ORIGINAL RESEARCH

Evaluation of Newer Antiplatelet Agent in Non-Interventional and Pre PCI Management of ST-Elevation Myocardial Infarction

Rakesh Kumar¹, P. Nigam²

ABSTRACT

Introduction: Treatment with primary percutaneous coronary interventions (PCI) decrease the mortality rate of patients with ST-elevation myocardial infarction (STEMI) presenting within 12 hours. Patients presenting after 12 hours are generally viewed to be ineligible for reperfusion therapy, and currently there are no specific treatment recommendations for this subgroup. Aim of the study was to confirm the role of newer anti-platelet agents in non-Interventional and Pre PCI management and optimal medical therapy (OMT) of STEMI.

Materials and Methods: An observational longitudinal study was conducted on patients attending in-patients department (IPD) and out-patients department (OPD) of Nehru Chikitsalay of B.R.D Medical College, Gorakhpur from December 2009 to November 2010. A total 43 diagnosed cases of STEMI who could not afford PCI and were ineligible for thrombolysis were included in the study. Patients were evaluated on the basis of Major Adverse Cardiac Events (MACE) after the therapy of glycoprotein (GP) IIb/IIIa inhibitors. Tirofiban (0.4 μg/kg/min for first 30 minutes followed by 0.01 μg/kg/min for next 24-48 hours as continuous infusion) in addition to aspirin and low molecular weight heparin (enoxaparin) were chosen for the treatment of STEMI.

Results: The mean age of study population (43) was 52.32±7.1 with male: female ratio of 5:1. Follow up of patients showed that on day 7, 7(18%) had sever recurrent ischemia (SRI), 3(8%) had arrhythmia, 10(26%) had heart block, 4 patients were having CHF. Till day 30, 5(14%) had SRI, 2(6%) had myocardial infarction (MI), 3(8.50%) had arrhythmia, 4(11.50%) had heart block and 4(11.50%) had congestive heart failure (CHF). Till second month, SRI was present in 4(12%) patients, 2 (6%) had arrhythmia, 6(18%) had heat block and 2(6%) had CHF.

Conclusion: The use of tirofiban a GP IIb/IIIa receptor antagonist as important component of optimal medical therapy of STEMI for the patients, who were ineligible for thrombolysis or cannot afford invasive therapy, seems to be reasonable and rational strategy.

Keywords: Tirofiban, STEMI, Glycoprotein inhibitors, Thrombolysis

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INTRODUCTION

Early reperfusion using fibrinolytic agents offer many benefits leading to decrease in morbidity and mortality in acute STEMI patients.¹ Platelet accumulation is a main step in the formation of thrombus on the busted atherosclerotic plaque and after percutaneous coronary intervention (PCI).² GP IIb/IIIa antagonists are potent inhibitors of platelet aggregation that provide noted protection from ischemia in patients undergoing PCI.³ Patients who does not experience reperfusion therapy, an optimal therapy in those patients remains to be defined. Guidelines from American College of Cardiology (ACC)/American Heart Association (AHA) recommend aspirin use every patient with acute coronary syndromes. Guidelines also suggest that patients who do not have a contraindication to heparin, UFH or low-molecular-weight heparin (LMWH) (eg, enoxaparin) may be useful in all patients not treated with thrombolytic therapy. In routine practice, combination of antithrombotic strategy (both aspirin and heparin) is widely used in the treatment of acute STEMI.¹ Present study focus on the role of newer anti-platelet agents in non-Interventional and Pre PCI management and Optimal Medical Therapy (OMT) of STEMI along with aspirin and heparin.
MATERIALS AND METHODS

