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## Hydroxylation index of omeprazole in relation to CYP2C19 polymorphism and sex in a healthy Iranian population

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**Background:** Polymorphism of *CYP2C19* gene is one of the important factors in pharmacokinetics of *CYP2C19* substrates. Omeprazole is a proton pump inhibitor which is mainly metabolized by cytochrome P450 2C19 (*CYP2C19*). The aim of present study was to assess omeprazole hydroxylation index as a measure of *CYP2C19* activity considering new variant allele (*CYP2C19**17) in Iranian population and also to see if this activity is sex dependent.

**Methods:** One hundred and eighty healthy unrelated Iranian individuals attended in this study. Blood samples for genotyping and phenotyping were collected 3 hours after administration of 20 mg omeprazole orally. Genotyping of *2C19* variant alleles **2, *3* and **17* was performed by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and semi-nested PCR methods. Plasma concentrations of omeprazole and hydroxyomeprazole were determined by high performance liquid chromatography (HPLC) technique and hydxroxylation index (HI) (omeprazole/ hydroxyomeprazole) was calculated.

**Results:** The *CYP2C19*17* was the most common variant allele in the studied population (21.6%). Genotype frequencies of *CYP2C19*17*17, *1*17,* and **2*17* were 5.5%, 28.8% and 3.3% respectively. The lowest and the highest median omeprazole HI was observed in **17*17* and **2*2* genotypes respectively (0.36 vs. 13.09). The median HI of omeprazole in subjects homozygous for *CYP2C19*1* was 2.16-fold higher than individuals homozygous for *CYP2C19*17* (P<0.001) and the median HI of *CYP2C19*1*17* genotype was 1.98-fold higher than CYP2C19 *17*17 subjects (P<0.001). However, subjects with CYP2C19*2*17 (median HI: 1.74) and *CYP2C19*1*2* (median HI: 1.98) genotypes and also *CYP2C19*1*17* (median HI: 0.71) and *CYP2C19*1*1* (mean HI: 0.78) did not show any significantly different enzyme activity. In addition, no statistically significant difference was found between women and men in distribution of *CYP2C19* genotypes. Furthermore, the hydroxylation index of Omeprazole was not different between women and men in the studied population.

**Conclusion:** Our data point out the importance of *CYP2C19*2* and *CYP2C19*17* variant alleles in metabolism of omeprazole and therefore *CYP2C19* activity. Regarding the high frequency of *CYP2C19*17* in Iranian population, the importance of this new variant allele in metabolism of *CYP2C19* substrates shall be considered.

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**Notes:**