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Guest Editorial

Platelet Glycoprotein IIb/IIIa Inhibitors in Acute Coronary Syndrome

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Platelet activation is believed to be the initial trigger of acute coronary syndromes. Indeed, the use of aspirin, a cyclooxygenase inhibitor of platelet aggregation, is part of standard therapy for myocardial infarction (MI) and unstable angina. As platelets can be activated by pathways other than through the cyclooxygenase system, agents that block the final common pathway of platelet activation (the glycoprotein IIb/IIIa receptor) have recently emerged as a new strategy in the treatment of acute coronary syndromes.

To date, four glycoprotein IIb/IIIa inhibitors have been evaluated clinically. The most extensively studied is abciximab, a c7E3 Fab monoclonal antibody (Reopro) that has to be given intravenously. Synthetic non-peptides of lower molecular weight and shorter biological half-lives include eptifibatide (Integrilin), lamifiban and tirofiban, are currently under extensive clinical trials.

During percutaneous transluminal coronary angioplasty (PTCA), the injury produced by balloon on the vascular wall results for platelet activation. It is therefore not surprising that initial trials on glycoprotein IIb/IIIa inhibitors were performed in the setting of PTCA. The first large-scale trial is the Prevention of Ischaemic Complication (EPIC) study, which compares the use of abciximab (borus followed by 12-hour infusion) in 2100 high-risk patients undergoing PTCA. Compared to placebo, abciximab resulted in a 35% reduction in 30-day primary endpoints of death, acute MI or urgent re-intervention. An increase of bleeding complications has been found in this study using concomitant standard dosage of heparin, but the risk could be reduced by appropriate heparin dosage adjustment. The benefit of abciximab appeared to last up to 3 years, with a 13% long-term reduction in these composite endpoints.

This landmark study changes the practice of interventional cardiology, and spurs the investigations of glycoprotein IIb/IIIa inhibitors in different patient subsets undergoing PTCA. Prophylactic use of abciximab is now warranted in all patient populations undergoing balloon angioplasty or atherectomy as defined in the following trials. These include patients with unstable angina (EPIC1 and CPATURE2), patients with high-risk angiographic or clinical characteristics (EPIC1), patients with acute MI for primary or rescue PTCA (EPIC1), and low-risk patients (EPILOG3). As most cases of PTCA are now performed with stenting, the EPISTENT trial documents maximum benefit in patient receiving stenting and abciximab to balloon angioplasty (with abciximab) or stenting along.

About 40% of patients in this trial have stable angina, and this implies the benefit of using abciximab to low-risk patients and appears to be particularly relevant to the diabetic (51% reduction events compared to stent alone) and found to be cost-effective (preliminary results presented in the American College of Cardiology meeting, 1999). Early results also suggest the role of abciximab in patients undergoing direct PTCA and stenting in acute MI. In the RESTORE trial using the IIb/IIIa antagonist tirofiban, a strong trend to improvement in acute ischaemic endpoints was also documented.

A natural extension of the use of glycoprotein IIb/IIIa inhibitors outside coronary intervention is its role in medical treatment of acute coronary syndromes. In the Platelet IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial, the effects of eptifibatide (bolus and 72-92 hours) infusion were compared in 10948 patients with unstable angina/non-Q-wave MI. A significant reduction in rate of death or MI was observed in eptifibatide treated group compared to the placebo group (14.2 vs 15.7%). Similarly, low-dose lamifiban in the PARAGON study in a similar

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group of patients showed a 6-month reduction in these endpoints. Tirofiban has been used in the PRISM (low-risk) and PRISM-PLUS (high-risk) cases of unstable angina/non-Q-wave MI. In conjunction with heparin, tirofiban reduces major 30-day ischaemic events by 36 and 28%, in the PRISM and PRISM-PLUS trials, respectively. A more rapid medical stabilisation of symptoms and reduction in subsequent periprocedural PTCA complications also occurred after abciximab infusion in this group of patients.

Thus for the interventionalists and cardiologists who take care of patients with acute coronary syndromes a powerful platelet-buster is in our hands. Glycoprotein IIb/IIIa inhibitors for PTCA in Hong Kong is not frequently employed at present, arguable because of a predominance of elective overacute PTCA cases, the absence of a formal 24-hour acute PTCA programme for acute MI in the Hospital Authority hospitals, and the observed increased susceptibility of Chinese patients to bleeding complications. Much more can be said, however, for the use of these agents in patients with unstable angina/non-Q-wave MI. This use is much simpler, and is translated to substantial reduction in mortality and major ischaemic events when applied routinely that only in the interventional laboratories. Further large-scale trials are awaited to assess its use as an adjunct to thrombolysis in the setting of acute MI.

References