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Research Article

EFFECT OF TIROFIBAN ON THE OUTCOME DURING HOSPITALIZATION IN PATIENTS WITH ACUTE CORONARY SYNDROME AN OBSERVATIONAL STUDY

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ABSTRACT

Objective: The present study was intended to know the effect of tirofiban on the prognostic outcome of patients with acute coronary syndrome (ACS) during their stay in the hospital.

Methods: Registers and case sheets of patients admitted for ACS during May 2014–April 2015 were analyzed retrospectively. The duration of stay in hospital/Intensive Care Unit (ICU) and the outcomes were recorded in patients who received tirofiban. ACS patients who did not receive tirofiban served as control. During the study period, there were 720 patients with ACS, and among them, 216 did not receive tirofiban and 504 patients received tirofiban.

Results: ICU stay (days, mean±standard deviation [SD]) for tirofiban group was longer (2.5±0.5) when compared to the controls (1.5±0.5). However, this was not statistically significant. The duration of hospitalization (days, mean±SD) was not significantly different in both groups (6±0.81 vs. 6±0.82). None of the patients developed reinfarction or persistent pain during their stay in the hospital. There were no major adverse events with tirofiban.

Conclusion: Therefore, it was concluded that tirofiban does not affect the outcome during hospitalization in patients with ACS.

Keywords: Acute coronary syndrome, ST-segment elevation myocardial infarction, non-ST segment elevation myocardial infarction, Tirofiban, Percutaneous coronary intervention.

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INTRODUCTION

Acute coronary syndrome (ACS) is a term used for any condition brought on by suddenly reduced blood flow to the heart. Common to most clinical presentations is disruption of a coronary plaque, leading to local platelet aggregation and thrombus at the arterial wall, with subsequent partial or total occlusion of the vessel [1].

Treatment pathways for ACS patients include antiplatelets, low molecular heparin (LMWH), anticoagulants, and other surgical methods of primary percutaneous coronary intervention (PCI)/percutaneous transluminal coronary angioplasty/coronary artery bypass grafting.

Tirofiban is an anti-integrin agent directed against the platelet integrin GPIIb/IIIa which is effective in combination with other antiplatelet agents and heparin [2]. Tirofiban is one of three glycoprotein IIb/IIIa (GPIIb/IIIa) receptor antagonists approved by the US FDA, beside abciximab and eptifibatide. Various clinical trials have shown that, when administered with a standard heparin and aspirin regimen, tirofiban reduces the risk of ischemic complications in patients with unstable angina/non-Q-wave myocardial infarction (MI) and in patients undergoing percutaneous revascularization. The approval of tirofiban covers conservative treatment of MI and unstable angina, as well as percutaneous coronary intervention, for which treatment with tirofiban is recommended in moderate-to-high-risk patients. Tirofiban has an acceptable tolerability profile. Therefore, intravenous tirofiban is likely to be used as an adjunct to heparin and aspirin in patients with ACSs including high-risk patients undergoing revascularization [18].

Aim

The present study is undertaken to study the effect of tirofiban on the prognostic outcome of patients with ACS during their stay at a tertiary care hospital in Chennai.

MATERIALS AND METHODS

Materials

Registers and case sheets of patients admitted for ACS during May 2014–April 2015 were analyzed retrospectively. The duration of stay in hospital/Intensive Care Unit (ICU) and the outcome were recorded in patients who received tirofiban. ACS patients who did not receive tirofiban served as control. During the study period, there were 720 patients with ACS; among them, 216 did not receive tirofiban and 504 patients received tirofiban.

Methods

Study design

This was a observational retrospective study.

Study center

This study was conducted at the Department of Cardiology, Government Stanley Medical College.

Sample size

The sample size included 720 patients (216 - control group + 504 - study group).

Inclusion criteria

Patients who presented with ST-segment elevation MI (STEMI) who had:

1. Chest pain for >30 min with ST-segment elevation of ≥1 mm in ≥2 contiguous electrocardiographic leads or with presumably new left bundle-branch block.
2. Admission either <12 h of symptom onset or between 12 and 24 h with evidence of continuing ischemia was eligible for enrolment.
3. Patients who underwent PCI for STEMI/non-ST segment elevation MI (NSTEMI).

