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CLINICAL RESEARCH **Interventional Cardiology**

The Clinical Results of a Platelet Glycoprotein IIb/IIIa Receptor Blocker (Abciximab: ReoPro)-Coated Stent in Acute Myocardial Infarction

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OBJECTIVES This study is a prospective randomized trial investigating clinical outcomes of patients with acute myocardial infarction (AMI) treated with abciximab (ReoPro)-coated stents.

BACKGROUND Recently we have demonstrated that abciximab-coated stents have inhibitory effects in the prevention of coronary restenosis.

METHODS Ninety-six patients with AMI were randomly allocated into two groups; group I received abciximab-coated stents (n = 48, 57.1 ± 12.0 years), and group II received bare metal control stents (n = 48, 58.4 ± 11.6 years).

RESULTS At baseline, clinical characteristics, percent diameter stenosis, and minimal luminal diameter were no different between the two groups. One patient in group II had reinfarction and target lesion reintervention during hospital stay. Follow-up coronary angiography was obtained in 77.1% (37 of 48) in group I and 75.0% (36 of 48) in group II. Percent diameter stenosis and late loss were significantly lower in group I than group II (18.9 ± 5.54% vs. 37.9 ± 6.25%, p = 0.008; and 0.39 ± 0.29 mm vs. 0.88 ± 0.45 mm; p = 0.008, respectively). At follow-up intravascular ultrasound, intrastent lumen area and intrastent neointimal hyperplasia (NIH) area were 5.4 ± 1.8 mm^2 and 2.2 ± 1.5 mm^2, respectively, in group I and 4.3 ± 1.6 mm^2 and 3.4 ± 1.8 mm^2, respectively, in group II (p = 0.045). And, in-stent restenosis rate was lower in group I than group II (p = 0.011 and p = 0.008, respectively). During 1-year follow-up, two patients in group II (4.1%) had AMI, whereas no patient in group I suffered AMI. Target lesion revascularization and total major adverse cardiac events rates were relatively lower in group I compared with those in group II (10.4% [5 of 48] vs. 20.8% [10 of 48], p = 0.261, and 10.4% vs. 25.0%, p = 0.107, respectively).

CONCLUSIONS Abciximab-coated stent implantation was safe and effective without stent thrombosis in AMI patients. (J Am Coll Cardiol 2006;47:933–8) © 2006 by the American College of Cardiology Foundation

The development of coronary artery stenting reduces the incidence of acute coronary occlusion after percutaneous transluminal coronary angioplasty to <1% (1). In-stent restenosis caused by intimal hyperplasia, however, still occurs in as high as 10% of patients even after drug-eluting stent (DES) and thereby remains a significant clinical problem to be solved (2). It has been shown that stents coated with antiproliferative agents such as sirolimus and paclitaxel are associated with lower restenosis rates, after percutaneous coronary intervention (PCI), than conventional bare-metal stents. More recent reports have also shown the efficacy of these DES under more challenging conditions, such as small vessels, lesions of in-stent restenosis, diabetics, and long and complex lesions (3–7).

Abciximab, a potent antiplatelet agent that blocks the final pathways to platelet aggregation, improves outcomes of high-risk PCI and decreases the incidence of major adverse cardiac events (MACE) (8–11). Differently from other kinds of platelet glycoprotein IIb/IIIa receptor blockers, it also binds to Mac-1 (CD11b/18) on vascular endothelial cells and macrophages, thereby inhibiting inflammatory responses and smooth muscle cell proliferation after vascular injury (12–17). Recently, we demonstrated that abciximab-coated stents were safe and effective in the prevention of coronary restenosis in humans as well as in a porcine model (18,19).

The aim of the present study is to evaluate clinical and angiographic outcomes of abciximab-coated stent implantation in patients with acute myocardial infarction (AMI).

METHODS

Study group. Ninety-six patients with AMI who underwent PCI at Chonnam National University Hospital

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Abbreviations and Acronyms

AMI = acute myocardial infarction
DES = drug-eluting stent
IVUS = intravascular ultrasound
MACE = major adverse cardiac events
PCI = percutaneous coronary intervention
TIMI = Thrombolysis In Myocardial Infarction

were recruited and then randomly divided into two groups: group I, which received abciximab-coated stents (n = 48), and group II, which received conventional bare-metal stents (n = 48). The inclusion criteria were AMI patients with age range from 18 to 80 years, target vessel diameter between 2.5 and 4.0 mm, lesion length <25 mm, and critical stenosis (>70%) on angiography. Patients with left main-stem stenosis, graft-vessel stenosis, cardiogenic shock, left ventricular ejection fraction <35%, or contraindications for antiplatelet agents were excluded from the study. The study protocol was reviewed and approved in sequence by the Korean Ministry of Health and Welfare and the Ethics Committee of Chonnam National University Hospital, and informed consent was obtained from all patients.

