Short bowel syndrome and clopidogrel non-responsiveness: a new indication for platelet aggregometry?

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DESCRIPTION

A 74-year-old woman presented with unstable angina. Coronary angiography demonstrated severe single-vessel coronary disease and a 3×12 mm bare metal stent placed in the right coronary artery. She had a history of short bowel syndrome following emergency resection for ischaemic bowel just 2 years prior to receiving a long-term total parenteral nutrition (TPN). In view of clinical uncertainty surrounding effects of short bowel syndrome and TPN on clopidogrel responsiveness,¹ platelet function testing was conducted.

Aspirin responsiveness was assessed by light transmission aggregometry (LTA; figure 1A–C) and whole blood impedance aggregometry (WBA) using the multiplate (figure 2A,B). Results by both approaches confirmed adequate aspirin

responsiveness. Clopidogrel responsiveness was only partial when assessed by LTA (figure 1) and absent when assessed by WBA (figure 2). When ticagrelor was used in place of clopidogrel, 90% inhibition of platelet aggregation was achieved by LTA. This was confirmed using the Verify Now P2Y12 test. Dual antiplatelet therapy with aspirin and clopidogrel showed a 4% inhibition of platelet aggregation compared with 69% with aspirin and ticagrelor. Medications were taken orally (not crushed).

Incidence of the rare but catastrophic complication of stent thrombosis² is substantially reduced by potent platelet inhibition with dual antiplatelet therapy, most commonly with aspirin and clopidogrel. Inhibition of platelet aggregation by clopidogrel shows considerable variation between patients.

Figure 1 Light transmission aggregation. Measurements are in percentage light transmission. Arachidonic acid (AA)—response to 1 mM AA (A, C and E). ADP—response to 20 μ M ADP (B, D and F). Control traces (A) aspirin and (B) clopidogrel. Patient's good response to aspirin (C, 10%) and partial response to clopidogrel (D, 50%). After switching to ticagrelor/aspirin and retesting 1 week later, good responses to aspirin (E, 3%) and ticagrelor were observed (F, 10%).

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Figure 2 Whole blood impedance aggregometry (WBA). Measurements are in arbitrary aggregation units against time and reported as the area under the aggregation curve (AUC). ASPI test uses arachidonic acid. ADPI test uses ADP. Control traces (A) and (B) showing no platelet inhibition. Patient's good response to aspirin (C) in ASPI test and no response to clopidogrel in ADPI test (D).

Clopidogrel resistance may be genetic,³ for example, cytochrome P450 2C19 polymorphisms accounting for about 4.6% of the variability in responsiveness, or acquired, for example, in patients with diabetes or chronic renal failure.

Learning points

- ▶ Clopidogrel hyporesponders are recognised in the population and have an increased risk of adverse events including stent thrombosis following percutaneous coronary intervention.
- ▶ Newer antiplatelet agents do not rely on enzymatic conversion of a prodrug (such as ticagrelor) and are effective alternatives to clopidogrel in hyporesponsive patients.
- ▶ Malabsorption states requiring parenteral nutrition may contribute to reduced clopidogrel responsiveness. Platelet aggregometry or use of ticagrelor may be considered in this population.

Contributors GH and DA wrote the manuscript and prepared the figures. GH looked after the patient and had the idea of writing the case report. PH conducted the platelet function tests and provided interpretation and expertise from a haematological perspective. DA looked after the patient and helped with the literature search and knowledge for the cardiovascular aspect of the paper. RC was in charge of patient's care and oversaw the whole case report and provided cardiovascular expertise.

Competing interests

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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