Pre-PCI Atorvastatin Reduces Cardiac Events

BY BETSY BATES
Los Angeles Bureau

NEW ORLEANS — Two doses of atorvastatin before percutaneous coronary intervention reduced the 30-day risk of major adverse cardiac events by 88% among patients with acute coronary syndromes in a study presented at the annual meeting of the American College of Cardiology.

A composite primary end point consisting of death, myocardial infarction, or target vessel revascularization occurred in 4 (5%) of 86 patients who received preprocedural atorvastatin, a significant difference from the 14 (17%) of 85 of those assigned to placebo in the randomized, multicenter trial.

A multivariate analysis found an 88% risk reduction among patients pretreated with atorvastatin.

"This is a much greater effect than that observed in other large studies using a high dose of statins in acute coronary syndromes," noted the investigators in an article timed for release during the meeting (J. Am. Coll. Cardiol. 2007;49:1272-8).

"Lipid-independent pleiotropic actions of atorvastatin may explain such effects," Dr. Germano Di Sciascio of the department of cardiovascular sciences at Campus Bio-Medio University in Rome said at the meeting.

Dr. Di Sciascio and associates in the ARMYDA (Atorvastatin for Reduction of Myocardial Damage During Angioplasty) study group previously documented reduced MI during percutaneous coronary intervention (PCI) in stable angina patients pretreated with atorvastatin. They undertook the current study to determine whether patients with acute coronary syndromes would get the same benefits.

Atorvastatin's 'lipid-independent pleiotropic actions' may account for its effects on the heart.

DR. DI SCIASCIO

The trial enrolled 171 patients who had been referred for coronary angiography within 48 hours after presenting with unstable angina or non–ST-segment elevation acute MI.

A multivariate analysis found an 88% risk reduction for cardiac events among patients pretreated with two doses of atorvastatin before PCI.

Eligible subjects were randomly assigned to receive placebo or atorvastatin in an 80-mg loading dose given 12 hours before PCI and a 4-mg dose approximately 2 hours before the procedure. Otherwise, patients were treated according to standard protocols, receiving aspirin, clopidogrel, and intravenous heparin prior to the procedure; some patients also received glycoprotein IIb/IIIa inhibitors.

Procedures were performed at Campus Bio-Medico University of Rome; Vito Fazzi Hospital of Lecce, Italy; or University La Spienza of Rome.

Post procedure, all patients received daily aspirin and clopidogrel throughout the 30-day target period and were prescribed 40 mg/day of atorvastatin regardless of whether they received the drug or placebo before PCI.

Procedural success, defined as a reduction of stenosis to less than 30% of residual narrowing, was achieved in all patients, and no patient died in the ensuing 30 days.

The highly significant difference in incidence of major adverse cardiac events at 1 month was largely driven by postprocedural MI, which occurred in 4 (5%) of 86 patients receiving pre-PCI atorvastatin, compared with 13 (15%) of 85 on placebo. One patient in the placebo arm required target vessel revascularization.

"Our study shows 70% reduction in the incidence of periprocedural myocardial infarction: According to these data, 10 patients should be treated with atorvastatin to avoid one case of myocardial infarction," they reported.

The investigators cautioned that the findings cannot be extrapolated to other patient groups. ■

Statin Pretreatment Reduces Contrast Nephropathy in PCI

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — Patients treated with a statin starting before percutaneous coronary intervention had a dramatic reduction in their rate of contrast-induced nephropathy, compared with patients who weren't pretreated, in a study with more than 400 patients.

Statin pretreatment might work by reducing inflammation and oxidative stress. In addition, lower incidence of contrast-induced nephropathy during and immediately after percutaneous coronary intervention (PCI) might lead to improved long-term outcomes, Dr. Annunziata Nusca and his associates reported in a poster at the annual meeting of the American College of Cardiology.

The Atorvastatin for Reduction of Myocardial Damage During Angioplasty (ARMYDA)-RENAL study enrolled consecutive patients who underwent PCI for either acute coronary syndrome or stable angina at the Campus Bio-Medico University in Rome. Patients scheduled for elective PCI were randomized to receive either 40 mg atorvastatin daily or placebo starting 7 days before their procedure. Patients who underwent PCI for acute coronary syndrome received either an 80-mg dose of atorvastatin 12 hours before the procedure and a second, 40-mg dose immediately before the procedure, or placebo. All patients received 40 mg atorvastatin daily after the procedure.

