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Recommended Citation
Anna Chan, Wilson Chan, Chun-Wai Chiu, Chi-Chiu Kum, Abciximab Usage in Percutaneous Coronary Intervention in High-Risk Patients: Early and Late Outcomes Journal of the Hong Kong College of Cardiology 2001;9(4) https://doi.org/10.55503/2790-6744.1173

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Abciximab Usage in Percutaneous Coronary Intervention in High-Risk Patients: Early and Late Outcomes

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CHAN ET AL.: Abciximab Usage in Percutaneous Coronary Intervention in High-Risk Patients: Early and Late Outcomes. Background: Clinical adverse cardiac events have been significantly reduced by the adjunctive usage of Glycoprotein IIb/IIIa receptor inhibitors in patients undergoing percutaneous coronary intervention (PCI). However, no information on its safety and efficacy is available for Asian. Methods: All patients who had PCI together with abciximab in the Prince of Wales Hospital from August 1998 to December 2000 were included. Hospital records, ECG records and laboratory results were reviewed retrospectively. The primary composite endpoint including death, myocardial infarction, target vessel revascularization or bypass surgery was assessed at index hospitalization, at 1 month, and 6 months after PCI. The safety of abciximab and any difference in outcomes between the prophylactic and standby group were studied. Results: One hundred and five patients had PCI together with abciximab during the study period. All received bolus abciximab of 0.25 mg/kg followed by 0.125 µg/kg/min infusion over 12 hours. Twenty-one patients had experienced the primary endpoint at the index hospitalization (7 from the prophylactic group and 14 from the standby group). Additional 3 patients in the prophylactic group had reached primary endpoint at 1 month. At 6 months, another 1 in the prophylactic group and 4 in the standby group reached primary endpoint. Total 5 deaths occurred during the index hospitalization, 2 from prophylactic group and 3 from standby group. The bleeding complication was similar in both groups and most of them were minor bleeding only. Three patients had severe thrombocytopenia (platelet count less than 20x10^9/l) and total 6 patients had thrombocytopenia of < 50x10^9/l. Conclusion: There was a trend towards better clinical outcome in the abciximab prophylactic group and the benefit seemed to be sustained at 6 months. Low incidence of major bleeding was observed in the usage of abciximab, but the incidence of thrombocytopenia after abciximab usage in Chinese was much higher than reported in current published studies. (J HK Coll Cardiol 2001;9:171-175)

Abciximab in PCI

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Received June 1, 2001; revision accepted September 30, 2001
Introduction

Several large clinical trials published in recent years have demonstrated the efficacy of Glycoprotein IIb/IIIa (GP IIb/IIIa) receptor inhibitors in preventing ischaemic complications associated with PCI. One of the proposed mechanisms for ischaemic complications is due to mechanical vessel endothelial damage which triggers platelet activation and aggregation. GP IIb/IIIa receptor inhibitors acting as potent inhibitors in the final common pathway of platelet aggregation will inhibit the above adverse platelet mediated thrombotic process. However, the usage of GP IIb/IIIa receptor inhibitors in Hong Kong has been limited. Apart from financial considerations as the drug is expensive, the other concern is the safety profile of the drug in Chinese as most of the data are from Western studies. Therefore, GP IIb/IIIa receptor inhibitors are often used as “standby” therapy i.e. administered when complications or unfavorable angiographic results were encountered during PCI in Hong Kong. We evaluated the usage of abciximab – a GP IIb/IIIa receptor inhibitor for PCI in high-risk patients in relation to the early and late outcomes, in particular efficacy difference between the prophylactic and standby strategies. The safety profile and bleeding risk were also determined.

Methods

All patients who had PCI together with abciximab in Prince of Wales Hospital from August 1998 to December 2000 were included. This was a retrospective study of total 105 patients in a single center. The study population was divided into prophylactic group – abciximab given before intervention, or standby group – abciximab given during intervention when complications or suboptimal angiographic results were encountered. Fifty-four were from the prophylactic group and 51 were from the standby group. All hospital records, ECG records and laboratory results were reviewed. The primary composite endpoint of death, myocardial infarction, target vessel revascularization or bypass surgery was assessed at index hospitalization, at 1 month and 6 months after PCI. Post-procedural diagnosis of MI was made if CK/CKMB was elevated two times the baseline or there were new ECG changes.

Study Population

Table 1 shows the baseline demographic characteristic of patients. Male predominates in both study groups. The baseline characteristics including risk

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prophylactic group</th>
<th>Standby group</th>
<th>P valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>76.9%</td>
<td>73.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>62.4</td>
<td>74.1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.6</td>
<td>61.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.0</td>
<td>160.6</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>78.8%</td>
<td>54.4%</td>
<td>NS</td>
</tr>
<tr>
<td>DM</td>
<td>26.9%</td>
<td>12.3%</td>
<td>NS</td>
</tr>
<tr>
<td>HT</td>
<td>46.2%</td>
<td>33.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Prior MI</td>
<td>7.7%</td>
<td>8.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>9.6%</td>
<td>14.0%</td>
<td>NS</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>5.8%</td>
<td>8.8%</td>
<td>NS</td>
</tr>
</tbody>
</table>
ABCIXIMAB USAGE IN PERCUTANEOUS CORONARY INTERVENTION

factors were similar in both groups except patients in the prophylactic group had a higher body weight (p=0.03).

