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Implications of a sub-optimal response to clopidogrel in vascular surgical patients

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BACKGROUND

Clopidogrel is a pro-drug converted by CYP450 enzymes which inhibits platelet function and is used more frequently in peripheral arterial disease since new NICE publications in 2010 and 2014.

Most guidelines recommend stopping clopidogrel 5-10 days before elective surgery. However, urgent surgery requires a risk-benefit analysis.

It is known ~30% of healthy individuals will not convert enough clopidogrel to its active form and are termed 'sub-optimal responders' defined as <30% platelet inhibition¹.

We noticed through routine testing that the sub-optimal responder rate was higher in vascular patients than healthy individuals.

METHODS

Results were generated from an audit of vascular patients in whom clopidogrel was not stopped prior to their surgery between 13th September 2017 and 9th June 2018 (~8 months) at The Royal Sussex County Hospital, Brighton.

Patients' blood was analysed using platelet mapping on the TEG 6s Hemostasis Analyser from Haemonetics to determine % platelet inhibition.

RESULTS

14 out of 20 (70%) vascular surgical patients tested showed a sub-optimal response to clopidogrel (Figure 2). Days since last dose of clopidogrel: mean 1.45 days, median 1 day. None of these patients had their procedures postponed.

10 out of 14 sub-optimal responders (71%) had their procedure performed using a neuraxial anaesthetic technique. None of these patients had any bleeding related complications.

Of the 6 patients who did have platelet inhibition due to clopidogrel, one was cancelled, one received pre-operative platelets followed by a CSE, 3 had a general anaesthetic and one had a peripheral nerve block instead of a neuraxial block.



Figure 1: TEG 6s haemostasis analyser showing minimal platelet inhibition due to ADP receptor blockade².



Figure 2: Example of a platelet mapping analysis on a TEG 6s haemostasis analyser².

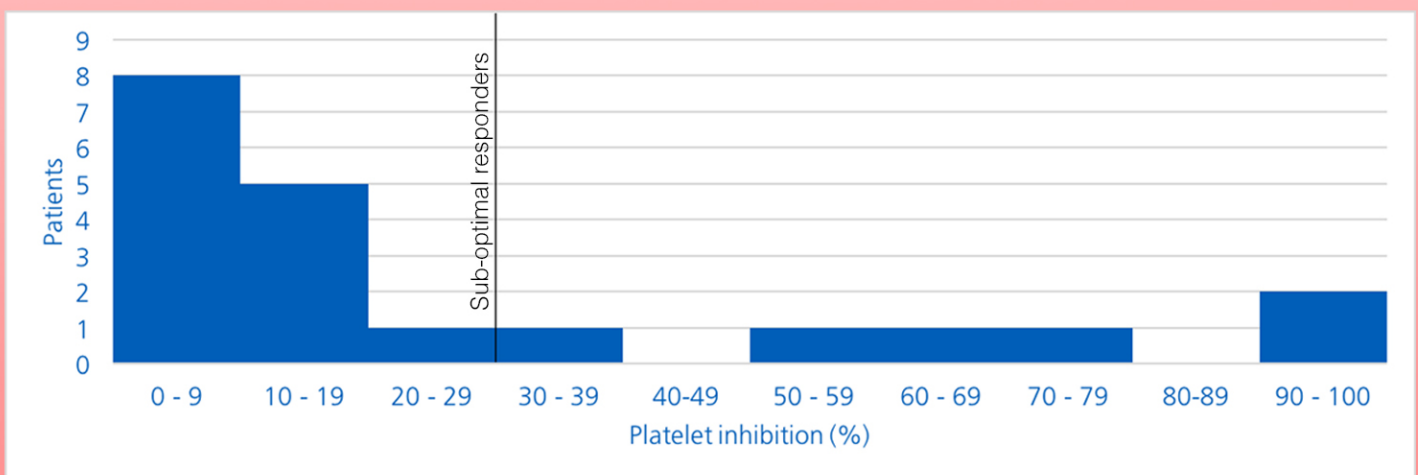


Figure 3: Histogram showing distribution of platelet inhibition from platelet mapping analysis in vascular surgical patients taking clopidogrel.

KEY MESSAGE

We found that vascular patients requiring surgery who are taking clopidogrel have a higher sub-optimal response rate than would be expected based on published data.

Unnecessary general anaesthesia could be avoided by platelet mapping vascular patients who have not omitted clopidogrel prior to urgent surgery.

Although this is a small study, these results raise questions about the efficacy of clopidogrel in vascular patients.

FUTURE RESEARCH

Based on these results, we are planning a cross-sectional study to investigate sub-optimal response to clopidogrel amongst patients with peripheral arterial disease.

We will sample patients with peripheral arterial disease taking clopidogrel who attend a claudication clinic. This study is planned to start in 2019.

Further work is required to inform individually tailored antiplatelet therapy.

1. Matetzky S, Shenkman B, Guetta V. Clopidogrel resistance is associated with increased risk of recurrent atherothrombotic events in patients with acute myocardial infarction. *Circulation*. 2004;109:3171-3175. [PubMed]

2. Gindrey C. TEG 6s presentation. Presentation presented at; 2018; Centre Hospitalier Universitaire de La Réunion.