

CYP2C19 genotypes and their impact on clopidogrel responsiveness in percutaneous coronary intervention.

[Mejin M](#), [Tiong WN](#), [Lai LY](#), [Tiong LL](#), [Bujang AM](#), [Hwang SS](#), [Ong TK](#), [Fong AY](#).

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Department of Pharmacy, Sarawak General Hospital Heart Centre, Kota Samarahan, Malaysia, melissamejin@crc.gov.my.

Abstract

Background Cytochrome P450 2C19 (CYP2C19) loss-of-function polymorphisms are more common in Asian populations and have been associated with diminished antiplatelet response to clopidogrel. In this era of 'personalised medicine', combining genotyping and phenotyping as a strategy to personalise antiplatelet therapy warrants further exploration. **Objective** This study aimed to investigate the prevalence and impact of CYP2C19*2, *3 and *17 genotypes on clopidogrel responsiveness in a multiethnic Malaysian population planned for percutaneous coronary intervention. **Setting** Between October 2010 and March 2011, a total of 118 consecutive patients planned for percutaneous coronary intervention were enrolled in Sarawak General Hospital, Borneo. All patients received at least 75 mg aspirin daily for at least 2 days and 75 mg clopidogrel daily for at least 4 days prior to angiography. **Method** Genotyping for CYP2C19*2 (rs4244285, 681G > A), *3 (rs4986893, 636G > A) and *17 (rs11188072, -3402C > T) alleles were performed by polymerase chain reaction-restriction fragment linked polymorphism method. Whole blood ADP-induced platelet aggregation was assessed with multiple electrode platelet aggregometry (MEA) using the Multiplate Analyzer. **Main outcome measures** The distribution of CYP2C19*2, *3 and *17 among different ethnic groups and the association between genotype, clopidogrel responsiveness and clinical outcome were the main outcome measures. **Results** The highest prevalence of poor metabolisers (carriers of at least one copy of the *2 or *3 allele) was among the Chinese (53.7 %), followed by the Malays (26.9 %), Ibans (16.4 %) and other races (3.0 %). Poor metabolisers (PMs) had the highest mean MEA (303.6 AU*min), followed by normal metabolisers (NMs) with 270.5 AU*min and extensive metabolisers (EMs) with 264.1 AU*min ($p = 0.518$). Among poor responders to clopidogrel, 65.2 % were PMs and NMs, respectively, whereas none were EMs ($p = 0.350$). Two cardiac-related deaths were reported. **Conclusion** There was a diverse inter-ethnic difference in the distribution of CYP2C19 polymorphism. The findings of this study echo that of other studies where genotype appears to have a limited impact on clopidogrel responsiveness and clinical outcome in low-risk patients.