All were high-risk patients as they either presented with unstable angina (23.1% vs 31.6%), post-MI angina (26.9% vs 40.3%), direct or salvage PTCA for acute myocardial infarction (23.0% vs 3.5%) in the prophylactic and standby group respectively. A higher percentage of patients in the prophylactic group had primary or salvage PCI for acute myocardial infarction than standby group (P=0.04). In setting like acute MI, abciximab is often given “prophylactically” before intervention in order to reduce ischaemic complications. Standby abciximab was given to those with unexpected suboptimal angiographic results after PCI. The main reasons for standby usage of abciximab were presence of thrombus (45.9%), slow flow (15.6%), dissection (11%) or abrupt vessel closure (4.6%) on angiogram during PCI.

Medication Regime

All patients received aspirin and intravenous conjunctive weight adjusted dose of heparin (average 84 units/kg in prophylactic group and 111 units/kg in the standby group) before or during procedure. Additional ticlodipine (500 mg loading before PCI then 250 mg QD for 4 weeks) or clopidogrel (300 mg loading before PCI then 75 mg QD for 4 weeks) were given with coronary stenting. Seventy-five percent were on beta blockers, 39% on ACEI, 47% on statins, indicating most patients were on optimal medical therapy. Abciximab was given as a bolus of 0.25 mg/kg followed by 0.125 µg/kg/min infusion over 12 hours. The mean heparin dose was statistical significantly lower in the prophylactic group than in the standby group (5590 units in the prophylactic group vs 6870 units in the standby group, P<0.05). Lower doses of heparin were given in the prophylactic group because of the concern of excessive bleeding risk associated with the conjunctive usage of abciximab and standard dose of heparin.

Study Endpoints

All primary endpoints were classified by reviewing hospital records. Serial ECG and cardiac enzymes CPK and CKMB were monitored 8 hourly for 24 hours after PCI. Post-procedural diagnosis of MI was made if CK/CKMB was elevated two times the baseline or there were new ECG changes. Haematologic profiles such as haemoglobin level and platelet counts were monitored at 0 hour, 8 hourly for 24 hours and on day of discharge. Thrombocytopenia was confirmed with film comment to avoid pseudothrombocytopenia.

Results

Twenty-one patients experienced the primary composite endpoints during the index hospitalization, 7 from the prophylactic group and 14 from the standby group. The difference was mainly due to the reduction of non-Q MI in the prophylactic group (5.8% vs 19.3%, P<0.05). A total 5 deaths occurred during the index hospitalization, 2 from prophylactic group and 3 from standby group. Most of deaths were from critically ill patients who presented with acute myocardial infarction or cardiogenic shock before intervention. An additional 3 patients in the prophylactic group had reached primary endpoint at 1 month. At 6 months, 1 in the prophylactic group and 4 in the standby group reached primary endpoint. The primary endpoint at 1 and 6 months were mainly due to target vessel revascularization.

The bleeding complication was similar in both groups despite the difference in conjunctive heparin dosage. The overall bleeding risk was 20.2% and was comparable with other studies. No serious clinical bleeding such as intracerebral haemorrhage or bleeding resulting in death was observed. Most bleeding complications were mild and majority were local complications such as groin haematoma or gum bleeding. But 3.7% of patients did have gastrointestinal bleeding and half of them requiring blood transfusions.
Three patients had severe thrombocytopenia (platelet count less than 20x10^9/l) and total 6 patients had thrombocytopenia of platelet count less than 50x10^9/l. All thrombocytopenia occurred within 24 hours after administration of abciximab. The platelet count recovered promptly usually within 24 hours to 48 hours after stopping the infusion.

**Discussion**

In this study, the overall clinical event rate is substantial in both groups (total 27.6% reached primary endpoints at 6 months). This was because our study populations mainly included high-risk patients whom were expected to have high mortality even with intervention. They were sicker patients presented with acute myocardial infarction and failed thrombolysis or with cardiogenic shock. Still, the clinical adverse events were reduced with usage of abciximab in the prophylactic group when compared to standby group (20.3% vs 35.3% respectively).

The potential usage of standby abciximab for PCI-related complications justified further evaluation. The delay administration of abciximab in standby strategy still found to be useful might be due to the rapid and persistent systemic inhibition of platelet inhibition. Subgroup analysis of abciximab efficacy needs exploration, though some studies suggested the benefit is independent of device or modality used.

Determination of optimal conjunctive heparin dose is important in order to maintain the efficacy of anticoagulation without concomitant increase in excessive bleeding risk. Heparin dose can either be weight-adjusted or guided by activated clotting time to achieve the optimal intensity of anticoagulation during PCI. From our limited experience, a standby strategy in presence of full systemic heparinization is not associated with excessive bleeding risk. From our data, the usage of closer device did not reduce the rate of local vascular complications but did improve patient comfort and allow early mobilization. Other anticoagulation options like the use of GP IIb/IIIa receptor inhibitors in combination with direct thrombin inhibitor or thrombolytic agents in PCI or in acute coronary syndrome needs further evaluation.

The risk of profound thrombocytopenia is reported to be rare (0.4% to 1%) in previous studies. The onset is known to be very early and prompt recovery is expected once the agent is stopped. The incidence of severe thrombocytopenia appears to be significantly higher in Hong Kong Chinese than reported in current published studies.

No hypersensitivity or anaphylactic reactions were noted after abciximab administration.

**Study Limitations**

The limitation of study was small sample size and was retrospective in nature and patients were not randomized to one of prophylactic or standby group. Nevertheless, our study reflects the daily clinical practice in our center.

**Conclusion**

The additional use of GP IIb/IIIa receptor inhibitors in prophylactic group tends to have lower ischaemia complications, particularly in the reduction of non-Q myocardial infarction when compared with bailout group. There was a trend towards better clinical outcome in the prophylactic group and the benefit seemed to be sustained at 6 months. Low incidence of major bleeding was observed in the usage of abciximab in Chinese. Further assessment of the cost-effectiveness of standby strategy is important.

**References**

4. Randomised placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina: the