Tailored Clopidogrel Dosing Cut Major Events

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CHICAGO — Monitoring platelet response using a novel measuring tool allowed for tailored clopidogrel dosing and was associated with reduced major adverse cardiovascular events after percutaneous coronary intervention in a small, prospective study of 162 patients.

After 30 days of follow-up, none of the 78 patients whose therapy was adjusted using the vasodilator-stimulated phosphoprotein (VASP) index assay experienced a major adverse cardiovascular event (MACE), compared with 8 (10%) of the 84 patients in the standard-dosing group, lead investigator Dr. Laurent Bonello reported at the Innovation and Intervention (i2) Summit. The between-group difference in MACE, defined as cardiovascular death, acute or subacute stent thrombosis, or revascularization, was significant.

Overall MACE rates were driven by acute and subacute thrombosis, which was reported in 4 (5%) of the controls.

Thrombolysis in myocardial infarction (TIMI) major bleeding was reported in one patient in each group, and TIMI minor bleeding occurred in three patients in the control group and two in the VASP-guided group.

The VASP index is an assay that measures the degree of phosphorylation of the vasodilator phosphoprotein, which is directly dependent on the $P2Y_{12}$ and adenosine diphosphate (ADP) receptors. These receptors are targets for clopidogrel, making the assay highly specific to the response to clopidogrel, said Dr. Bonello, of the Hôpital Universitaire Nord, Marseilles, France.

Several studies have established a link between low response to clopidogrel and ischemic events, including stent thrombosis, he said at the meeting, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions.

All patients in the study were undergoing elective percutaneous coronary intervention for unstable angina or non–ST-elevation acute coronary syndrome, and were defined as low responders to clopidogrel, based on a platelet reactivity of 50% or more using the VASP index after a standard loading dose of 600 mg clopidogrel and 250 mg aspirin.

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Patients in the control group underwent PCI after the standard clopidogrel dose, whereas patients in the VASP tailored–therapy group could receive three additional 600-mg doses, up to a maximum of 2,400 mg, every 24 hours until platelet activity dropped below 50% before undergoing PCI.

The dose adjustment was effective in 67 (86%) patients. Despite having received 2,400 mg of clopidogrel, 11 (14%) patients remained low responders, he said. The average clopidogrel dose was 1,620 mg in the VASP tailored–therapy group.

Baseline characteristics were similar between the VASP and control groups. In both groups, the mean age was 66 years and the mean body mass index was 27 kg/m^2. Prior MI had occurred in 22 of the VASP patients and 20 of the control patients, a nonsignificant difference.

"Reaching a post-treatment platelet activity below 50% using the VASP index seems optimal to prevent MACE in patients without increasing bleeding," Dr. Bonello concluded.

Discussant Dr. Paul Gurbel, of Sinai Hospital in Baltimore, said the study suffered from some data-collection and analysis issues, but was an initial attempt to move away from the "one-size-fits-all" dosing of $P2Y_{12}$ inhibitors. It also identified a "ceiling effect" of clopidogrel on high platelet reactivity in select patients.

"The final take-home message is that high platelet reactivity is a quantifiable and modifiable cardiovascular risk factor, and we can't ignore it anymore," Dr. Gurbel said.

Dr. Bonello said that the assay is commercially available, but that its use is currently restricted to the research setting.

Dr. Bonello did not disclose any conflict of interest. The study was supported by a grant from the French Federation of Cardiology. ■