Recovery of Coronary Flow and Left Ventricular Function After Abciximab

To the Editor:

I read with great interest the article by Neumann et al1 on the “Effect of Glycoprotein IIb/IIIa Receptor Blockade on Recovery of Coronary Flow and Left Ventricular Function After the Placement of Coronary-Artery Stents in Acute Myocardial Infarction.” In particular, the recovery of coronary flow and left ventricular function provided by abciximab were related to improvement of perfusion of the coronary microvasculature beyond mere restoration of epicardial vessel patency. Indeed, the efficacy of abciximab in preventing distal embolization and reducing periprocedural myocardial infarction was observed previously among various subsets of patients in the EPIC (Evaluation of c7E3 for the Prevention of Ischemic Complications) trial.2,3

In the article by Neumann et al,1 patients with myocardial infarction were randomized to receiving standard-dose heparin or abciximab plus low-dose heparin. A total of 15 000 U was administered to those in the standard-heparin group compared with 30 000 U of heparin for those treated with abciximab plus low-dose heparin. In addition, patients in the standard-heparin group continued to receive heparin infusion for 12 hours after sheath removal. I suppose the total dose of heparin in the abciximab plus low-dose heparin group was 7500 U (typographical error in the text, I believe). Nonetheless, this dose is not particularly low, because the median dose among patients in the low-dose heparin group of the EPILOG (Evaluation in PTCA to Improve Long-term Outcome by c7E3 GPIIb/IIIa receptor blockade) study4 was 5500 U (interquartile range 4700 to 6600 U). On the other hand, the median doses for those patients in the standard-dose heparin and standard-dose plus abciximab groups were 9400 U (interquartile range 7800 to 11 800 U) and 8600 U (interquartile range 7000 to 10 000 U), respectively. It would be useful to know the activated clotting and partial thromboplastin times, because subsequent complications may be related to the level of anticoagulation.5

Immediately after stent placement, the basal and peak flow velocity reserve, degree of angiographic residual stenosis, and hemodynamic data were similar between these 2 groups, which suggests that optimal results were obtained between these 2 groups of patients. However, at 14 days, the recovery of coronary flow and left ventricular function was substantially greater among those treated with abciximab. The authors attributed these benefits to platelet glycoprotein IIb/IIIa blockade. Although these results are impressive, an important confounding factor was that heparin infusion was continued for 12 hours in the standard-dose group. Its significance was not discussed. The sudden discontinuation of heparin after 12 hours may promote coagulation, the so-called “rebound” phenomenon,6 and hence lead to formation of microthrombi and subsequent “clogging” of the coronary microvasculature. This effect may account, in part, for the results at 14 days.

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Response

We appreciate the interest Dr Mak expressed in our article. As Dr Mak correctly points out, the dose of heparin in patients assigned to abciximab was indeed 7500 U. Compared with the 15 000 U of heparin administered in the control group, this was a low dose. Dr Mak objects that our dose of heparin in the abciximab group was similar to standard-dose and not to low-dose heparin in EPILOG (Evaluation of PTCA to Improve Long-term Outcome by c7E3 GPIIb/IIIa receptor blockade).1 We chose this dose because in EPILOG, the outcome in patients with recent myocardial infarction was better with standard-dose heparin than with low-dose heparin.1 We did not routinely measure activated clotting times (ACTs), because we are not aware of any prospective randomized study showing a benefit from this practice. We do not think that the lack of routine ACT measurements created a bleeding hazard for our patients. In patients without previous thrombolysis, transfusion rates were very similar to those in EPISTENT (Evaluation of IIb/IIIa Platelet Inhibitor for STENTing),2 2.4% in the abciximab group and 2.6% in the control group. All transfusions were necessitated by access-site problems, and there were no other major bleeding complications.

For the control group, we chose the regimen validated in ISAR (the Intracoronary Stenting and Antithrombotic Regimen trial), which was the only published randomized trial on antithrombotic treatment after stenting at the time we designed the study.3 We do not share Dr Mak’s concerns that the continuation of heparin for 12 hours in the control group represents an important confounding factor. In the first place, heparin was discontinued in both groups. If anything, delayed discontinuation in the control group might have allowed for better plaque stabilization. Second, in Theroux’s classic work,4 cited by Dr Mak to postulate a rebound phenomenon after discontinuation of heparin, heparin rebound was not detectable in patients taking aspirin, which all of our patients received.

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