





Impaired response to aspirin and clopidogrel: how do we treat?

"..newer antiplatelet agents such as cangelor and prasugrel ... may be the solution for patients with impaired response to ASA and clopidogrel. However, we should be cautious to make such a recommendation as data with newer antiplatelet agents are limited and bleeding risks are high."

The two most important antiplatelet therapies used in the management of cardiovascular disease are acetylsalisylic acid (ASA) and clopidogrel. The response to ASA and clopidogrel in terms of antiplatelet effects is not 100%. An impaired antiplatelet response is noted both in laboratory studies and patient outcomes [1]. Impaired responses to clopidogrel and ASA are due to several factors: first, inadequate dosing; second, noncompliance by patients; and third, drug-drug interactions and our genetic polymophisms [2-4]. Such impaired responses have manifested as acute coronary syndrome (ACS) or stent thrombosis in patients with cardiovascular disease [5]. Patients with ACS who present with angina despite being on ASA are considered to be high risk.

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The incidence of impaired response to ASA and clopidogrel is astonishingly high. The impaired response to ASA is 0-65% and for clopidogrel is 4-58% [6]. There is no direct correlation between the laboratory findings of impaired response to clinical significance. However, an association between the laboratory finding and clinical adverse events has been well described [7].

The study carried out by Bhatt et al. eloquently demonstrates the correlation of the impaired incidence in the study to the published literature [8]. The physicians appropriately increased the dose of ASA and clopidogrel in patients with impaired response as recommended by guidelines [9]. The limitations of the study are that it was a retrospective analysis and lacks a correlation between laboratory findings and clinical adverse events. An easy rapid clinical test such as urine or blood analysis to demonstrate the impaired response would be useful. Such a test could be administered to all patients with ACS and patients undergoing percutaneous angioplasty and interventions. Patients with impaired response can then be pre-emptively treated with higher doses of ASA and clopidogrel. The authors further recommend that newer antiplatelet agents such as cangelor and prasugrel, owing to their higher effectiveness, may be the solution for patients with impaired response to ASA and clopidogrel. However, we should be cautious to make such a recommendation as data with newer antiplatelet agents are limited and bleeding risks are high [10].

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Bibliography

- Wang TH, Bhatt DL, Topol EJ: Aspirin and clopidogrel resistance: an emerging clinical entity. Eur. Heart J. 27, 647-654 (2006).
- Eikelboom JW, Hankey GJ: Aspirin resistance: a new independent predictor of vascular events? J. Am. Coll. Cardiol. 41, 966-968 (2003).
- Hankey GJ, Eikelboom JW: Aspirin resistance. BMJ 328, 477-479 (2004).
- Cambria-Kiely JA, Gandhi PJ: Aspirin resistance and genetic polymorphisms. J. Thromb. Thrombolysis 14, 51-58 (2002).

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- Gum PA, Kottke-Marchant K, Welsh PA, White J, Topol EJ: A prospective, blinded determination of the natural history of aspirin resistance among stable patients with cardiovascular disease. J. Am. Coll. Cardiol. 41, 961-965 (2003).
- Tseeng S, Arora R: Aspirin resistance: biological and clinical implications. J. Cardiovasc. Pharmacol. Ther. 13, 5-12

30

- Eikelboom JW, Hirsh J, Weitz JI, Johnston M, Yi Q, Yusuf S: Aspirin-resistant thromboxane biosynthesis and the risk of myocardial infarction, stroke, or cardiovascular death in patients at high risk for cardiovascular events. Circulation 105, 1650-1655 (2002).
- Depta JP, Bhatt DL, Kottke-Marchant K et al.: Management of patients with aspirin and clopidogrel impaired response. Intervent. Cardiol. 1(1), 31-40 (2009).
- Smith SC, Feldman TE, Hirshfeld JW et al.: ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). Circulation 113, 156-175 (2006).
- Wiviott SD, Braunwald E, McCabe CH et al.: Prasugrel versus clopidogrel in patients with acute coronary syndromes. N. Engl. J. Med. 357, 2001–2015 (2007).

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