Study examines outcomes of high-dose antiplatelet drug after stent placement

March 15 2011

Modifying a patient's dosage of the antiplatelet drug clopidogrel for 6 months depending on the patient's level of platelet reactivity did not result in combined lower rates of nonfatal heart attack, stent thrombosis (clot) and cardiovascular death in patients who had a procedure such as balloon angioplasty and received a drug-releasing coronary stent, according to a study in the March 16 issue of *JAMA*.

Current guidelines recommend treating patients undergoing percutaneous coronary intervention (PCI; procedure such as balloon angioplasty used to open narrowed coronary arteries) and drug-eluting stent implantation with a combination of aspirin and P2Y12 (compound found on the surface of blood platelet cells and an important regulator in blood clotting) antagonist for at least 1 year. But several studies have suggested that patients with high platelet reactivity during treatment with clopidogrel are at an increased risk of cardiovascular events after PCI. A treatment strategy for this issue has not been well defined, according to background information in the article.

Matthew J. Price, M.D., of Scripps Translational Science Institute, La Jolla, Calif., and colleagues conducted the Gauging Responsiveness with A VerifyNow assay—Impact on Thrombosis And Safety (GRAVITAS) trial to determine whether high-dose clopidogrel is superior to standard-dose therapy for the prevention of cardiovascular events after PCI in patients with high on-treatment reactivity. The randomized trial included 2,214 patients with high on-treatment reactivity (measured 12 to 24 hours after PCI) with drug-eluting stents at 83 centers in North America

between July 2008 and April 2010. Patients received high-dose clopidogrel (600-mg initial dose, 150 mg daily thereafter) or standard-dose clopidogrel (75 mg daily) for 6 months. The primary outcome measured was the 6-month incidence of death from cardiovascular causes, nonfatal heart attack, or stent thrombosis. Safety measurements included severe or moderate bleeding.

The researchers found that the rate of death from cardiovascular causes, nonfatal heart attack, or stent thrombosis was not different with high-dose compared with standard-dose clopidogrel in the patients with high on-treatment reactivity (25 (2.3 percent) vs. 25 [2.3 percent]). In an analysis, the event rates in the 2 groups after 30 days were (20 [1.9 percent] vs. 17 [1.6 percent]), respectively.

The reduction in on-treatment reactivity at 30 days and at 6 months after randomization was significantly greater with high-dose than with standard-dose clopidogrel. High-dose clopidogrel was associated with an absolute 22 percent lower rate of high on-treatment reactivity compared with standard-dose clopidogrel at 30 days and 6 months (40 percent vs. 62 percent; and 36 percent vs. 60 percent, respectively).

Severe or moderate bleeding was not increased with the high-dose regimen.

"In conclusion, high-dose clopidogrel for 6 months in patients with high on-treatment platelet reactivity 12 to 24 hours after PCI with drug-eluting stents did not reduce the rate of death from cardiovascular causes, nonfatal myocardial infarction, or stent thrombosis compared with standard-dose clopidogrel. The results of GRAVITAS do not support a uniform treatment strategy of high-dose clopidogrel in patients with high on-treatment reactivity identified by a single platelet function test after PCI. Alternative treatment strategies incorporating platelet function testing merit further investigation," the authors write.

More information: *JAMA*. 2011;305[11]1097-1105.