The CYP2C19*1/*2 Genotype Does Not Adequately Predict Clopidogrel Response in Healthy Malaysian Volunteers

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Background.
The CYP2C19*2 allele may be associated with a reduced antiplatelet effect for clopidogrel. Here, we assessed whether CYP2C19*2 alleles correlate with clopidogrel responsiveness following the administration of clopidogrel in healthy Malaysian volunteers. Methods. Ninety volunteers were genotyped for CYP2C19*2 and CYP2C19*3 alleles. Forty-five of 90 volunteers were included in the clopidogrel response studies and triaged into three genotypes, namely, CYP2C19*1/*1 , CYP2C19*1/*2 and CYP2C19*2/*2. All subjects received 300 mg of clopidogrel, and platelet reactivity was assessed after a four-hour loading utilizing the VerifyNow-P2Y12 assay. Platelet activity was reported using P2Y12 reaction units (PRUs), and nonresponder status was prespecified at PRU ≥ 230. Results. Following clopidogrel intake, CYP2C19*2/*2 carriers had a significantly higher mean PRU compared to the CYP2C19*1/*2 and CYP2C19*1/*1 (291.0 ± 62.1 versus 232.5 ± 81.4 versus 147.4 ± 87.2 PRU,) carriers. Almost half of the participants (46.7%) were found to be nonresponders (3 were CYP2C19*1/*1, 11 were CYP2C19*1/*2, and 7 were CYP2C19*2/*2). Conclusion. In healthy Malaysian volunteers, CYP2C19*2 allele was associated with a decrease in platelet responsiveness to clopidogrel. However, clopidogrel nonresponders can be found not only in the carriers of CYP2C19*2/*2, but also in the carriers of CYP2C19*1/*2 and CYP2C19*1/*1. The present paper demonstrated that genotype information does not correlate with clopidogrel response, and genotyping may represent a less robust approach compared to platelet activity testing in guiding clopidogrel therapy.