Manufacturing process of the abciximab-coated stent. Abciximab-coated stents were used according to the protocol previously described (18,19). Briefly, a plasma polymerization reaction was performed to attach amine radicals to the stent surface. For the attachment of amine radicals to the stent surface, diaminocyclohexane monomer was drifted to the tubular reactor in a constant dose, and plasma was generated with a radiofrequency power generator. The abciximab used was a human-murine chimeric antibody Fab fragment, ReoPro (Eli Lilly and Company, Indianapolis, Indiana). The carboxy radical of abciximab was introduced to the amine radicals attached to the stent to achieve covalent bonding and improved attachment power between the stent and abciximab. The abciximab coating on the surface of the stent was confirmed by scanning electron microscopy. For the release, kinetics of abciximab from the stent was done.

Study procedure, stent implantation, angiography, and IVUS. All other procedures were performed by standard techniques: randomly selected stents were deployed at 10 to 16 atmospheric pressure after predilation with a balloon catheter. In cases with residual stenosis, additional balloon dilatation was performed after stenting. None of the study patients received glycoprotein IIb/IIIa receptor blockers. All patients received aspirin (300 mg loading and 100 to 200 mg/day indefinitely) and clopidogrel (300 mg loading and 75 mg/day for 2 months). Heparin was administered as 5,000-U bolus, followed by 1,000 U/h and additional 5,000 U immediately before PCI to keep the activated clotting time (ACT) at 250 to 300 s. Successful PCI was defined as a patent vessel at the treatment site with anterograde Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 and angiographic residual stenosis <20% without occurrence of any cardiac events.

Acute myocardial infarction was defined as the presence of typical chest pain, ischemic change on the electrocardiogram in two or more contiguous leads, and peak elevation of plasma creatine kinase (CK) and CK-MB to at least twice normal. Stent thrombosis was defined as an acute coronary syndrome with angiographic documentation of either vessel occlusion (TIMI flow grade 0 or 1) or thrombus within or adjacent to a previously successfully stented vessel (TIMI flow grade 1 or 2).

Bleeding events were classified as major, minor, or insignificant according to the criteria of the TIMI Study Group. Major bleeding events were defined as intracranial bleeding or a bleeding event that caused fall in hemoglobin of >4 g/dl or that required transfusion of >3 U of blood. Thrombocytopenia was defined as a platelet count $<100 \times 10^3/mm^3$.

Coronary angiography was performed at baseline, immediately after the procedure, and 6 months later. Quantitative diameter measurements of the coronary arteries were obtained by a blinded reviewer using a workstation with dedicated software (Philips H5000 or Allura DCI program, Philips Medical Systems, Eindhoven, the Netherlands) by a standard technique. In-stent restenosis was defined as an in-stent luminal diameter stenosis ≥40%. Late lumen loss was defined as the difference between the minimal luminal diameter immediately after stenting and the minimal luminal diameter at follow-up. The intravascular ultrasound (IVUS) imaging was performed in all patients before and after procedure and at follow-up. The IVUS images were acquired with motorized pullback at a constant speed of 1 mm/s (Galaxy, Boston Scientific, Natick, Massachusetts, or Endosonics, EndoSonics Corporation, Rancho Cordova, California).

Study end points. Clinical evaluation was done at 30 days, 6 months, and 1 year to assess patient symptom frequency and cardiac event rates. The primary end point was in-stent late lumen loss and the secondary end point was intrastent luminal volume by IVUS and composite of major cardiac events, including cardiac death, any myocardial infarction, and percutaneous or surgical revascularization of the target lesion 12 months after procedure.

Statistical analysis. We calculated that with a sample of 96 patients, the study would have 80% power to detect a difference in the mean late luminal loss of 0.30 mm between the two groups, assuming a standard deviation of 0.5 mm in each group, with the use of a two-group *t* test and a two-sided significance level of 0.5. All analyses were based on the intention-to-treat principle. For continuous variables, differences between the treatment groups were evaluated by analysis of *t* test. For categorical variables, differences were expressed as counts and percentages and were analyzed with the chi-square test. Statistical analysis was performed with the aid of commercially available software (SPSS Version 10.0, SPSS Inc., Chicago, Illinois).