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## Research Letter

# Duration of antiplatelet therapy cessation before coronary artery bypass surgery: Relation with platelet count



## A B S T R A C T

## Keywords:

Platelets  
Antiplatelet therapy  
Coronary artery bypass grafting  
Aspirin  
Clopidogrel

As of now, no study or data is available to determine the period of discontinuation of antiplatelet therapy and the timing of elective surgery in clopidogrel treated patients. The 2011 ACCF/AHA Guidelines have a Class-I recommendation for withdrawing clopidogrel for 5 days before elective coronary artery bypass grafting. However, 5 days period may not suit all patients as platelet count varies from  $150 \times 10^9/L$  to  $450 \times 10^9/L$ . Based on our retrospective data analysis, we have proposed a hypothesis to determine no of days of discontinuation of antiplatelet therapy while taking in consideration the basal count and life-span of platelets.

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Antiplatelet therapy with aspirin and/or clopidogrel is common practice in the management of vaso-occlusive events (e.g., stroke, acute myocardial infarction, coronary artery disease, unstable angina, percutaneous coronary intervention, primary and secondary cardiovascular disease prevention).<sup>1,2</sup> Aspirin irreversibly inactivates a key platelet enzyme cyclooxygenase (COX-1) thus inhibiting thromboxone (TX-A<sub>2</sub>) generation. Clopidogrel, a prodrug has no direct antiplatelet activity of its own, but its active metabolite (R130964) binds to the platelet P2Y<sub>12</sub> receptor and irreversibly inhibits adenosine diphosphate (ADP)-induced platelet aggregation.<sup>3</sup> This inhibition persists for the entire life span of the platelet, that varies from 8 to 10 days.<sup>4</sup> This effect can only be reversed by formation of new platelets.<sup>5</sup>

Continuation of antiplatelet drugs is associated with increased risk of intraoperative and postoperative bleeding and transfusion requirements during the perioperative period.<sup>2,6</sup> On the other hand, stopping antiplatelet therapy for prolonged period may put such patients at increased risk of ischemic insult. Most tests used to demonstrate inhibitory effects of antiplatelet drugs are expensive, too time consuming for routine practice and are not widely available, especially in developing countries. As of now, no study or data is available to determine the period of discontinuation of antiplatelet therapy and the timing of surgery in clopidogrel treated patients. The 2011 ACCF/AHA Guidelines have a Class-I recommendation for withdrawing clopidogrel for 5 days before elective coronary artery bypass grafting.<sup>7</sup>

Though there are no definite evidence-based guidelines advocating a minimum number of platelets for major elective surgeries, most prefer an uninhibited and functional platelet count of more than  $120 \times 10^9/L$ . Assuming life span of a platelet 8–10 days, about one tenth of platelets are newly formed and a same number destroyed daily. Hence, following cessation of antiplatelet therapy in a patient whose basal platelet count is  $150 \times 10^9/L$  it will take about 10 days to produce new platelet count of  $150 \times 10^9/L$ . Therefore, a discontinuation period of 5 days may produce fresh and fully functional platelets of  $75 \times 10^9/L$  only, which is a grossly insufficient number for effective control of bleeding. On the other hand, with the same rate of platelet formation in a patient whose platelet count is more than  $400 \times 10^9/L$ , it may take only four days or less to have more than  $150 \times 10^9/L$  newly formed platelets, a sufficient number to control bleeding.

This hypothesis is based on our retrospective patient data analysis. During the period from January 2009 to December 2013, fifty-two patients aged between 38 and 76 years, who were on Aspirin 75 mg OD and clopidogrel 75 mg OD, had undergone CABG following cessation of antiplatelet therapy for five to seven days. Basal platelet count varied from  $137 \times 10^9/L$  to  $355 \times 10^9/L$  and hematocrit from 35% to 42%. None of the patients had known coagulopathy, liver or kidney dysfunction. Postoperatively, 44 patients had an uneventful course however, 8 patients had blood loss ranging from 600 ml to 1100 ml in the first six hours of which five required redo surgery for control of bleeding. Six out of those eight had

preoperative platelet count between  $135 \times 10^9/L$  and  $155 \times 10^9/L$ , and two had  $180 \times 10^9/L$  and  $205 \times 10^9/L$ , respectively and required more than ten units of platelet transfusion, perioperatively. Other 44 patients, who did not have significant bleeding perioperatively, were found to have preoperative platelet count of more than  $260 \times 10^9/L$  and required no or less than two units of platelet transfusion.

Thus, it seems logical not to generalize the discontinuation period of antiplatelet drugs for all patients irrespective of their preoperative basal platelet count.

Literature search failed to find any study that shows a direct relation of discontinuation period of antiplatelet therapy in days before major surgery with the platelet count of the patient. We feel that while advising a discontinuation period of antiplatelet therapy before major surgery, apart from other hematological parameters 'Basal platelet count divided by Ten' multiplied by number of days in order to get newly formed fully functional platelets of more than  $120 \times 10^9/L$ , at least. However, a prospective study is warranted to prove this hypothesis.

#### REFERENCES

- Hirsh J, Guyatt G, Albers GW, Harrington R, Schunemann HJ. Executive summary: American College of Chest Physicians evidence-based Clinical practice guidelines (8th Edition). *Chest*. 2008;133:71S–109S.
- Hall R, Mazer D. Antiplatelet drugs: a review of their pharmacology and management in the perioperative period. *Anesth Analg*. 2011;112:292–318.
- Farid NA, Payne CD, Small DS, et al. Cytochrome P450 3A inhibition by ketoconazole affects prasugrel and clopidogrel pharmacokinetics and pharmacodynamics differently. *Clin Pharmacol Ther*. 2007;81:735–741.
- Roth GJ, Stanford N, Majerus PW. Acetylation of prostaglandin synthase by aspirin. *Proc Natl Acad Sci U S A*. 1975;72:3073–3076.
- Burch JW, Stanford N, Majerus PW. Inhibition of platelet prostaglandin synthetase by oral aspirin. *J Clin Invest*. 1978;61:314–319.
- Dunning J, Versteegh M, Fabbri A, et al, EACTS Audit and Guidelines Committee. Guideline on antiplatelet and anticoagulation management in cardiac surgery. *Eur J Cardiothorac Surg*. 2008;34:73–92.
- Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update of the Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction (updating the 2007 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Am J Coll Cardiol*. 2011;57:1920–1959.

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Available online 3 July 2015

0019-4832/\$ – see front matter

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<http://dx.doi.org/10.1016/j.ihj.2015.05.013>