Association of the CYP2C19 *2 allele on the occurrence of in-stent restenosis in patients undergoing coronary stenting

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Background

Proper functioning of the CYP2C19 enzyme is required to convert clopidogrel to its active metabolites to be able to exert its antiplatelet effect. Presence of the CYP2C19 loss-of-function (LoF) *2 variant allele is associated with a decreased response to clopidogrel which may lead to adverse cardiac events post-percutaneous coronary intervention (PCI).

Objectives

To genotype patients undergoing PCI for carriage of the CYP2C19 LoF *2 allele and to analyse whether there is an association between presence of the LoF allele and occurrence of in-stent restenosis (ISR) in these patients.

Method

- University Research Ethics Committee approval was granted.
- After obtaining informed written consent, 5mL of peripheral blood were collected from 82 patients undergoing PCI at the cardiac catheterisation suite (time of recruitment, t=0) into a purple-top EDTA tube. Patients were recruited by non-probability sampling and all patients had a previous history of PCI with stenting.
- Genomic DNA purification was undertaken using the QiAamp DNA Mini Kit with the fully automated QiaCube (Qiagen) and CYP2C19 SNP genotyping for variant allele *2 (rs4244285) was undertaken using a TaqMan® SNP drug metabolism assay (Life Technologies) on the 7500 Real-Time PCR system (Applied Biosystems).
- Patients were divided into two groups: Patients with ISR (Group 1) and without ISR (Group 2) at t=0. Group 1 patients were further divided into two sub-groups: Patients with ISR ≤ 1 year and patients with ISR > 1 year.
- Genotype results were also classified into two groups: Non-carrier of *2 allele (genotype 1) and carrier of at least one *2 allele (genotype 2).
- The chi-square test was used to retrospectively assess whether there is an association (p<0.05) between presence of the LoF *2 allele and ISR.

Setting

Mater Dei Hospital (Cardiac Catheterisation Suite, Cardiology Department and Molecular Diagnostics Unit, Pathology Department)

Results

In-stent restenosis at t=0 (N=82)

Out of the 82 patients with previous stenting, 29 (35.4%) presented with angiography-confirmed ISR at t=0 and were undergoing PCI to the same previously stented vessel. In 13 of these patients, the stent was deployed ≤ 1 year before t=0 (patients still on maintenance dose clopidogrel).

Patient demographics (N=82)

Mean age of the patients was 65 years (range 40-85 years), 65 patients were male and 17 were female, 81 patients were Caucasian and 1 patient was Asian.

Presence of CYP2C19*2 allele and ISR occurrence

A statistically significant higher percentage of *2 allele carriers than non-carriers presented with ISR at t=0 (p<0.05) (Table 1).

Conclusions and implications to practice

The findings indicate a statistically significant association between presence of the CYP2C19 LoF *2 allele and coronary ISR. These patients may benefit from an alternative antiplatelet agent. Clinical pharmacist-led optimisation of antiplatelet therapy directed by CYP2C19 genotyping may limit the occurrence of coronary ISR in patients who carry the CYP2C19 LoF *2 allele.

References


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