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.

Int J Clin Pharm. 2013 May 10. [Epub ahead of print]

Source

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.