4. Both male and female patients above the age of 18 years.
5. Patients who gave written informed consent.

Exclusion criteria

1. Patients who were managed other than PCI.
2. Administration of fibrinolytic agents in the previous 30 days.
3. History of bleeding diathesis or allergy to the study drugs and major surgery within 15 days.
4. Active bleeding or previous stroke in the past 6 months.
5. Patients not willing to give written informed consent.

METHODOLOGY

After obtaining the Institutional Ethics Committee Clearance, the study was conducted in the Cardiology Department of Goverment Stanley Medical College, Chennai, India. It is an observational retrospective study. Data of patients subjected to PCI for STEMI/NSTEMI were obtained from registers maintained in Cardiology Department, Cath Lab, and Case sheets from MRD and ICU/ward and analyzed during the period of May 2014–April 2015.

Parameters observed [9-11]

- Subjective well-being.
  - — Post-PCI stay in ICU/Ward.
  - — Reinfarct.
  - — Mortality during hospital stay.
  - — Adverse events.

Statistical methods

Collected data were manually entered into Microsoft Excel 2015, and statistical analysis was done in SPSS version 20. The categorical attributes are reviewed using the proportions and the continuous attributes with the mean or median, whichever is appropriate. The relationship between these attribute proportions is computed using Chi-square test.

RESULTS

After a loading dose (aspirin 300 mg, clopidogrel 325 mg, isosorbide 5–10 mg, and atorvastatin 80 mg) and heparin, 720 patients underwent PCI [12], of which 259 were female (36%) and 461 were male (64%). 199 females were associated with comorbidities (77%) and 304 males were associated with comorbidities (66%). Table 1 shows the percentage of patients with comorbidities in study group and control group, respectively.

Table 1: Patients with comorbidities in tirofiban group and control group

S.no	Comorbidities	n (%)	
		Study group	Control group
1	Smoking	181 (36.00)	77 (35.70)
2	Hypertension	332 (65.80)	140 (65.10)
3	Dyslipidemia	235 (46.60)	101 (46.70)
4	Diabetes mellitus	125 (24.90)	54 (25.10)

*Sample size of 720 patients. Comorbidities are shown in percentage %

On post-PCI, injection tirofiban was given to 504 patients (5 ml bolus followed by 6 ml/h for 24 h) and 216 patients were not. Patients' selection for tirofiban was decided by interventional cardiologists [13]. ICU stay for tirofiban was longer (2.5±0.5) when compared with controls (1.5±0.5) which were statistically not significant (p=0.5). Duration of hospital stay (ward) after PCI was not significantly different in both the groups (6±0.81 vs. 6±0.82). Pain relief was better with tirofiban group which was not measured by the scoring system. Table 2 shows the parameters observed in tirofiban and non-tirofiban groups. None of the patients developed reinfarction or persistent pain during their stay in the hospital. There were no serious adverse events noted in both the groups, and minor adverse events were noted in tirofiban group (hematuria 1.0% and gum bleeding 0.2%) [14,15].

DISCUSSION

ACSs clinically include unstable angina and NSTEMI and STEMI. The early and strong inhibition of activated platelet plays a vital role in preventing serious thromboembolic complication for these patients. At present, the drug commonly used to prevent thrombosis is combined use of both aspirin and clopidogrel. However, these drugs are partially effective. Recently, antagonists to platelet GPIIb/IIIa have been found to be useful in the treatment of patients with ACS.

In the past years, large interest has been focused on the adjunctive administration of tirofiban, a specific non-peptide antagonist of the platelet GPIIb/IIIa receptor. The administration of tirofiban has been incorporated in clinical practice for the treatment of patients with ACS. Lately, several studies [1-3] showed that GPIIb/IIIa inhibitors improve outcome in ACS patients with or without any coronary intervention. However, various studies [4-7] showed that the adjunctive treatment with tirofiban does not confer any clinical benefit, as compared with placebo or other antiplatelet drugs, such as abciximab and ticagrelor [8]. Thus, controversy still exists in the clinical efficacy of tirofiban on ACS. The aim of the present study was to systemically evaluate the efficacy and safety of tirofiban in patients with ACS.

On post-PCI, recurrent ischemia can result from restenosis, development of progressive disease in the same or different coronary territory, or increased myocardial demand from various causes [3]. Dual antiplatelet therapy with aspirin and clopidogrel is mandatory initially in patients who had coronary stents implanted [4].

