Clopidogrel Before PCI Improves Outcomes

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STOCKHOLM — Clopidogrel pretreatment markedly reduced the rate of cardiovascular events in patients with ST-segment elevation MI 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 for all patients undergoing PCI, Marc S. Sabatine, M.D., said at the annual congress of the European Society of Cardiology.

Until now, usual care has been to administer a loading dose of clopidogrel when PCI begins, he said in an interview.

For every 23 patients in the study, pretreatment with clopidogrel prevented one major cardiovascular event. "That is an amazingly big 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 coinvestigator on the study.

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

The study was sponsored by Sanofi-Aventis and Bristol-Myers Squibb, which market clopidogrel (Plavix) worldwide. Dr. Sabatine and Dr. Cannon have received honoraria and research support and have been 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, showed that patients who had a STEMI and initially received thrombolytic therapy had better outcomes when a clopidogrel regimen 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

Equivocal Data on Peripheral Drug-Eluting Stents

LAS VEGAS — Drug-eluting stents have not worked as well in the peripheral vasculature as they have in the coronary arteries, but that doesn't mean that investigations should be abandoned, Gary Ansel, M.D., said at a meeting on vascular interventions sponsored by Medical Media Communications.

So far, clinical trials in which drug-eluting stents were compared with bare stents in the periphery have shown that restenosis in distant vessels is a different process, said Dr. Ansel, a peripheral vascular disease specialist who practices in Columbus, Ohio.

Trials in the renal arteries and the superficial femoral artery have not shown any demonstrable benefit from drug elution, but there has been some indication of benefit. In addition, most of the trials have been small and, therefore, not definitive.

The findings of the Sirolimus-Coated Cordis SMART Nitinol Self-Expanding Stent for the Treatment of Obstructing Superficial Femoral Artery Disease (SIROCCO) trial, for example, suggested that the drug sirolimus might have had some positive benefit for distant vessels, and that a significant benefit might be found with longer follow-up of the patients.

The trials have been complicated by the fact that the bare nitinol stents used for comparison have performed better than was expected at the outset of the trials, Dr. Ansel added.

On the negative side, one study of sirolimus in renal arteries suggested the drug may have an adverse effect on kidney function.

Drugs still considered worth investigating in stent trials include paclitaxel and bisphosphonates.

The way to get better results with stents in the periphery may not be in the use of a different agent, but, rather, in using stents with different drug delivery rates from those in coronary stents, Dr. Ansel said.

—Timothy F. Kirn

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 933 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 stent implantation followed by ongoing treatment with 75 mg/day.

PCI was done a median of 3 days after the start of fibrinolytic treatment—in some cases within 6 hours, and in others after 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 significant 46% reduction. 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 their 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, associated with a 0.5% rate of major bleeds and a 1.4% rate of minor bleeds, compared with 1.1% and 0.8% , respectively, in the placebo group. 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. "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 accompanying 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. ■