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Original Research Article

Effect of varied times of tirofiban administration on post-emergency percutaneous coronary intervention in patients with acute myocardial infarction

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Abstract

Purpose: *To determine the impact of time profile of tirofiban hydrochloride administration on short-term outcomes in patients with acute myocardial infarction (AMI) undergoing emergency percutaneous coronary intervention (PCI).*

Methods: *A total of 112 patients with AMI who received PCI treatment in The First People's Hospital of Tianshui, Tianshui, China were randomly and equally assigned to study and control groups. The study group received intravenous tirofiban hydrochloride bolus (10 μg/kg) 1 - 2 h before PCI, followed by sustained infusion at 0.15 μg/kg/min for 36 h after the procedure. Control group received the same regimen immediately after PCI. Myocardial injury markers, cardiac functional parameters, ST-segment resolution, myocardial perfusion changes, bleeding complications, and adverse cardiovascular events over 6 months were evaluated.*

Results: *When compared with control group, the study group exhibited significantly lower cardiac troponin T (cTnT) levels and lower serum creatine kinase-MB (CK-MB) levels at 7 days post-PCI ($p < 0.05$). Furthermore, the study group showed significantly reduced left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD), along with higher left ventricular ejection fraction (LVEF) after 7 days ($p < 0.05$). The study group also exhibited superior ST-segment resolution and significant improvement in myocardial perfusion 90 min post-treatment and significantly lower incidence of reperfusion arrhythmias ($p < 0.05$). Both groups had similar rates of minor bleeding events and no incidence of severe complications or fatalities.*

Conclusions: *Administering tirofiban preoperatively enhances coronary blood flow, improves myocardial perfusion, and reduces the risk of distal embolic events without increasing severe bleeding complications. Larger-scale, multicenter studies with longer follow-up periods are required to confirm these findings and evaluate the safety and efficacy of different administration time for tirofiban infusion in patients with AMI undergoing PCI.*

Keywords: *Acute myocardial infarction, Tirofiban, Emergency percutaneous coronary intervention, Infusion timing, Short-term prognostic outcomes*

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INTRODUCTION

Acute Myocardial Infarction (AMI) is primarily characterized by pathological changes in coronary atherosclerosis, in which sudden rupture of unstable atherosclerotic plaques leads to total occlusion of one or more arteries. This condition manifests abruptly and predisposes patients to complications like heart failure, shock, arrhythmias, and sudden death; factors that contribute to relatively high mortality rate [1]. Percutaneous Coronary Intervention (PCI) is an essential therapeutic approach for myocardial reperfusion in patients with AMI, as it rapidly and sustainably reopens the affected arteries [2]. This intervention utilizes catheter-based techniques to relieve constricted or obstructed coronary arteries, with the aim of enhancing coronary microcirculation and myocardial blood flow [3,4].

Intra-procedural administration of antiplatelet agents also plays a crucial role in augmenting myocardial perfusion by inhibiting platelet aggregation and thrombus formation [3]. Conventional treatment often involves administering medication after the procedure. However, a significant number of patients do not achieve complete myocardial reperfusion postoperatively, which negatively affects prognosis [5]. Tirofiban, a widely-used antiplatelet agent, has been extensively applied in the prevention of no-reflow phenomena in emergency AMI cases during and post-PCI. Given the absence of standardized guidelines for tirofiban use, this study investigated the effects of varying times of infusion administration of tirofiban on the short-term prognosis of patients with AMI undergoing emergency PCI.

METHODS

Participants

This study involved 112 patients with AMI who received PCI treatment in The First People's Hospital of Tianshui, Tianshui, China between January 2019 and July 2023. All participants were duly informed and provided signed consent forms. Ethical clearance for this study was granted by The First People's Hospital of Tianshui Ethics Committee (approval no. 2024017), and conducted in accordance with the guidelines of Declaration of Helsinki [6]. The participants were evenly and randomly allocated into study and control groups.

Inclusion criteria

Participants who met the AMI diagnostic standards corroborated by coronary angiography, onset of symptoms within 12 h, and requiring treatment with APCI.

Exclusion criteria

Individuals with cardiogenic shock, compromised hepatic or renal function, presence of severe arrhythmias, hematological or coagulation impairments, contraindications to PCI or allergies to medications used in the study.