An observational study was conducted on patients attending IPD and OPD of Nehru Chikitsalay of B.R.D Medical College, Gorakhpur from December 2009 to November 2010. A total 43 diagnosed cases of STEMI who could not afford PCI and were not eligible for thrombolysis were selected for the study. Patients with bleeding disorders, intracranial hemorrhage, neoplasm, Arteriovenous malformation, acute pericarditis, myocarditis and chronic kidney disease (CKD) patients were excluded from the study. A written informed consent and approval from Institutional Ethics Committee was taken before starting study. Patients were evaluated on the basis of Major Adverse Cardiac Events (MACE) after the therapy of GP IIb/IIIa inhibitors. SRI, MI, arrhythmias, heart blocks, CHF, revascularization and death were evaluated under MACE. All patients were followed up for one year and they were evaluated in reference to parameters of MACE as primary endpoints and bleeding and thrombocytopenia as a secondary end point at day 7, 30 and at month 2 of diagnosis and treatment. A detailed history including type and onset of chest pain, aggravating and relieving factors, duration, severity and frequency of pain, diaphoresis, palpitation, breathlessness, heartburn and vomiting was done for every patient. Laboratory test including serial electrocardiogram (every 6 hourly), Troponin T (cardiac marker), bleeding Time, clotting time, prothrombin time, partial thromboplastin time and international normalized ratio was done. 2D ECHO and TMT were also performed. Tirofiban (0.4 μg/kg/min for first 30 minutes followed by 0.01 μg/kg/min for next 24-48 hours as continuous infusion) in addition to aspirin and low molecular weight heparin (enoxaparin) were chosen for the treatment of STEMI. Statistical analysis was done using fisher’s exact test.

RESULTS

The mean age of study population (43) was 52.32±7.1 with male: female ratio of 5:1. Out of 43 patients, 21 (48%) had hypertension, 26 (60%) were smokers, 19 (44%) had diabetes mellitus, 20 (46%) had dyslipidemia and 6 (13%) patients had positive family history of CAD as a risk factor. On day 7, out of 43 patients, 5(11.62%) were lost in follow up. Results of primary endpoints showed that 7 (18%) had SRI, 3(8%) had arrhythmia, 10(26%) had heart block and 4 patients were having CHF. Two (5.26%) patient died due to unknown reason. As a secondary endpoints, 2 (5.26%) had minor bleeding and 6(16%) had decreased platelet count. Occurrence of primary outcomes till day 30 showed that, 5(14%) had SRI, 2(6%) had MI, 3(8.50%) had arrhythmia, 4(11.50%) had heart block and 4(11.50%) had CHF. Two (6%) mortality was seen till day 30. As a secondary end point no patients had bleeding or decreased platelet count. Outcomes till second month showed that sever recurrent ischemia was present in 4(12%) patients, 2 (6%) had arrhythmia, 6(18%) had heat block and 2(6%) had CHF as a primary end point. One died at the end of two months. No patient had bleeding or decreased platelet counts as a secondary end point. Association between gender and occurrence of primary (p=0.189) and secondary (p=0.405) outcomes till day 7 revealed that there was no significant difference between male and female groups. Till day 30, primary (p<0.0001) outcomes were more in female group. Same results were seen till 2 month, primary outcomes were more in female group of the study population (p=0.0191). Both Primary and secondary outcomes were not found more in diabetic patients at day 7. Primary outcomes were more associated in higher frequency in diabetic patients at day 30 and till two month.

DISCUSSION

An unstable atherosclerotic plaque with superimposed platelet deposition forms the basis of unstable angina/NSTEMI and STEMI and such patients are at a significant risk of thrombotic complications, which can further trigger recurrent ischemia, MI or death. Potent platelet inhibitors such as GP IIb/IIIa receptor antagonist have been shown to prevent thrombotic complications associated with percutaneous revascularization. GP IIb/IIIb inhibitors have the potential of being a reasonable alternative and go a long way in improving clinical outcome and survival among this group of patients. The current study demonstrates additional benefits when tirofiban, a potent inhibitor of platelet GP IIb/IIIa is added to standard therapy with heparin and aspirin. Patients in present study suffered no MI, 18% recurrent ischemia and 5% mortality on 7 day and 6% MI, 14% recurrent ischemia and 6% mortality on day 30 of follow up. Event rates were comparable at 30 days for
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patients who were not eligible for reperfusion therapy treated with tirofiban in TETAMI trial. Mortality rate for the patients of killip class 1 in TETAMI trial of 30 day was 7%, who were treated with tirofiban in addition to aspirin and enoxaparin. In terms of safety data, the episodes of haemorrhages were 5% on day 7 and 0% on day 30 in our study which was comparable to the major haemorrhages on 30 day of TETAMI trial.1

