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Letter to the Editors-in-Chief

Study on a novel polymorphism in the *VKORC1* promoter region using bioinformatic tools and warfarin dosing data

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Highlights

- Optimal dose of warfarin should be personalized for each person.
- Polymorphism in the promoter region of VKORC1 is effective in warfarin medication.
- Changes in the binding sites of the transcription factors can affect the expression of the VKORC1 gene.

Introduction

Warfarin, an antagonist of vitamin K, interferes with coagulation by disrupting the vitamin K cycling pathway [1]. The VKOR enzyme which is the target of warfarin is encoded by the *VKORC1* gene [2]. Several studies have demonstrated that genetic variation in *VKORC1* led to differences in the amount of required warfarin doses between geographically-distinct or ethnic groups [3]. Oldenburg, et al. found that polymorphism in this gene is responsible for 30% difference in warfarin therapeutic dose among various races [4]. However, reports on the *VKORC1* role in thrombogenicity are apparently suffering from the notable gaps of information about enriched transcription factor-binding sites (TFBSs) in the promoter and the potential transcription factors, which would influence the gene expression. Finding effects of polymorphisms in warfarin sensitive or resistant patients on TFBSs of the *VKORC1* gene promoter can offer valuable clues in order to determine transcription factors involved in *VKORC1* gene expression. In this study, for the first time, variants of *VKORC1* gene promoter and the relation between these variants and warfarin maintenance dose in Iranian patients taking warfarin were investigated.

Section snippets

Materials and methods

This study was approved by the Scientific and Ethical Committee of Urmia University of Medical Sciences (code: 1394.282). 2ml blood samples obtained from 29 warfarin receiving patients of Seyyed alshohada Hospital in Urmia, Iran. Genomic DNA extracted with DNA Extraction mini kit (YTA Company, Iran). To investigate *VKORC1*-1639G>A polymorphism in the studied cohort PCR-RFLP analysis was carried out according to Sconce et al. [11]. Additionally, primers were specifically designed for 849bp of …

Results

Patients who received warfarin dose less than 1.5 mg/day considered as warfarin sensitive (12 patients), between 1.6 and 7.5 mg/day as control group (8 patients) and more than 7.5 mg/day as high dose taker (10 patients). Among 29 patients, there were 15 males and 14 females.

All patients were genotyped for rs9923231 in the promoter region of *VKORC1*. A novel mutation with a single base substitution (located at -330 C→A in the upstream region of *VKORC1*), along with the *VKORC1*-1639G>A in 3 out of the …

Discussion

A specific dose of warfarin cannot be applied for all patients due to differences between individuals, one of which is genetic differences. Appropriate dose was determined according to the individual's resistance or sensitivity to warfarin. This study included patients with different warfarin dose requirements, thus allowing the determination of the genetic variants related to pharmacological response in sensitive, resistant and control groups. This study introduced the genetic polymorphism …

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Conflict of interest statement

None declared. …