Procedures and treatments

All patients underwent percutaneous coronary intervention (PCI). Prior to the procedure, patients were given 300 mg aspirin and 600 mg clopidogrel orally. Unless contraindicated, all patients were administered statin (40 - 80 mg atorvastatin orally) and nitrate. Low molecular weight heparin was administered at 0.4 mL every 12 h till 5th day after procedure.

Study group received intravenous tirofiban hydrochloride injection at a dose of 10 μg/kg every 1 - 2 h before PCI procedure and completed within 3 min followed by continuous intravenous infusion at 0.15 μg/kg/min for 36 h after the procedure. Control group received intravenous infusion immediately after PCI completion following the same procedure as study group.

In cases where blood flow was not adequately restored, sodium nitroprusside was administered through intracoronary injection at 10 μg/kg/min or intra-aortic balloon pumping (IABP) may be utilized as adjunctive treatment [7]. As soon as the patient’s circulation returned to normal, treatment was discontinued. Routine anticoagulant and anti-inflammatory treatments were administered after the procedure.

Evaluation of parameters/indices

Cardiac injury

Venous blood samples were drawn (5 mL) from patients in a fasting state before and 7 days after treatment. Levels of serum creatine kinase-MB (CK-MB) and cardiac troponin T (cTnT) were assessed. Also, cTnT concentrations were monitored 24 and 48 h following concurrency.

Cardiac function

Left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and the left ventricular ejection fraction (LVEF) were evaluated at day 7 after treatment.

Resolution of ST-segment

The amplitude of ST-segment elevation in the most significant lead of an 18-lead electrocardiogram (ECG) was evaluated before and 90 mins after the procedure. Using T-P segment as a baseline, point 20 ms post the J point was identified. The difference between post-procedure and pre-procedure readings represented the ST-segment resolution, classified as complete (> 70 % decline), partial (30 - 70 % decline), or absent (< 30 % decline) [8].

Myocardial reperfusion

Thrombolysis in myocardial infarction (TIMI) risk score was employed to evaluate the level of blood flow restoration in the infarct-related arteries before and after treatment [9].

Adverse effects

A six-month follow-up was undertaken to document and analyze instances of platelet diminution, complications related to bleeding, and adverse cardiovascular effects such as angina, reperfusion-induced arrhythmias, and recurrent myocardial infarctions.

Statistical analysis

Data was analyzed using Statistical Packages for Social Science (SPSS) 25.0 software (IBM, Armonk, NY, USA). Normally distributed data were represented as mean ± standard deviation (SD), and intergroup variances were examined using student t-test. Categorical variables were expressed as percentages (%) and analyzed using Chi-square (χ^2) test. Ordinal data were analyzed using Mann-Whitney U test. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

There was no significant difference in baseline characteristics (gender, age, time elapsed from symptom onset to PCI intervention, Killip classification (Class I, II, III), site of myocardial infarction (left anterior descending artery, right coronary artery, left circumflex artery, left main trunk), associated conditions (hypertension, diabetes, hyperlipidemia), or smoking status ($p > 0.05$) between study and control groups (Table 1).

Table 1: Baseline characteristics

Indicator	Study	Control	t/χ^2 value	*P*-value
Male	37 (66.1)	32(57.1)	0.154	0.621
Female	19(33.9)	24(42.9)		
Age	64.3±5.3	65.3±4.8	1.047	0.298
Time from symptom onset to PCI treatment (h)	4.3±1.3	4.5±1.2	0.846	0.399
Killip classification				
Class I	14(25.0)	16(28.6)	0.573	0.472
Class II	29(51.8)	30(53.6)		
Class III	13(23.2)	10(17.8)		
Infarct location				
Left anterior descending	37(66.1)	35(62.5)	0.07	0.915
Right coronary	10(17.9)	12(21.4)		
Left circumflex	5(8.9)	6(10.7)		
Left main trunk	4(7.1)	3(5.4)		
Hypertension				
Yes	15(26.8)	16(28.6)	0.785	0.351
No	41(73.2)	40(71.4)		
Diabetes				
Yes	18(32.1)	20(35.7)	0.983	0.278
No	38(67.9)	36(64.3)		
Hyperlipidemia				
Yes	20(35.7)	19(33.9)	0.619	0.311
No	36(64.3)	37(66.1)		
Smoking				
Yes	32(57.1)	36(64.3)	0.103	0.714
No	24(42.9)	20(35.7)		

