Prevalence of the CYP2D6*10 (C100T), *4 (G1846A) and *14 (G1758A) alleles in Iranian populations of different ethnicities

ABSTRACT

The presence of polymorphisms in the CYP2D6 gene may modulate enzyme level and activity, thereby affecting individual responses to pharmacological treatment. Here, we compared the prevalence of the CYP2D6*10, *4, and 14* alleles in an Iranian population of different ethnicities with those of other populations. Allele and genotype frequency distributions of CYP2D6*10 variants and predicted phenotypes including extensive metabolizers, intermediate metabolizers, and poor metabolizers were analysed in blood samples of 300 unrelated healthy individuals in an Iranian population using polymerase chain reaction (PCR)-restriction fragment length polymorphism, PCR-single-strand conformation polymorphism, and direct genomic DNA sequencing. The CYP2D6*4 (G1846A) and *14 (G1758A) allelic frequencies were not detected in different ethnicities, demonstrating the absence of a significant contribution of these alleles in Iranian populations. However, the T/T, C/T, and C/C genotype frequencies of the CYP2D6*10 allele were significantly different ($P<0.01$) in all Iranian ethnic groups. Additionally, the frequency of the homozygous T/T variant of the CYP2D6*10 allele was significantly high in the Lure ($P<0.017$) and low in the Kurd ($P<0.002$) ethnicities. The frequency of the T/T variant of the CYP2D6*10 allele in central Iran was the highest ($P<0.001$), while the south of Iran had the lowest frequency ($P<0.001$). The frequency of the C/T variant of the CYP2D6*10 allele was significantly a bit high ($P<0.001$) in females compare to males, while the frequencies of the T/T variant in females is similar to males, which are 24.4% and 24.3%, respectively. In contrast to absence of the CYP2D6*4 (G1846A) and *14 (G1758A) alleles in Iranian populations of different ethnicities, the prediction of the CYP2D6*10 allele is required in drug research and routine treatment, where the information would be helpful for clinicians to optimize therapy or identify persons at risk of adverse drug reactions before clinical trials. Approximately 39.3% of subjects (24.3% homozygous T/T CYP2D6*10 as poor metabolizers and 15% heterozygous C/T CYP2D6*10 as intermediate metabolizers) had this allele; therefore, the harmful effects of drugs are relatively common among Iranians.

Keyword: Pharmacogenetics; Polymorphism; Cytochrome P450 genes; CYP; Iranian population; Antipsychotics; Antidepressants