Percutaneous coronary intervention (PCI) is performed in more than 1 million patients worldwide each year. Although very effective in improving the symptoms of ischemia and quality of life, acute complications remain the major drawback of this procedure. Studies have demonstrated that the treated vessel closes abruptly during or shortly after the procedure in 4–9% of cases, causing considerable morbidity and an approximately tenfold increase in mortality.1-4

The arterial injury that accompanies PCI makes vascular surfaces vulnerable to platelet deposition, aggregation, and later thrombosis.5 Platelet aggregation is inhibited by glycoprotein (GP) IIb/IIIa inhibitors in a dose-dependent manner. More than 80% GP IIb/IIIa receptor blockade (resulting in more than 80% inhibition of platelet aggregation) is required to prevent thrombus formation in a highly thrombogenic environment.6-8 Eptifibatide (Integrilin), a GP IIb/IIIa inhibitor, has been approved for the treatment of patients undergoing PCI. In this setting, eptifibatide has been shown to decrease the rate of the combined endpoint of death, new myocardial infarction, or the need for urgent intervention.9 In this study, we assessed the efficacy and safety of eptifibatide in low-risk patients undergoing percutaneous coronary intervention.

Methods

Sixty low-risk patients undergoing PCI at Huntsville Hospital, Huntsville, AL, were included in this open-label pilot study. Patients were excluded if they were at high risk — that is, if they had (1) acute evolving myocardial infarction within 24 hours of symptoms that necessitated direct or rescue intervention, (2) unstable angina or peri-infarction pain, or (3) hypertension requiring urgent medical or pharmacological treatment. Patients were stratified into low-risk and intermediate-risk subgroups. Patients in the low-risk group underwent PCI without stenting. The treatment protocol involved the use of eptifibatide in a bolus dose sufficient to produce more than 80% platelet inhibition that was not followed by the continuous infusion.

Results and Conclusions

None of the patients in either study group had a MACE or thrombocytopenia during the follow-up period. Patients who received a conventional eptifibatide dose had a higher incidence of minor bleeding. It appears that, in low-risk patients, a shorter duration of treatment with eptifibatide may prevent the ischemic complications of percutaneous coronary intervention.
a non–Q-wave myocardial infarction 24 hours prior to procedure, or (3) angiographic characteristics indicating high risk (type B or C lesions). Patients were also excluded if they had any contraindication for eptifibatide use or if their serum creatinine concentrations were greater than or equal to 2 mg/dL.

The first group (bolus-only group) included 30 patients (23 men) aged 63.0 ± 11.4 years of age (mean ± SD). Their platelet functions were monitored at baseline and again 10 minutes after a bolus dose of eptifibatide 90 µg/kg, given over 1 minute, using AccuMetrics Ultegra RPFA, a point-of-care, rapid platelet function assay. According to this measuring technique, platelet function is measured based on the ability of activated platelets to bind fibrinogen. If less than 80% platelet inhibition was achieved, another bolus dose of eptifibatide 90 µg/kg was given 5 minutes after the first bolus. The second group (bolus + infusion group) included 30 patients (20 men) aged 65.2 ± 11.6 years. This group received a bolus dose of eptifibatide 180 µg/kg, given over 1 minute, followed by an infusion of 2 µg/kg/min for 20–24 hours. All patients received oral aspirin 325 mg before PCI and daily thereafter. Oral clopidogrel was initiated (300-mg load followed by 75 mg/d for 30 d) after coronary stent deployment. Patients also received heparin titrated to achieve a target activated clotting time of 200–300 seconds during the procedure.

Patients were followed for major adverse cardiovascular events (MACE) for 90 days after the procedure. MACE complications included death, myocardial infarction (raised creatine kinase-MB to at least 3 times the upper limit of normal or development of Q-waves in 2 or more contiguous leads), or any treatment for recurrent angina (percutaneous transluminal coronary angioplasty, stent placement, coronary artery bypass grafting). Patients were also contacted by phone after hospital discharge to determine whether they were hospitalized in another institution for any cardiac event.

Major safety endpoints assessed during hospitalization were bleeding and thrombocytopenia, defined as platelet count less than 100 × 10^3/mm³. Severity of bleeding was classified according to the TIMI (Thrombolysis in Myocardial Infarction) study bleeding classification. Using this scale, bleeding was characterized as being either minor or major, with major bleeding defined as any intracranial hemorrhage, a bleeding event associated with a decrease in hemoglobin of 5 g/dL, or a decrease in hematocrit of 15%.

**Results**

In the bolus-only group, 22 patients (73%) achieved more than 80% platelet inhibition 10 minutes after administration of the eptifibatide 90 µg/kg-bolus dose, which did not necessitate giving another bolus dose. None of the patients in either study group experienced a MACE during the follow-up period. However, 2 patients in the bolus-only group who received 1 bolus of eptifibatide 90 µg/kg had cardiac catheterization: 1 at 7 days and 1 at 11 days after the PCI because of recurrent chest pain. Catheterization laboratory reports showed that the previous angioplasty site was widely patent in both patients, with no evidence of restenosis. The first patient was diagnosed as having gastroesophageal reflux disease, and his chest pain improved after he was started on a proton-pump inhibitor. The other patient was diagnosed as having Prinzmetal’s angina, and a calcium-channel blocker was added to his medications, which resolved his symptoms.

**Lower doses of eptifibatide appear to be associated with fewer bleeding complications.**

Major bleeding was not reported in any of the patients in either group. In the bolus-only group, 6 patients (20%) had minor bleeding compared with 15 patients (50%) in the bolus plus infusion group. Bleeding involved mainly the vascular access site. Thrombocytopenia was not reported in any of the patients in both groups. Although the use of GPIIb/IIIa inhibitors has been associated with thrombocytopenia, which in some cases can be severe, it appears that this adverse effect occurs less frequently with eptifibatide.

**Discussion**

This trial is the first to have evaluated lower doses and shorter duration of treatment with eptifibatide in routine, elective coronary intervention that includes only patients with low-risk clinical and angiographic characteristics. The results demonstrate that the administration of eptifibatide at a bolus dose leading to more than 80% platelet inhibition that is not followed by a continuous infusion could be sufficient to prevent ischemia in low-risk patients undergoing PCI up to 90 days after the procedure. In addition, lower doses of eptifibatide appear to be associated with fewer bleeding complications. It may be that, in this population, a shorter duration of treatment with eptifibatide is sufficient because the thrombogenicity of the disrupted artery is most likely at its highest and the risk of abrupt vessel closure is greatest during and shortly after the procedure compared with an estimated 18–24 hours postprocedure in high-risk patients.
Summary

It appears that, in low-risk patients, a shorter duration of treatment with eptifibatide may prevent the ischemic complications of PCI. In addition, it appears to decrease the risk of minor bleeding. A major limitation of this study is that it was not sufficiently powered to provide statistically significant clinical efficacy or safety results. However, these results suggest that further study with a larger population is warranted.

References