News and Views from the Literature

Myocardial Infarction

Meta-Analysis of Abciximab Trials Confirms Benefit

Reviewed by Norman E. Lepor, MD, FACC, FAHA
The David Geffen School of Medicine,
Cedars-Sinai Medical Center, Los Angeles, CA
[*Rev Cardiovasc Med.* 2005;6(3):180-181]

Efficacy and Safety of Abciximab in Acute Myocardial Infarction Treated With Percutaneous Coronary Interventions: A Meta-Analysis of Randomized, Controlled Trials.

de Queiroz Fernandes Araujo JO, Veloso HH, De Paiva JM, et al.

Am Heart J. 2004;148:937-943.

Although the news is not new, it is enduring. Data remain consistent regarding the efficacy of the glycoprotein IIb/IIIa agent abciximab in patients undergoing primary percutaneous coronary intervention (PCI) for acute ST elevation myocardial infarction (MI). The purpose of this analysis was to evaluate the efficacy and safety of abciximab when administered following PCI to treat acute MI.

Six clinical trials were identified by the authors as fulfilling the criteria for inclusion in the meta-analysis. In each of the trials, patients underwent PCI within 48 hours of symptom onset, fulfilling the clinical and ECG diagnostic criteria for acute MI. All patients were followed up for at least thirty days.

The RAPPORT,[1] ISAR-2,[2] ADMIRAL,[3] Petronio,[4] CADILLAC,[5] and ACE[6] trials were included in this analysis. A total of 3755 patients were randomized to either abciximab therapy or control. A significant 30% reduction in mortality was observed with abciximab, from 4.9% to 3.4% ($P = .03$). Though there was no significant reduction in reinfarction, a 21% reduction in target vessel revascularization ($P = .02$) and a 24% reduction in major adverse cardiac events ($P = .001$) were observed.

There was an increased incidence of major bleeding with the use of abciximab (5.9% vs. 4.3%, $P = .03$). However, there was no significant increase in major bleeding in those patients who received the lower-dose intravenous heparin bolus (70 u/kg), as opposed to those receiving a high dose (100 u/kg).

In analyzing these data, researchers observed the benefit of abciximab in patients who underwent stent implantation, whereas those patients who underwent coronary angioplasty for acute MI did not seem to accrue any benefit.

These results reinforce previous clinical trial data illustrating the benefit of abciximab in patients treated

for acute MI with PCI. On-going concerns regarding excessive major bleeding seem to have been allayed by the use of lower doses of intravenous heparin. Whether the small molecule glycoprotein IIb/IIIa inhibitors (eptifibatide, tirofiban) or the intravenous direct thrombin inhibitors (lepirudin) are effective in the setting of PCI and acute MI has not yet been clarified by clinical trial data. In addition, abciximab's metabolizing independent of renal function makes it the ideal agent for use in patients with chronic renal insufficiency. In patients undergoing PCI for acute MI, the clinical data clearly support the adjunctive use of abciximab.

References

1. Brener S, Barr L, Burchenal J, et al. Randomized, placebo-controlled trial of platelet glycoprotein IIb/IIIa blockade with primary angioplasty for acute myocardial infarction. *Circulation*. 1998;98:734-741.
2. Neumann G, Kastrati A, Schmitt C, et al. Effect of glycoprotein IIb/IIIa with abciximab on clinical and angiographic restenosis rate after the placement of a coronary stent following acute myocardial infarction. *J Am Coll Cardiol*. 2000; 35:915-921.
3. Montalescot G, Barragan P, Wittenberg O, et al. Platelet glycoprotein IIb/IIIa inhibitor with coronary stenting for acute myocardial infarction. *N Engl J Med*. 2001;344:1895-1903.
4. Petronio A, Musumeci G, Limbruno U, et al. Abciximab improves 6-month outcome after rescue coronary angioplasty. *Am Heart J*. 2002;143:334-341.
5. Stone G, Grines C, Cox D, et al. Comparison of angioplasty with stenting with or without abciximab, in acute myocardial infarction. *N Engl J Med*. 2002;346:957-966.
6. Antoniucci D, Rodriguez A, Hempel A, et al. A randomized trial comparing primary infarct artery stenting with or without abciximab in acute myocardial infarction. *J Am Coll Cardiol*. 2002;89:126-131.

Percutaneous Interventions

Statins: Adjunctive Pharmacotherapy for Percutaneous Coronary Intervention?

Reviewed by Dean J. Kereiakes, MD, FACC, FAHA

The Lindner Center for Research and Education, Ohio Heart Health Center, Cincinnati, OH

[*Rev Cardiovasc Med.* 2005;6(3):181-183]

HMGCoA reductase inhibitors (statins) have recently been shown to possess direct, white-cell-mediated, anti-inflammatory effects that are distinct from (and operate in addition to) their well established low-density lipoprotein cholesterol-lowering effects. Indeed, statins directly impede leukocyte adhesion, rolling, and transmigration in addition to upregulating endothelial nitric oxide synthase activity (producing nitric oxide)[1,2] and downregulating neutrophil-monocyte, CD llb/18 (MAC-1) receptor expression.[3] The degree of mononuclear cell plaque infiltrate has been directly correlated with the presence of plaque rupture,[4] clinical disease activity (unstable syndromes),[5] and the propensity for restenosis following percutaneous coronary intervention (PCI).[6] The administration of either atorvastatin (80 mg daily) or simvastatin (40 mg daily) orally for 1 to 4 months prior to carotid endarterectomy significantly reduces the degree of macrophage and activated T-lymphocyte infiltration observed in excised plaque.[7,8] Thus, "plaque stabilization" appears to occur rapidly following the initiation of statin therapy. Observational studies have previously suggested that statin treatment prior to PCI (especially stent deployment) reduces the frequency and magnitude of periprocedural myocardial infarction as reflected by CK-MB or troponin measurements.[9-11] Clinically, statin treatment (vs. no statin treatment) has been associated with a reduction in hospital length-of-stay and 6-month and 1-year mortality following coronary stent deployment.[12-14] However, neither the requisite minimum time course required for pretreatment with statins, nor proof of efficacy derived from a placebo controlled randomized trial of statin administration prior to PCI, have been defined.

Randomized Trial of Atorvastatin for Reduction of Myocardial Damage During Coronary Intervention. Results from the ARMYDA (Atorvastatin for Reduction of Myocardial Damage during Angioplasty) Study.

Pasceri V, Patti G, Nusca A, et al. on behalf of the ARMYDA investigators.

Circulation. 2004;110:674-678.

The Atorvastatin for Reduction of Myocardial Damage during Angioplasty (ARMYDA) study randomly assigned 153 patients with stable angina undergoing elective PCI to receive either atorvastatin (40 mg, po, daily, n = 76) or placebo (n = 77) for 7 days prior to the procedure. Markers of myocardial injury (CK-MB, troponin I, and myoglobin) were assessed systematically prior to and following PCI. All patients received aspirin (100 mg/d) and either ticlopidine (250 mg, po, twice daily) for at least 3 days prior to PCI or clopidogrel (300 mg, po) at least 6 hours before PCI. All patients continued either oral ticlopidine, 250 mg twice daily, or oral clopidogrel, 75 mg