Early Clopidogrel Can Improve MI Outcome

Benefit seen in patients with ST-segment elevation who undergo percutaneous coronary interventions.

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STOCKHOLM — Clopidogrel pretreatment improves outcome of cardiovacular events in patients with ST-segment elevation myocardial infarction who underwent percutaneous coronary interventions in a study with more than 1,800 patients. 

On the basis of these and previous findings, clopidogrel pretreatment should be considered the standard of care, both for patients with ST-segment elevation myocardial infarction (STEMI) and for all other patients who are undergoing percutaneous coronary intervention (PCI), Marc S. Sabatine, M.D., said at the annual congress of the European Society of Cardiology.

Until now, no patients had received clopidogrel before PCI, Dr. Sabatine said in an interview. Usual care has been to administer a loading dose of clopidogrel when PCI begins. For every 23 patients in the study, pretreatment with clopidogrel prevented one major cardiovascular event. “That is an amazing benefit: from one to three extra doses of clopidogrel,” commented Christopher P. Cannon, M.D., a cardiologist at Brigham and Women’s Hospital in Boston and a co-investigator on the study.

Even if clopidogrel is not given at the initial presentation, it should be started once the decision is made to perform coronary angiography, said Dr. Sabatine, who is also a cardiologist at the hospital.

The study was sponsored by Sanofi-Aventis and Bristol-Myers Squibb, the companies that market clopidogrel (Plavix) and aspirin. Dr. Cannon has received honoraria and research support and have served as advisers to both companies.

Clopidogrel pretreatment was effective both before and after PCI was performed, noted Keith Fox, M.B., professor of cardiology at the University of Edinburgh. “The most convincing evidence of [clopidogrel’s efficacy] is the consistency of the clinical effect across all subgroups examined in the study,” he commented.

The new analysis was a prespecified substudy of the Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY) study. Results from the parent study, which involved nearly 3,500 patients, were reported last March.

Those results showed that patients who had a STEMI and initially received thrombolytic therapy had better outcomes when a clopidogrel regimen (a 300-mg loading dose followed by 75-mg/day) was begun immediately, along with the first dose of aspirin and the thrombolytic agent (N. Engl. J. Med. 2005;352:1179-89).

All patients in the CLARITY study were scheduled to undergo angiography 2-8 days following thrombolytic treatment, and the PCI substudy focused on the more than 1,800 patients (53%) from this group who wound up having PCI after angiography.

Although the study did not randomize patients to PCI, the 931 patients from the clopidogrel group who had PCI were very similar in their baseline measures to the 930 patients from the placebo group who had PCI.

The study protocol recommended that all patients who received a coronary stent after angiography receive a loading dose of 300 mg of clopidogrel at the time of planned revascularization followed by ongoing treatment with 75 mg/day. PCI was done a median of 3 days after the start of thrombolytic treatment—in some cases as quickly as within 6 hours, and in other cases after a delay as long as 8 days.

During this phase, the incidence of MI or stroke was 4% in the clopidogrel-treated patients and 6.2% in the placebo group, a 38% relative reduction that was statistically significant.

After PCI, up to a total of 30 days after initial treatment, the rate of cardiovascular death, MI, or stroke was 3.6% in the clopidogrel group and 6.2% in the placebo group, a 46% reduction that was statistically significant.

Overall, patients who began clopidogrel treatment immediately and then had PCI had a 7.5% incidence of cardiovascular death, MI, or stroke, compared with a 12% rate in those who did not start on clopidogrel until after PCI began. The results were published on the same day that they were reported at the meeting (JAMA 2005;294:1224-32).

Clopidogrel pretreatment was safe. It was associated with a 0.5% rate of major bleeds and a 1.4% rate of minor bleeds, compared with a major bleed rate of 1.1% and a minor bleed rate of 0.8% in the placebo group. Clopidogrel pretreatment was also safe and effective in the one-third of patients who received a glycoprotein IIb/IIIa inhibitor at the time they got their stents.

A major issue left unresolved by the study is whether patients would fare even better with a larger loading dose.

Some physicians order a 600-mg or even a 900-mg loading dose in order to produce a maximum antiplatelet effect more quickly.

Clinicians should consider giving 600 mg of clopidogrel as a loading dose, even though this approach has not been formally tested with thrombolytic therapy, David J. Moliterno, M.D., and Steven R. Steinhubl, M.D., of the University of Kentucky, Lexington, wrote in an editorial that accompanied the published report (JAMA 2005;294:1271-3).

“I think that there is evidence that the 600-mg dose is effective and safe, especially if given less than 6 hours before PCI. If it’s going to be 6 or more hours before PCI is done, then I’d use 300 mg,” Dr. Sabatine told this newspaper.

Thrombolytic Tx in Kidney Patients

Thrombolytic therapy is delayed in patients with kidney disease who develop MI, which is “particularly unfortunate” in this patient population because of their large burden of cardiovascular disease and high CVD mortality, according to Britt B. Newsome, M.D., of the Birmingham (Ala.) Veterans Affairs Medical Center, and associates.

The researchers analyzed data from 109,169 MI patients who were treated at more than 6,000 U.S. acute-care hospitals, and found that “door-to-needle time” in one Minnesota county between 1970 and 2000 was reviewed. The incidence of infection, reported Imad M. Tleyjeh, M.D., M.P.H., a nephrologist at Brigham and Women’s Hospital in Boston, was 1.9% in patients treated at 103 acute-care hospitals across Ontario.

Among patients hospitalized with heart failure, those who are at the highest risk of death are the least likely to be given drugs of proven benefit, according to Douglas S. Lee, M.D., Ph.D., of the University of Toronto, and his associates.

They assessed drug treatment in relation to predicted 1-year mortality risk, using data from a study of 1,418 heart-failure patients treated at 103 acute-care hospitals across Ontario.

The number of prescriptions written at hospital discharge for ACE inhibitors, angiotensin II-receptor blockers, and β-adrenoreceptor antagonists decreased as mortality risk increased, the investigators said (JAMA 2005;294:1240-7).

The mismatch between mortality risk and drug prescriptions persisted even in patients who had no perceived contraindications to the drugs and no life-limiting comorbidities that could confound a risk-benefit assessment. It seems likely that clinicians undertreated these patients because either they didn’t appreciate the benefits of therapy or they mistakenly believed that high-risk patients are more susceptible to the medications’ adverse effects, Dr. Lee and his associates said.

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