1639G>A and CYP2C9 were 80.6 and 2.9%, respectively. PT-INR value was significantly higher in the patients with VKORC1-1639 AA compared to those with GA (p=0.0076) and GG (p=0.0079). On the other hand, S-warfarin concentration was significantly higher in the patients with CYP2C9 hetero mutant (*1/*3) compared to those with wild type (*1/*1, p=0.0027). The genetic variation of VKORC1-1639G>A has affected the PT-INR as a pharmacodynamic indices and genetic variation of CYP2C9 has affected the S-warfarin concentration as a pharmacokinetic indices.