Investigation of allele and genotype frequencies of \textit{CYP2C9}, \textit{CYP2C19} and \textit{VKORC1} in Iran

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Abstract:
Research has shown that there are significant ethnic variations in the frequency of highly functional mutations in genes coding for metabolic enzymes. However, few studies have examined the frequency distribution of major allelic variations within the population of Iran. The present study focused on the genotype profile of southern Iranians in order to compare the allelic frequencies of \textit{CYP2C9}, \textit{CYP2C19}, and \textit{VKORC1} –1639G>A (all of which have been shown to have significant roles in the metabolism of warfarin) with those of other populations. Therefore, genotyping was carried out on 150 subjects (50 healthy volunteers and 100 outpatient subjects) by polymerase chain reaction- restriction length polymorphism (PCR-RFLP). Findings indicated both similarities and differences in the distribution of polymorphic alleles of \textit{CYP2C9}, \textit{CYP2C19} and \textit{VKORC1} between southern and northern Iranians. For example, the frequency of \textit{CYP2C9*3} among southern Iranians (9.8\%) was found to be similar to the frequency found among Caucasians (9.7\%) but was higher than the frequency found among Africans (1\%), Japanese (2.3\%), and northern Iranians (0\%). These findings confirmed significant inter-ethnic differences in \textit{CYP2C9} frequencies between southern and northern Iranians. The reported frequency of \textit{CYP2C9*2} in our subjects (25.3\%) was different from the frequencies seen in Caucasian (10–13\%), African (2\%) and Asian (0\%) populations. The \textit{CYP2C19*2} and \textit{CYP2C19*3} allelic frequencies were similar to the Caucasian population. For \textit{VKORC1}, the allelic frequency of –1639A (55.6\%) was in accordance with Caucasian, but different from Chinese (96\%) and African-American populations (13\%).

The findings confirmed some important interethnic differences in the metabolic capacity for drug clearance. Because the population of Iran consists of several ethnicities, this type of analysis can help explain the genetic diversity between the populations of northern and southern Iran. In addition, the results of this study will be useful for understanding clinical pharmacokinetics and drug dosage recommendations for Iranians.

Key words: \textit{CYP2C9}, \textit{CYP2C19}, \textit{VKORC1}, Iranian, genotype