PHARMACIST-LED RAPID POINT-OF-CARE CYP2C19 GENOTYPING FOR INDIVIDUALISATION OF ANTIPLATELET THERAPY

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BACKGROUND

Presence of the CYP2C19 loss-of-function (LoF) *2 allele is associated with reduced antiplatelet effect in clopidogrel-treated patients.[1] Since about 50% of major adverse cardiac events occur within the first few days after percutaneous coronary intervention (PCI)[2], a rapid *CYP2C19*2* genotype result is important to individualise antiplatelet therapy at the start of treatment.[3]

OBJECTIVE

To apply a pharmacist-led process to individualise antiplatelet therapy guided by *CYP2C19*2* genotype using the novel rapid point-of-care (POC) genetic testing system in patients undergoing PCI.

STUDY DESIGN

1. Ethical approval for the study was granted.
2. Following informed written consent, patients undergoing PCI with stent deployment for ACS or stable angina and who were candidates for DAPT were recruited by a clinical pharmacist researcher from the catheterisation laboratory over a 3-month period (October to December 2014).
3. Exclusion criteria were patients < 18 and > 75 years, body weight < 60 kg, history of stroke or transient ischaemic attack, active bleeding, coagulation or platelet disorders and/or chronic liver disease.
4. A buccal sample was collected by the clinical pharmacist researcher for automated *CYP2C19*2* genotyping with the Spartan™ RX assay *(Spartan Bioscience)* within 60 minutes.
5. Each patient was genotyped as a non-carrier of the *2 allele (*1/*1), a carrier of one *2 allele (*1/*2) or a carrier of two *2 alleles (*2/*2).
6. Carriers of the *2 allele were verbally communicated by the clinical pharmacist researcher to the cardiologist together with suggested antiplatelet therapy recommendations.[4] Treatment decision was taken by the cardiologist.

RESULTS

Patient baseline characteristics

The total patient cohort consisted of 34 patients. Twenty-five patients were male and 9 were female, mean age was 66 years (range 49-75 years) and all patients were Caucasian.

CYP2C19 genotype results

Thirteen patients (38%) were genotyped as carriers of the CYP2C19 LoF *2 allele (Table 1).

Table 1: Distribution of CYP2C19 *2 allele (N=34)

CYP2C19 genotype	Number of patients
Non-carrier of *2 allele	21
Carrier of one *2 allele*	12
Carrier of two *2 alleles*	1

**Candidates for alternative antiplatelet therapy to clopidogrel*

CONCLUSIONS

The Spartan™ RX assay rapidly identifies carriers of the LoF *2 allele (13 patients in this cohort), is user-friendly requiring minimal training and is portable enabling testing at the patient's bedside. The main limitation is the cost of the tests. According to the Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations for CYP2C19 genotype and clopidogrel therapy[4] these patients are candidates for a newer and more potent $P2Y_{12}$ receptor, such as prasugrel. This assay can be implemented for pharmacist-led *CYP2C19*2* genotype-guided personalisation of antiplatelet therapy in the critical period post-PCI.

References

1. Scott SA, Sangkuhl K, Shuldiner AR, Hulot JS, Thorn CF, Altman RB *et al*. PharmGKB summary: Very important pharmacogene information for cytochrome P450, family 2, subfamily C polypeptide 19. *Pharmacogenet Genom*. 2012;22(2):159–65.
2. Giusti B, Gori AM, Marcucci R, Saracini C, Sestini I, Paniccia R *et al*. Relation of cytochrome P450 2C19 loss-of-function polymorphism to occurrence of drug-eluting coronary stent thrombosis. *Am J Cardiol.* 2009;103(6):806–11.
3. Knauer MJ, Diamandis EP, Hulot JS, Kim RB, So DY. Clopidogrel and CYP2C19: Pharmacogenetic testing ready for clinical prime time? *Clin Chem.* 2015;61(10):1235-40.
4. Scott SA, Sangkuhl K, Stein CM, Hulot JS, Mega JL, Roden DM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. *Clin Pharmacol Ther.* 2013; 94 (3): 317-23.

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