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The VCORK1 alleles involved in the pharmacogenetics of warfarin anticoagulant among Emiratis

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Introduction: Warfarin is one of the most prescribed anticoagulant drugs used in the prevention and treatment of thromboembolic vascular diseases. However, warfarin has a low therapeutic index and therefore has high risk of side effects and/or therapeutic failure. Individual variation in drug response depends on variation in patient weight, height, gender, use of other anticoagulant drugs, co-medications, diet, patient compliance, and most importantly genetic variation. Recently, more studies are focusing on determining the initial warfarin dosing based on the genetic profile of these patients rather than a trial and error based dosing. Warfarin targets the vitamin K epoxide reductase VKORC1 and blocks its activity and therefore any functional mutations in the gene encoding this enzyme will perturb the balance between the influence of warfarin and vitamin K on the enzyme activity. The purpose of this study is to determine the alleles and genotypes and their frequencies among UAE nationals.

Methods: Blood samples from Emirati subjects were collected and the promoter and allexonic and intronic regions were amplified by PCR and sequenced using Sanger Sequencing.

Results: The alleles harboring the –promoter region variant (-1639G >A,rs9923231) have been observed in a large proportion of the population. Other variants includingrs7294, rs9934438 and rs2884737 have also been observed.

Conclusion: In Emirati population the promoter variant-1639G > A is common. The A allele is associated with the need of lower doses than the G allele. Homozygous carriers of the A allele require a warfarin dose approximately 50% of that of an individual that is homozygous for the G allele.

Biography

Hayat Aljabeiji is a pharmacist graduate from Dubai Pharmacy College and holds MBA from Griggs University. She is a pharmacogenomic researcher/ candidate for master program at UAE University. Prior to that, she worked as program manager at Institute of HealthCare Research at Cambridge Academy for Higher Education where she worked on a number of pharmaceutical and healthcare projects. Before that, she worked at Boots, Bin Sina Pharmacies as a pharmacist and at AXA Insurance as a Medical Advisor.

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