Evidence of interethnic differences in the pharmacokinetics of a marker of cyp1a2 activity

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It has been reported that CYP3A4 activity is reduced in Mexicans and frequently, lower doses of drugs metabolized by this pathway are employed in our population. Recently, we have observed that the reduction of doses in Mexicans is also present with drugs that are not metabolized by CYP3A4. One of them is tizanidine. This drug is a muscle relaxant that is widely used in therapeutics. It is considered as a narrow therapeutic index drug and sedation and hypotension may be present with higher doses of the drug. It has been described that tizanidine is a marker of CYP1A2 activity. In order to establish if the reduction of doses in Mexicans is due to a reduced metabolism of tizanidine in Mexicans, this study was conducted to evaluate the pharmacokinetics of this drug and to compare with data reported in other populations in order to establish if interethnic differences are present. Twenty-five Mexican adult healthy volunteers received an oral dose of 6 mg tizanidine under fasting conditions and plasma samples were obtained at selected times during 12 hours. Plasma tizanidine concentrations were determined by a validated high-performance liquid chromatographic method. Pharmacokinetic parameters were obtained by a non-compartmental approach and values obtained were compared with those reported in other populations. Parameters obtained in this study were as follows (mean +/- SD): Cmax 11.93 +/- 5.46 ng/ml, tmax 1.30 +/- 0.68 h, AUC 36.16 +/- 23.43 ng.h/ml and t1/2 1.57 +/- 0.57 h. Values of Cmax and AUC are at least twice the values reported in other populations. This study gives evidence about the existence of interethnic differences in the oral pharmacokinetics of tizanidine, suggesting a lower activity of CYP1A2 in Mexicans. Therefore, it is important to review dosage regimes of this drug in Mexicans to avoid side effects due to increased exposure to the drug.