

Influence of *CYP2D6* Deletion, Multiplication, -1584C→G, 31G→A and 2988G→A Gene Polymorphisms on Dextromethorphan Metabolism among Mexican Tepehuanos and Mestizos

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Abstract

The aim of this study was to explain the variability of *CYP2D6* activity by the identification of *CYP2D6* deletion and multiplications, and the single-nucleotide polymorphisms (SNPs) -1584C→G, 31G→A and 2988G→A in Mexican Mestizo and Tepehuano subjects. One hundred twelve Mestizos and 99 Tepehuano Amerindians were studied, who were previously phenotyped with dextromethorphan. The frequencies of *CYP2D6**2A [-1584C→G] and *35 [-1584C→G, 31G→A] were 10.7 and 4.1%, respectively, in Mestizos, which is evidently a trend towards an extensive metabolism in carriers of the -1584G change. In Tepehuanos, *2A was identified with a frequency of 20%, and the allele *35 was not found. The frequencies of *CYP2D6**5 (deletion) and *41/2988G→A were 1.3 and 2.2% in Mestizos and 0.5 and 1% in Tepehuanos, respectively. The SNP 2988A was found to be significantly related with the intermediate metabolizer phenotype in Mestizos ($R = 0.309$; $n = 88$; $p = 0.006$). The multiplications had frequencies of 4.1% in Mestizos and 1.5% in Tepehuanos. Only in the Mestizos did the presence of multiplication significantly decrease the DM/DX (dextromethorphan/dextrorphan) values ($R = 0.273$; $n = 88$; $p = 0.016$). The polymorphisms studied had different frequencies between Tepehuanos and Mestizos ($p < 0.001$); however, in the Tepehuano group these had a low influence on their phenotypic expression. It helps to understand the genotype-phenotype relationships of *CYP2D6* in our studied populations.