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Frequency of functional drug disposition gene polymorphism in Thai population: relevance to antiretroviral drugs

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Purpose of the study

Significantly higher plasma exposure of some protease inhibitors (PIs) has been observed in Thai subjects compared to Caucasians. These differences may partially be explained by factors such as body weight and diet. However, pharmacogenetic differences may also contribute. The aim of this study was to investigate, in a Thai population, the frequency of functional polymorphisms in genes known to influence plasma concentrations of antiretroviral drugs.

Methods

Eighty-four Thai subjects were included in this study. Genotyping for *CYP2B6* (516G>T and 983T>C), *CYP3A4* (-392A>G), *CYP3A5* (6986A>G), *ABCB1* (1236C>T, 3435C>T and 2677G>T), *ABCC1* (-260G>C), *ABCG2* (421C>A), *SLCO1B1* (521T>C) and *PXR* (63396C>T and 44477T>C) was conducted by real-time PCR based allelic discrimination. Hardy-Weinberg equilibrium was assessed by χ^2 test of observed versus predicted genotype frequencies. Fisher's exact test was used to determine differences in allele frequency between Thai and previously reported Caucasian populations.

Summary of results

All genotype frequencies were in the Hardy-Weinberg equilibrium. The minor allele frequency for 516G>T, 983T>C, -392A>G, 3435C>T, 2677G>T, -260G>C and 521T>C was 0.35, 0, 0.02, 0.45, 0.45, 0.03 and 0.12, respectively and not significantly different from Caucasians. The G allele frequency for *CYP3A5* 6986A>G was lower in Thai (0.65) than in Caucasians (0.92; $p < 0.0001$). Similarly, the minor allele frequencies for ABCB1 1236C>T and ABCG2 421C>A were significantly higher in Thai compared to Caucasian populations (0.65 vs. 0.46, $p = 0.002$ and 0.24 vs. 0.10, $p = 0.003$, respectively). Finally, *PXR* SNPs were both at different frequency in Thai vs. Caucasian populations (0.34 vs. 0.40, $p = 0.006$ for 63396 C and 0.45 vs. 0.16, $p < 0.0001$ for 44477 T).

Conclusion

Although the different allele frequencies for ABCB1 and ABCG2 could have a modest impact on the bioavailability, the over-representation of CYP3A5 6986 G would be expected to result in lower drug concentrations of PIs. However, we have previously shown an association of PXR SNPs with atazanavir plasma concentrations and so genotype-phenotype studies for these SNPs in Thai populations are now warranted.