Personalized antiplatelet treatment improves outcome after PCI

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Personalized antiplatelet treatment leads to better outcomes than standard antiplatelet treatment in patients undergoing coronary stent implantation, according to results from the MADONNA study presented at ESC Congress 2012.

The findings were presented by Dr Jolanta Siller-Matula from Medical University of Vienna.

Standard antiplatelet treatment in patients undergoing percutaneous coronary intervention (PCI) consists of a dual antiplatelet therapy with aspirin and an ADP receptor inhibitor such as clopidogrel.

But measurements of platelet aggregation in clopidogrel treated patients indicate that one patient in four is a non-responder to the drug. Such non-responsiveness is attributed to clopidogrel's extensive hepatic metabolism, polymorphisms of metabolising enzymes and drug-drug interactions, with additional contributions coming from clinical variables such as diabetes, body mass index, acute coronary syndrome, ejection fraction and renal failure. Multiple studies have demonstrated a clear association between non-responsiveness to clopidogrel and adverse clinical events. The strongest relationship was found between poor clopidogrel response and short term events, particularly stent thrombosis.

Personalized antiplatelet treatment involves choosing a therapy based on the results of platelet function testing, a measurement which shows how effective an antiplatelet drug such as clopidogrel is at inhibiting platelet

aggregation. Non-responders to the drug can be given a higher dose of clopidogrel or an alternate antiplatelet therapy such as the more potent platelet inhibitors prasugrel or ticagrelor. Personalized antiplatelet treatment only in clopidogrel non-responders would be a therapeutic strategy reaching two goals: increase of clinical efficacy only in patients who are at increased risk for ischemic events without exposing patients with a proper clopidogrel response to bleedings with use of very potent platelet antagonists.

In the MADONNA study (Multiple electrode Aggregometry in patients receiving Dual antiplatelet therapy tO guide treatmeNt with Novel platelet Antagonists), Austrian investigators led by Dr Jolanta Siller-Matula from the Medical University of Vienna and Professor Günter Christ from Kaiser Franz Josef Hospital in Vienna, investigated whether individualized treatment with platelet inhibitors according to the results of whole blood aggregometry improves clinical outcomes in patients undergoing percutaneous coronary intervention.

A total of 798 patients underwent platelet testing with whole blood aggregometry using the multiple electrode aggregometry (MEA) technique, which allowed patients to be classified as clopidogrel responders or non-responders. Patients were then allocated to the guided group or the non-guided group. In the guided group (n=403) clopidogrel non-responders (26%) received up to four loading doses of clopidogrel or after prasugrel became available, the more potent platelet inhibitor prasugrel. In the non-guided group (n=395) clopidogrel non-responders (25%) were further treated with the standard treatment consisting of clopidogrel and aspirin.

Results showed that patients in the non-guided group were at a 7.9-fold higher risk to develop stent thrombosis compared to the patients in the guided group (1.9% versus 0.2%; p=0.027). Furthermore acute coronary syndrome occurred in 0% of patients in the guided group versus 2.5% in

the non-guided group (p=0.001). There were no differences between the two groups in the rates of cardiac death or major bleeding.

"Introducing clopidogrel testing into clinical practice might be feasible: it involves a blood sample and takes ten minutes to get a result," said Dr Siller-Matula, first author of the study. "Providing individualized treatment based on the results of MEA instead of using novel antiplatelet drugs in each patient would save costs of drug therapy of about €410 per patient each year. As individualized antiplatelet therapy seems to be cost-effective, it might be of interest to health authorities."

"Physicians would never adjust doses of antihypertensive drugs without knowing blood pressures; statins, without knowing cholesterol levels; or antidiabetic drugs without knowing the HbA1C levels," she added. "So why are we still treating our patients with platelet inhibitors without being aware of levels of platelet inhibition?"

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