Editorial

Is there a safe time to stop clopidogrel in patients on dual antiplatelet therapy after a percutaneous coronary intervention and placement of drug-eluting stents?

Nureddin Almaddah, Rami N. Khouzam

Department of Internal Medicine, Division of Cardiovascular Diseases, University of Tennessee Health Science Center, Memphis, TN, USA

Correspondence to: Rami N. Khouzam. Department of Internal Medicine, Division of Cardiovascular Diseases, University of Tennessee Health Science Center, Memphis, TN, USA. Email: rkhouzam@uthsc.edu.

Provenance: This is an invited Editorial commissioned by the Section Editor Feng Zhang (Department of Cardiology, Zhongshan Hospital of Fudan University, Shanghai, China).

Comment on: Piccolo R, Feres F, Abizaid A, *et al.* Risk of Early Adverse Events After Clopidogrel Discontinuation in Patients Undergoing Short-Term Dual Antiplatelet Therapy: An Individual Participant Data Analysis. JACC Cardiovasc Interv 2017;10:1621-30.

Submitted Oct 02, 2017. Accepted for publication Nov 06, 2017.
doi: 10.21037/jtd.2017.11.69
View this article at: http://dx.doi.org/10.21037/jtd.2017.11.69

No clear evidence determines the most effective duration for dual antiplatelet therapy (DAPT) after drug-eluting stents (DES). Although DES reduces the rate of restenosis compared with bare-metal stents (BMS), it is of concern that they may be associated with a risk of stent thrombosis beyond 1 year post treatment. Many randomized clinical trials demonstrated the effectiveness of DAPT in preventing stent thrombosis; a serious complication of PCI. Additionally, it is believed that DAPT prevents adverse occurrences consequent to plaque rupture at a location other than the stented one. Such are the results of a study that compared medical treatment of acute coronary syndrome with Aspirin versus DAPT with clear reduction in the rate of myocardial infarction (MI) in patients who received DAPT (1).

After stent placement, which is considered a foreign body, the blood tends to thrombose. Such risk decreases soon after the metal part of the stent is endothelialized. Studies such as the Stent Anticoagulation Restenosis Study (STARS) trial showed that patients who received DAPT have a lower rate of stent thrombosis compared to those who received aspirin alone (2). The DAPT study is the largest of the randomized trials that compared a longer duration of 30 months versus a shorter 12-month duration of DAPT post DES placement. Results showed that with longer duration of DAPT, both cardiovascular and cerebrovascular events decreased, however, the rate of death from a non-cardiac causes increased (3). Additionally, the largest meta-analysis of randomized trials was conducted in 2016 and included ten sub- trials with a total of 33,051 patients. It compared 3–6 months duration versus 12 months, and it concluded that there is no difference of all-cause of death or MI, or stent thrombosis. Also, comparing 18–48 to 12 months durations showed no difference in the incidence of all cause of death, however a decrease in MI and in stent thrombosis was noted (4). Furthermore, another large study: PEGASUS-TIMI 54 trial that assigned 21,162 patients with MI 1 to 3 years earlier to placebo versus Ticagrelor (90 and 60 mg bid) showed a lower incidence of MI, stroke, and cardiovascular death in the Ticagrelor group (5).

Fear of a 'rebound' of prothrombotic platelet activity upon stopping the drug has been investigated as a possible cause of acute ischemic event in the short time after discontinuing P2Y12 inhibitors. The basic idea behind the rebound phenomenon is the production of hyper-reactive platelets following the cessation of Clopidogrel. A systematic review by Gaglia and Waksman, found earlier studies to be flawed and more recent detailed analyses elicited doubt on a clinical rebound particular to Clopidogrel. This leads to the belief that the increase in acute coronary and other vascular events after stopping

DAPT is due to premature discontinuation or disruption of treatment while the thrombotic risk is still high (6).

The strengths of this meta-analysis are rooted in the fact of comparing data from six randomized clinical trials totaling 11,473 patients. However, most of the selected patients presented with stable ischemic heart disease at the time of PCI with only less than 15% of them presenting with acute coronary syndrome. A higher risk of MI with 3 *vs.* 12 months DAPT duration was noted among patients with acute coronary syndrome. The findings of Piccolo *et al.* have major clinical implications that show no indication for routinely targeting 12 months of DAPT for patients who had DES placed in stable ischemic heart disease but not in the setting of acute coronary syndrome.

Current recommendations for patients with ACS treated with DAPT after BMS or DES implantation call for P2Y12 inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) to be given for a minimum of 12 months (Class I, Level B-R). If DES is placed in a stable ischemic heart disease, the recommendation for DAPT calls for a minimum of 6 months (Class I). After the 6 months duration, if no high risk or significant bleeding is noted, DAPT could be continued for more than 6 months (Class IIb) (7).

The authors' personal approach and practice is to evaluate each patient individually. After 6 and 12 months post DES placement, and for patients who have not had clinically significant bleeding and are at low risk for bleeding, it is reasonable to continue DAPT, while keeping a close eye and frequently evaluating each patient at follow up visits (8). The authors also find the HASBLED score to be a very helpful tool to assess for bleeding risk.

Guidelines are supposed to help physicians practice good evidence-based medicine, nevertheless, the art of sound clinical judgement and common clinical sense should not go obsolete.

Acknowledgements

None.

Cite this article as: Almaddah N, Khouzam RN. Is there a safe time to stop clopidogrel in patients on dual antiplatelet therapy after a percutaneous coronary intervention and placement of drug-eluting stents? J Thorac Dis 2017;9(12):4806-4807. doi: 10.21037/jtd.2017.11.69

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345:494-502.
2. Leon MB, Baim DS, Popma JJ, et al. A clinical trial comparing three antithrombotic-drug regimens after coronary-artery stenting. Stent Anticoagulation Restenosis Study Investigators. N Engl J Med 1998;339:1665-71.
3. Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014;371:2155-66.
4. Bittl JA, Baber U, Bradley SM, et al. Duration of Dual Antiplatelet Therapy: A Systematic Review for the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2016;68:1116-39.
5. Bonaca MP, Bhatt DL, Cohen M, et al. Long-term use of ticagrelor in patients with prior myocardia infarction. N Engl J Med 2015;372:1791-800.
6. Ford I. Coming safely to a stop: a review of platelet activity after cessation of antiplatelet drugs. Ther Adv Drug Saf 2015;6:141-50.
7. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2016;68:1082-115.
8. Sibbing D, Massberg S. Dual antiplatelet treatment after stenting: is longer better? Lancet 2014;384:1553-5.

