

Omeprazole might decrease the antiplatelet effect of Clopidogrel

Andrei Dumitru MARGULESCU, MD

Department of Cardiology, University and Emergency Hospital, Bucharest, Romania

Clopidogrel in association with aspirin is the standard treatment for patients with acute coronary syndromes or who are receiving coronary stents. Omeprazole is frequently prescribed on top of these medications in an attempt to decrease the incidence of gastrointestinal bleeding. However, the concern that the antiplatelet activity of clopidogrel might be reduced by omeprazole (and other protein pump inhibitors, PPIs) has not been verified. This concern has been put forward by the dependent activation of clopidogrel on the cytochrome P-450 (CYP) isoforms; the site of activation is competitive with other drugs such as statins and PPIs.

The Omeprazole Clopidogrel Aspirin (OCLA) study included 140 patients undergoing elective implantation of coronary stents that were randomized in a 1:1 fashion to receive omeprazole 20 mg/day or placebo for 7 days. All patients received standard antiplatelet treatment with aspirin 75 mg/day and clopidogrel (300 mg loading dose, followed by 75 mg maintenance dose). After excluding 16 patients for various reasons, the analysed groups contained 64 patients receiving omeprazole and 60 patients receiving placebo.

The primary objective was the change of the mean platelet reactivity index (PRI). The PRI index was measured by the vasodilator stimulated phosphoprotein phosphorylation (VASP) method. The PRI is inversely correlated with the antiplatelet activity (the higher the PRI, the lower the antiplatelet activity).

At inclusion, the mean PRI of the two groups was similar, at around 84%. At day 7, the mean PRI decreased by 32.6% in the omeprazole group compared with 43.3% in the placebo group ($p < 0.0001$). This corresponded to a mean PRI of 51.4% vs. 39.8%, respectively ($p < 0.0001$). Thus, after 7 days, the antiplatelet effect of aspirin plus clopidogrel was lower in the group receiving omeprazole compared with the group receiving placebo.

In conclusion, this study suggests that omeprazole has a negative effect on the antiplatelet activity of clopidogrel, as measured by the surrogate marker of PRI. The clinical impact of this finding has to be studied in large prospective trials. However, since the decrease in the platelet activity of clopidogrel in association with the use of PPIs may lead to an increased risk of stent thrombosis, the unwarranted use of omeprazole and other PPIs in this group of patients should be discouraged.

Comment on the paper:

Gilard M, Arnaud B, Cornily JC, et al. – Influence of omeprazole on the antiplatelet action of clopidogrel associated with aspirin: the randomized, double-blind OCLA (Omeprazole CLopidogrel Aspirin) study. *J Am Coll Cardiol* 2008;51:256-60