Impact of aspirin resistance on antiplatelet therapy management after coronary artery surgery

Mate Petricevic*, Bojan Biocina, Sanja Konosic and Visnja Ivancan

* Department of Cardiac Surgery, University Hospital Center Zagreb, Zagreb, Croatia
b Department of Anaesthesiology, University Hospital Center Zagreb, Zagreb, Croatia

c Corresponding author. Department of Cardiac Surgery, School of Medicine, University of Zagreb, Kispaticeva 12, 10000 Zagreb, Croatia. Tel: +385-1-2367529; fax: +385-1-2367531; e-mail: petricevic.mate@gmail.com (M. Petricevic).

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We read with great interest the recently published study by Wang et al. [1]. In a group of patients with off-pump coronary artery surgery (CAS), aspirin resistance (AR) was observed in 29.7% of patients on the first postoperative day [1]. To patients who developed AR, 75 mg of clopidogrel/day was prescribed in addition to 100 mg of aspirin/day [1]. By postoperative days 4 and 10, postoperative AR incidence decreased to 16.2 and 4.5%, respectively [1]. Dual antiplatelet therapy (APT) provides incremental platelet inhibition compared with either agent alone and more effective suppression of adverse ischaemic events [2]. This finding is confirmed by Awidi and coworkers who found that the combination of aspirin and clopidogrel had greater inhibitory effects on platelet aggregation than either agent alone in patients with coronary artery disease [3]. In our opinion, the addition of clopidogrel in the group of patients with AR inevitably affected both the observed clinical outcomes and the decrease in AR proportion. Following CAS, extensive evidence supports the use of aspirin, in doses of 100–325 mg/day, to be administered postoperatively and continued indefinitely [4]. A daily 100 mg dose of aspirin administered postoperatively in a study by Wang et al. [1], allows the possibility of different APT management strategies. For example, a stepwise increase in the aspirin dose with a subsequent platelet function assessment could probably bring a further decrease in the AR proportion and therefore, eliminate the need for dual APT. However, it still remains unclear, whether an aspirin dose increase would be superior to dual APT, in the context of a clinical outcome. Of note, a meta-analysis by Snoep et al. showed an overall prevalence of 21% of laboratory-defined clopidogrel low response [5]. We believe that these two different APT approaches should be evaluated in a large cohort randomized trial with an outcome evaluation of both ischaemic and bleeding events. The authors hypothesized that the Chinese population is more sensitive to aspirin therapy and presented no AR at a 6-month follow-up. It would be interesting if the authors analyzed the bleeding event occurrence at the 6-month follow-up in the group of patients on dual APT. APT management in cases of AR should be individually tailored, with aspirin dosage stepwise increased (up to 325 mg/day), and clopidogrel administration in cases of AR to high aspirin doses. Temporary AR requires temporary APT adjustment. The duration and intensity of the APT adjustment should be tailored according to drug specific platelet function tests in order to minimize both ischaemic and bleeding events. In conclusion, it is difficult to investigate by what amount the laboratory AR corresponds to the clinical AR. Prospective studies, with a large study sample necessitated by the infrequency of adverse ischaemic events, must determine the optimal threshold for AR, taking into consideration both the laboratory and clinical outcome findings.
REFERENCES


LETTER TO THE EDITOR RESPONSE

Reply to Petricevic et al.

Zanxin Wang and Minxin Wei*

Department of Cardiovascular Surgery, Tianjin Medical University General Hospital, Tianjin, China

* Corresponding author. Department of Cardiovascular Surgery, Tianjin Medical University General Hospital, 154# Anshan Road, Heping District, Tianjin 300052, China. Tel: +86-22-60363501; e-mail: minxinw@126.com (M. Wei).

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We thank Petricevic et al. for their comments [1] on our manuscript [2]. We also appreciate the editor giving us the opportunity to reply. For patients undergoing coronary artery bypass grafting surgery (CABG), current guidelines recommend aspirin monotherapy in doses of 75–162 mg per day starting within 48 h of surgery [3]. This has been based on the clopidogrel in unstable angina to prevent recurrent ischemic events (CURE) trial, which indicated that dual antiplatelet therapy was beneficial in reducing adverse outcomes in patients presented with acute coronary syndrome and those who ultimately underwent CABG. However, that benefit was totally preoperative while patients were awaiting surgery, and no benefit for clopidogrel was demonstrated for CURE patients after coronary surgery [4]. So in our study, only patients who developed aspirin resistance were prescribed clopidogrel. And laboratory assays of aspirin resistance (0.5 mg/dl arachidonic acid-induced platelet aggregation) were used very commonly. It is effective to evaluate aspirin resistance and the results will not be influenced by clopidogrel, because the pathway of clopidogrel (adenosine diphosphate (ADP)-induced platelet aggregation) is different.

In our study, only one dose of aspirin (100 mg/day) was used. This is one of the limitations of our article which has been mentioned in the discussion. The generation of new platelets after surgery make the common dosage of aspirin not suitable for antiplatelet therapy. That is a plausible mechanism for aspirin resistance. There are also other risk factors of aspirin resistance such as female gender, smoking and genetic background. They will be evaluated in our further research including ischaemic and bleeding events.

In summary, we thank Petricevic et al. for their valuable recommendation which might be of great value in further studies. We concur that it is necessary to make sure of the risk factors of aspirin resistance and reach the aim of individual antiplatelet therapy.

REFERENCES