Values are either mean ± SD or n (%)

Cardiac injury

Both groups showed an increase in cTnT levels 24 h following symptom onset. This was followed by a decline in cTnT concentrations 48 h and 7 days after treatment, with study group exhibiting significantly lower levels compared to control group ($p < 0.05$). Serum levels of CK-MB similarly decreased in both groups, with significantly lower levels in study group 7 days after the procedure compared to control group ($p < 0.05$; Table 2).

Cardiac function

There was no significant difference in pre-treatment levels of left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular ejection fraction (LVEF) between both groups ($p > 0.05$). However, 7 days following treatment, study group showed significantly lower LVEDD and LVESD values but a significantly higher LVEF compared to control group ($p < 0.05$; Table 3).

ST-segment recovery status

Ninety minutes following treatment, Study group showed significantly higher levels of ST-segment resolution as well as higher rates of complete resolution compared to control ($p < 0.05$) 90 mins following treatment (Table 4).

Complications and adverse effects

There was no significant difference in gingival bleeding, gastrointestinal hemorrhage, and puncture site hematomas between the two groups ($p > 0.05$). No fatalities were recorded in either group. Also, study group showed significantly lower rate of reperfusion-induced arrhythmias compared to control group ($\chi^2 = 11.529$, $p < 0.05$; Table 6).

Table 2: Serum cardiac troponin T (cTnT) and creatine kinase-MB isoenzyme (CK-MB; mean ± SD; n=56)

Group	Treatment time	cTnT/ng/mL	CK-MB/U/L
Study group	Pre-treatment	1.73±0.26	19.61±5.84
	24h post-onset	2.42±0.62[a]	-
	48h post-onset	1.83±0.14[a]	-
	7days post-treatment	1.00±0.11[a]	8.10±1.10[a]
Control group	Pre-treatment	1.73±0.22	18.64±5.85
	24h post-onset	2.40±0.66[a]	-
	48h post-onset	1.88±0.50[a]	-
	7days post-treatment	1.07±0.18[a,c]	12.36±3.77[a,c]

[a]$P < 0.05$ vs pre-treatment levels, and [c]$p < 0.05$ vs study group

Table 3: Cardiac function parameters (mean ± SD; n = 56)

Group	LVEDD (mm)		LVESD (mm)		LVEF (%)	
	Pre-treatment	***7days post-treatment***	***Pre-treatment***	***7d post-treatment***	***Pre-treatment***	***7d post-treatment***
Study	58.76±3.28	49.93±2.83[a]	37.94±2.50	21.72±2.24[a]	44.46±3.42	59.99±2.44[a]
Control	58.55±3.11[b]	54.94±2.96[a,c]	38.67±2.51[b]	34.20±2.04[a.c]	45.59±2.95[b]	54.18±2.49[a.c]

Note: [a]$P < 0.05$ vs pre-treatment levels, [b]$p > 0.05$, [c]$p < 0.05$ vs study group

Table 4: Comparative analysis of ST-segment recovery 90 mins after treatment

Group	ST-segment resolution values/mm	No resolution	Partial resolution	Complete resolution
A	1.64±0.28	2(3.6)	18(32.1)	36(64.3)
B	1.11±0.22*	5(8.9)	31(55.4)	20(35.7)*

*$P < 0.05$ vs study group, values are either mean ± SD or n (%)

Table 5: Myocardial reperfusion (n=56; %)

Group	Time	Grade0	Grade 1	Grade 2	Grade 3
Study	Pre-treatment	24(42.9)	18(32.1)	9(16.1)	5(8.9)
	Post-treatment	2(3.6)[a]	2(3.6)[a]	6(10.7)[a]	46(82.1)[a]
Control	Pre-treatment	26(46.4)[b]	15(26.8)[b]	11(19.7)[b]	4(7.1)[b]
	Post-treatment	3(5.4)[a,c]	5(8.9)[a,c]	14(25.0)[a,c]	34(60.7)[a,c]

