Frequency of VKORC1 (C1173T) and CYP2C9 genetic polymorphisms in Egyptians and their influence on warfarin maintenance dose: proposal for a new dosing regimen

Abstract:

Introduction: Warfarin is one of the most widely used anticoagulants, yet interindividual differences in drug response, a narrow therapeutic range and a high risk of bleeding or stroke complicate its use. We aimed to determine the allele and genotype frequency of VKORC1 1173 C>T, CYP2C9*2 and CYP2C9*3 variant polymorphisms in the Egyptian population and to evaluate their influence on the interindividual differences in warfarin dosage. **Methods:** A total of 154 unrelated healthy adult patients and 46 warfarin-treated patients were included. SYBR Green-based real-time polymerase chain reaction (PCR) assay was used for studying VKORC1 (C1173T) and CYP2C9*3 polymorphisms. Mutagenically separated PCR assay was used to detect the CYP2C9*2 allele. **Results:** VKORC1 genotype frequencies were 11%, 24% and 65% for CC, CT and TT, respectively. The prevalence of CYP2C9 haplotypes was 81% (*1*1), 3.3% (*1*2), 9.7% (*1*3), 4.5% (*2*2) and 0.65% (2*3 and *3*3). VKORC1 TT and CYP2C9*2*2 were associated with a significantly lower warfarin dose. VKORC1 and CYP2C9 accounted for 31.7% and 15.6% of warfarin dose variability, respectively, and together with clinical factors explained 61.3% of total variability. **Conclusion:** VKORC1-TT and CYP2C9 *1/*1 are the most prevalent genotypes among Egyptians. Patients with VKORC1-TT genotype required a lower warfarin dose.

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