Tirofiban is currently regarded as the most potent inhibitor of platelet aggregation. It is given in the dose of 5 ml bolus (0.25 mg) followed by 6 ml (0.3 mg)/h for 24 h along with standard antiplatelet drugs and heparin [5].

Our study was conducted to see if the addition of tirofiban improved the outcomes such as subjective well-being, post-PCI Stay in ICU/ward, reinfarct, and mortality during hospital stay [9-14].

On post-PCI, injection tirofiban was given to 504 patients (5 ml bolus followed by 6 ml/h for 24 h) and 216 patients were not given tirofiban. ICU stay for tirofiban was longer (2.5±0.5) when compared with controls (1.5±0.5) which were statistically not significant (p=0.5). Duration of hospital stay (ward) after PCI was not significantly different

Table 2: Parameters observed and compared in tirofiban group and non-tirofiban group

S.No	Factors	Mean±SD		p
		Tirofiban group	Non-tirofiban group	
1	ICU stay (days)	2.5±0.5	1.5±0.5	0.5
2	Duration hospital stay (days)	6±0.81	6±0.82	0.64
3	Adverse events	Hematuria (1.2%) Hemoptysis (0.2%)	Nil	
4	Recurrent MI	-	-	
5	Emergency revascularization	-		
6	Death	-	-	

*Sample size of 720 patients. Outcomes are shown in mean±standard deviation (SD). ICU: Intensive care units, MI: Myocardial infarction

in both the groups (6±0.81 vs. 6 ±0.82). We observed that there was no significant difference in a number of days stayed in ICU/ward post-PCI [17]. Furthermore, there was no significant difference in mortality in both the groups. Addition of tirofiban did not produce any serious adverse events [15,16].

Limitations

Several limitations must be noted when interpreting the results of the study [18,19].

First, administration of tirofiban was mainly concentrated on South Indian population, due to the lower costs compared with other kinds of GPIIb/IIIa such as abciximab and eptifibatide, which are used more commonly in developed counties. Thus, the current study may be more valuable in South Indians.

Second, substantial heterogeneity was considered to exist. At the same time, we performed subgroup analysis to explore resource heterogeneity.

Third, the treatment in control group differed which may have affected our outcomes.

Fourth, our analysis failed to show the risk stratification.

Fifth, the follow-up was not done after discharge. Therefore, further studies should be performed to confirm long-term outcomes of tirofiban.

Sixth, percentage of reinfarction in both the groups could not be evaluated since the period of hospital stay was limited

Finally, sensitivity analysis for tirofiban was not done.

CONCLUSION

Bollhalder *et al.* [20] declared that the key to the block the formation of thrombosis was to block the platelet GPIIb/IIIa receptor antagonist. Representative platelet GPIIb/IIIa inhibitors currently used are abciximab, eptifibatide, and tirofiban. Tirofiban is a highly selective, short-acting GPIIb/IIIa receptor inhibitor, and it inhibits platelet aggregation by preventing the combination of fibrinogen and GPIIb/IIIa, consequently preventing acute myocardial ischemic events resulting from coronary thrombosis [12-14]. Compared to abciximab, which binds near irreversibly to the receptor, resulting in a considerably longer effect, the anti-aggregatory effects of tirofiban reverse within hours after the completion of the infusion [15,16]. Moreover, tirofiban does not inhibit other β3 integrins, which have been traditionally regarded as crucial targets to explain abciximab effect on microcirculation [17]. In addition, unlike eptifibatide, tirofiban shares the property of high-affinity IIb/IIIa receptor binding with abciximab [14]. However, due to the lower cost, tirofiban represents a very attractive strategy and is more commonly used in clinical practice in Asia, compared with abciximab and eptifibatide, which are mainly used in the developed country.

Our findings suggest that treatment with tirofiban was not associated with a reduction in the odds of all-cause mortality in ACS patients. Our study also shows that tirofiban does not affect the outcome during hospitalization in patients with ACS.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this research article.

AUTHORS' CONTRIBUTIONS

Dr. Thamayanthi K contributed to the design, intellectual content, and protocol for the conduct of the research, analysis of obtained data, and authored the article.

Dr. Arun Ranganathan provided the design, intellectual content, and the protocol for the conduct of the research along with mentorship and authored the article.

Dr. Vasanthira K provided the design, intellectual content, and the protocol for the conduct of the research along with mentorship and authored the article.

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