This was identical to patients enrolled in the Global Utilization of streptokinase and t-PA for occluded coronary arteries (GUSTO V trial) using combination reduced fibrinolytic therapy and platelet GP IIb/IIIa inhibition.6 In this study patients with chest pain of less than 6 hours duration and either ST elevation or LBBB were treated with reteplase or half doses of reteplase combined with abciximab. Mortality with combination therapy was “not inferior” to reteplase (5.6% vs 5.9%; p=0.43). Patients aged 75 and older, combination therapy was associated with an insignificant increase in mortality (18.3% vs 17.9%; p=0.83) compared with reteplase.

The combination of abciximab and half dose reteplase failed to produce a significant reduction in 30 days mortality, the primary end point: 468 (5.6%) patients in the reteplase-alone group. No difference in death rates within 24 hours or 7 days after enrolment were observed. In our study 6%, 30 day mortality rate was observed, which was comparable to the group who received half doses of reteplase combined with abciximab. Re-infarction and recurrent ischemia within 7 days occurred in significant fewer patients receiving the combination: 2.3% vs 3.5% had re-infarction (p<0.0001), and 11.3% vs 12.8% had recurrent ischemia (p=0.004). Furthermore, the need for PCI within 6 hours of randomization was significantly reduced (5.6% vs 8.6%,

<table>
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<th>Parameter</th>
<th>Day 7</th>
<th>Day 30</th>
<th>Two months</th>
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<td></td>
<td>&lt;60y</td>
<td>&gt;60y</td>
<td>P value</td>
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<td>Primary outcome</td>
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<tr>
<td>MI</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>CHF</td>
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<td>3</td>
<td>0.035</td>
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<tr>
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<td>1</td>
<td>0.422</td>
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<tr>
<td>Secondary Outcome</td>
<td>B/throcyto</td>
<td>3</td>
<td>5</td>
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<tr>
<td>Total patients</td>
<td>29</td>
<td>9</td>
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</tbody>
</table>

*data are expressed in no of patients, 1Years. Sever recurrent ischemia; SRI, Myocardial infarction; MI, Congestive heart failure; CHF, Bleeding or Thrombocytopenia; B/throCyto

Table-1: Association between age and occurrence of primary and secondary outcome at day 7, 30 and 2 months*
p<0.001) in the combination therapy group. There were no re-infarction within 7 days in our study and recurrent ischemia within 7 days occurred in 18% of the patients. Our study, which were diagnosed with CHF on follow up were those who had presented with CHF at the time of presentation. Episodes of CHF in patients of our study were not high in comparison to other studies as they were not classified according to Killip classes at the time of treatment.¹,² So, the response in attenuation of severity of CHF could not be evaluated after the therapy and the other co-morbidity of the patients which could have played important role in outcome of CHF were not well correlated.

None of the study till date has dealt with issues of arrhythmias in these patients after therapy. In our study population the episodes arrhythmias were 8% on day 7, 6% on day 30 and 6% on month 2. These episodes were more frequently associated with patients had higher incidence of CHF and mortality. These arrhythmias were mostly Supraventricular tachycardia and ventricular tachycardia in less than 1% of patients. Heart block rates were not include in the arrhythmias as over 26% of the patients on day 7 and this was not associated with poor outcome of the patients. These episodes of 1º heart block and 2º blocks were considered to be a predictor of better ECGs recovery to baseline after use of tirofiban therapy. The rates of heart block declined to 11.5% on day 30 follow up.

None of the patients in our study went under PCI in follow up over the period of one year follow up. To conclude, tirofiban has a definite role in improving outcomes in patients who cannot afford invasive therapy or those who presents out window period for thrombolysis or ineligible for thrombolysis for other contraindication like age, other co-morbidities like bleeding diathesis.

CONCLUSION

The use of tirofiban a GP IIb/IIIa receptor antagonist as important component of optimal medical therapy of STEMI for the patients who care ineligible for thrombolysis or cannot afford invasive therapy, seems to be reasonable and rational strategy.

REFERENCE