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Clopidogrel pharmacokinetics and pharmacogenetics in Iranian patients

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Background and Aims: Clopidogrel is a prodrug which requires transformation into an active metabolite by cytochrome P-450 (CYP2C19) enzymes for its antiplatelet effect. The genes encoding CYP enzymes are polymorphic, with common alleles conferring reduced function.
Methods: We tested the association between functional genetic variants in CYP genes (by Polymerse Chain Reaction, PCR) and plasma concentrations of active drug metabolite (by HPLC) and studied association between these genetic variants in 130 patients (from Tehran Heart Center and Shahid Rajai Heart Hospital) with coronary syndromes treated by Precotaneous Coronary Intervention(PCI) and to whom clopidogrel were administrated.
Results: In our patients who were treated with clopidogrel, carriers of at least one CYP2C19 reduced-function allele (approximately 25% of the study population) had a relative reduction of 49% in plasma exposure to the active metabolite of clopidogrel. A two-sided P value was used to test for significance (threshold, $P<0.05$). A significant difference between genotype classification CYP2C19*1*1 and CYP2C19*2*2 and the mean plasma concentrations was identified ($p=0.038$), (1560+/- 2300 and 765+/- 752 ng/ml respectively).
Conclusions: Among persons treated with clopidogrel, carriers of a reduced-function CYP2C19 allele had significantly lower levels of the active metabolite of clopidogrel. There were several potential limitations to our study that we try to overcome it in future studies.

Keywords: Clopidogrel; Pharmacokinetics; Pharmacogenetics; CYP2C19