World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:15, No:12, 2021

The Impact of CYP2C9 Gene Polymorphisms on Warfarin Dosing

Authors : Weaam Aldeeban, Majd Aljamali, Lama A. Youssef

Abstract : Background & Objective: Warfarin is considered a problematic drug due to its narrow therapeutic window and wide inter-individual response variations, which are attributed to demographic, environmental, and genetic factors, particularly single nucleotide polymorphism (SNPs) in the genes encoding VKORC1 and CYP2C9 involved in warfarin's mechanism of action and metabolism, respectively. CYP2C9*2rs1799853 and CYP2C9*3rs1057910 alleles are linked to reduced enzyme activity, as carriers of either or both alleles are classified as moderate or slow metabolizers, and therefore exhibit higher sensitivity of warfarin compared with wild type (CYP2C9*1*1). Our study aimed to assess the frequency of *1, *2, and *3 alleles in the CYP2C9 gene in a cohort of Syrian patients receiving a maintenance dose of warfarin for different indications, the impact of genotypes on warfarin dosing, and the frequency of adverse effects (i.e., bleedings). Subjects & Methods: This retrospective cohort study encompassed 94 patients treated with warfarin. Patients' genotypes were identified by sequencing the polymerase chain reaction (PCR) specific products of the gene encoding CYP2C9, and the effects on warfarin therapeutic outcomes were investigated. Results: Sequencing revealed that 43.6% of the study population has the *2 and/or *3 SNPs. The mean weekly maintenance dose of warfarin was 37.42 ± 15.5 mg for patients with the wild-type allele (CYP2C9*1*1), whereas patients with one or both variants (*2 and/or *3) demanded a significantly lower dose (28.59 ±11.58 mg) of warfarin, (P= 0.015). A higher percentage (40.7%) of patients with allele *2 and/or *3 experienced hemorrhagic accidents compared with only 17.9% of patients with the wild type *1*1, (P = 0.04). Conclusions: Our study proves an association between *2 and *3 genotypes and higher sensitivity to warfarin and a tendency to bleed, which necessitates lowering the dose. These findings emphasize the significance of CYP2C9 genotyping prior to commencing warfarin therapy in order to achieve optimal and faster dose control and to ensure effectiveness and safety.

Keywords : warfarin, CYP2C9, polymorphisms, Syrian, hemorrhage
Conference Title : ICTH 2021 : International Conference on Thrombosis and Hemostasis
Conference Location : Vienna, Austria
Conference Dates : December 27-28, 2021