Oral

[O26-3] O26-3: Pharmacogenomics (1)

Chairs: Ichiro Ieiri, Japan / Vincent Haufroid, Belgium
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[O26-3-2] Pharmacogenetic profiling of CYP2D6 in western Indian population

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Background

Cytochrome P450 2D6 (CYP2D6) is responsible for the metabolism of numerous classes of clinically important drugs. More than 100 CYP2D6 alleles have been detected which shows differences in frequencies between worldwide populations. CYP2D6 genotyping and phenotype prediction has led to strong guidelines by Clinical Pharmacogenetics Implementation Consortium (CPIC) for various drug classes such as antidepressants, opioids, antipsychotics etc. There is lack of data from Mumbai, Western India on the allele frequencies of major CYP2D6 alleles, gene deletion, duplication or multiplication. Hence a pilot study was undertaken to determine the distribution of *2, *3, *4, *5, *10 and *41 CYP2D6 alleles, and CYP2D6 gene multiplication alleles in healthy individuals from Western India. Furthermore, to determine pharmacogenetic implications of CYP2D6 genotypes by detecting the distribution of predicted phenotypes.

Methods

Fifty-two healthy individuals were screened for major CYP2D6 alleles *2, *3, *4, *5, *10 and *41 using Taqman SNP genotyping assay and Copy number variation (CNV) assay by realtime PCR. Validation of Taqman SNP genotyping assays was performed by sending representative samples for Bi-directional sequencing.

Results

The allele frequencies of CYP2D6*2, *3, *4, *5, *10 and *41 alleles were observed to be 30.8%, 0%, 11.5%, 3.9%, 19.2% and 17.3% respectively. The frequency of CYP2D6 multiplication alleles *1XN, *2XN and *4XN was observed to be 9.6%, 1.9% and 3.9% respectively. The predicted phenotype frequency was observed to be 78.9%, 3.9% and 9.6% for extensive metabolizers (EMs), Intermediate metabolizers (IMs), and Ultrarapid Metabolizers (UMs) respectively. Poor metabolizers (PMs) were not detected in the present study.

Conclusions

High frequency (17.3%) of reduced function allele CYP2D6*41 allele observed in the present study were similar to West Asian and Middle East populations (16.9%). Lack of data in Indian population, and contribution of CYP2D6*41 allele to IMs in combination with null alleles necessitates its screening in Indian population for better therapeutic modulation. Present study demonstrated high frequency of *1xN alleles (9.6%) as compared with Indian and worldwide populations. High frequency of Ums (9.6%) observed in the present study and scarcity of data in Indian populations further emphasizes pharmacogenetic implications of CYP2D6 genotyping testing.