The study did not receive commercial support. The impact of atorvastatin pretreatment on the incidence of death, myocardial infarction, or need for revascularization in patients with acute coronary syndrome was the focus of a second report at the meeting from the same researchers, ARMYDA-ACS. (See story above.)

The primary end point of the ARMYDA-RENAL study was postprocedural incidence of contrast-induced nephropathy, defined as an increase in serum creatinine of at least 25% over the baseline level, or by at least 0.5 mg/dL.

Among the 260 patients who received statin pretreatment, the incidence of contrast-induced nephropathy was 3%, vs. 27% in patients who weren't pretreated, a statistically significant difference. Prior to PCI, the average creatinine clearance rate was about 83 mL/min in all patients. Immediately after PCI, the rate was about 80 mL/min in statin-pretreated patients, and about 64 mL/min in those with no pretreatment, also a statistically significant difference, reported Dr. Nusca, a cardiologist at the university, and his associates.

In a multivariable analysis that controlled for several differences between the two study groups at baseline, patients who received atorvastatin pretreatment had a 90% drop in their rate of contrast-induced nephropathy, compared with patients who did not get pretreatment. The only patient characteristic that blunted the benefit from statin pretreatment was a baseline creatinine clearance rate of less than 40 mL/min.

Pretreated patients also had significantly better outcomes with follow-up out to 4 years. For example, the rate of major adverse cardiac events after 4 years was 6% in statin-pretreated patients and 36% in those with no pretreatment. ■

Low-Dose Aspirin as Effective and Safer Than High-Dose After PCI

BY BRUCE JANCIN
Denver Bureau

NEW ORLEANS — Low-dose aspirin appears to be as effective as—but considerably safer than—the higher doses favored by most American cardiologists for prevention of recurrent cardiac events after percutaneous coronary intervention, Dr. Sanjit S. Jolly said at the annual meeting of the American College of Cardiology.

He presented a retrospective observational analysis of the Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events in Patients Undergoing Percutaneous Coronary Intervention (PCI-CURE) trial database, which concluded that the adjusted risk of major bleeding within 8 months after the procedure was 2.2-fold greater in patients on aspirin at a dosage of at least 200 mg/day, compared with those on 100 mg/day or less.

"This analysis suggests low-dose aspirin may be superior with regard to a lower rate of serious bleeding compared to high-dose aspirin, and with similar efficacy in terms of death, MI, and stroke," said Dr. Jolly of McMaster University, Hamilton, Ont.

Moreover, these PCI-CURE findings are supported by two other large observational analyses in patients with acute coronary syndrome that reached the same conclusions. One, led by Dr. Eric J. Topol, involved nearly 9,200 participants in a study of the failed oral glycoprotein IIb/IIIa inhibitor lotrafiban (Circulation 2003;108:399-406). The other included more than 12,500 patients in a clopidogrel trial (Circulation 2003;108:1682-7).

"I personally have increasingly been prescribing low-dose aspirin after PCI because of the data from these three observational studies. However, I don't think we have the final word yet," Dr. Jolly commented.

He stressed that observational data such as these must be considered hypothesis generating. But a large, prospective, randomized clinical trial is well underway under the leadership of his colleagues at McMaster. The seventh Optimal Antiplatelet Strategy for Interventions/Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent Events trial (OASIS-7/CURRENT) is randomizing 14,000 patients with unstable angina or non–ST-elevation MI to either a 300- or 600-mg loading dose of clopidogrel and low- or high-dose aspirin. Results should be available in 12-18 months.

The PCI-CURE analysis involved 2,658 patients with acute coronary syndrome on four continents who underwent PCI. Aspirin dosing was left to physician preference, which in Europe strongly favored the use of 100 mg/day or less in accord with the latest European Society of Cardiology practice guidelines. In contrast, the great majority of American cardiologists prescribed at least 200 mg/day—and most commonly 325 mg/day—as recommended in current American College of Cardiology/American Heart Association guidelines.

"When there's such a practice difference between Europeans and Americans, it tells us that perhaps we need more data," he said.

At 8-month follow-up in PCI-CURE, the major bleeding rate was 1.9% in the low-dose aspirin group, compared with 3.9% with high-dose therapy. The 2.2-fold increased risk in the high-dose group was derived after adjusting for potential confounders, including age, gender, weight, hypertension, and use of clopidogrel versus placebo.

The combined end point of cardiovascular death, MI, or stroke was 7.1% in the low-dose aspirin group and 8.6% with high-dose therapy, a nonsignificant difference. ■