[a]$P < 0.05$ vs pre-treatment levels, [b]$p > 0.05$, [c]$p < 0.05$ vs study group

Table 6: Incidence of adverse effects (n, %)

Adverse effect	Features	Study	Control	χ^2	*P*-value
Adverse reaction	Gum bleeding	7(36.8)	8(33.3)	0.047	0.962
	Gastrointestinal Bleeding	3(15.8)	5(20.8)	0.034	0.977
	Puncture Site Hematoma	9(47.4)	11(45.9)	0.196	0.819
Adverse cardiovascular effects	Reperfusion Arrhythmia	5(55.6)	13(61.9)	11.529	0.001
	Angina	3(33.3)	5(23.8)	3.03	0.081
	Recurrent Myocardial Infarction	1(11.1)	3(14.3)	0.146	0.702

DISCUSSION

Pathogenesis of acute myocardial infarction (AMI) is principally rooted in coronary artery atherosclerosis, marked by the accumulation of unstable atherosclerotic plaques. Subsequent disintegration or rupture of these plaques instigates a cascade of thrombus formation, ultimately leading to vascular occlusion [10]. The condition poses significant morbidity and mortality rates and is a leading cause of mortality among cardiovascular diseases. Timely and enduring revascularization of the occluded vessels emerges as a quintessential strategy for preserving myocardial viability, alleviating clinical symptoms, and enhancing long-term patient prognoses.

Percutaneous coronary intervention (PCI), an integral component of modern AMI treatment, offers substantial benefits but is not devoid of limitations. Evolving evidence indicates that PCI may exacerbate the likelihood of untoward effects, including hemorrhagic complications, de novo thrombogenesis, and distal vascular re-occlusion. Hence, concomitant administration of anticoagulant agents alongside PCI becomes an imperative therapeutic option. This adjunctive approach aims to dampen platelet aggregation, thereby serving as a prophylactic measure against the incidence and worsening of thrombotic complications. Glycoprotein inhibitors, typified by their modulatory effects on platelet aggregation, function through targeted inhibition of platelet membrane glycoprotein IIb/IIIa receptors. Three pivotal agents in this category (eptifibatide, abciximab, and tirofiban) have gained widespread clinical application [11].

Tirofiban hydrochloride, a non-peptide antagonist, is distinguished by its high specificity for the GPIIb/IIIa receptor. It competitively binds to the receptor's cross-linking site through an aspartic acid, arginine, and glycine sequence, thus exerting potent inhibition against platelet aggregation triggered by either plasma factors or fibrinogen [12]. In patients with AMI undergoing percutaneous coronary intervention (PCI), numerous clinical investigations have revealed the efficacy of tirofiban in substantially mitigating postoperative incidences of myocardial infarction and mortality, compared to control groups devoid of tirofiban treatment. Nevertheless, the therapeutic impact appears to be modulated by administration time [13]. Two principal windows for drug delivery include; pre-procedural initiation and immediate post-procedural application. Conventional protocols often advocate for the administration of tirofiban immediately after PCI. Empirical studies have revealed that the coronary vascular milieu of patients with AMI during PCI is in a dynamic equilibrium between thrombus formation and dissolution [14].

Incomplete inhibition of platelet aggregation may compromise myocardial perfusion and escalate risk of adverse cardiovascular effects resulting in unfavorable prognosis. Complementary research corroborates that preemptive anti-coagulant regimens aimed at attenuating platelet aggregation prior to PCI may serve as a prophylactic measure against reperfusion injuries and severe cardiovascular complications [15]. Hence, a critical examination of the temporal effects of tirofiban administration on myocardial perfusion and complications in patients with AMI is imperative for implementing clinical guidelines.

The study revealed that study group showed lower cardiac troponin T (cTnT) levels within 24 h following symptom onset compared to control group. Given that all participating patients with AMI were admitted within 12 h after symptom onset and were treated within 24 h, it suggests that tirofiban manifests its myocardial effects in a relatively prompt fashion after administration. Furthermore, serum concentrations of creatine kinase-MB (CK-MB) decreased in both groups following treatment but were significantly reduced in study group, suggesting that preemptive pharmacotherapy substantially ameliorates myocardial injury. At the seventh day after

treatment, key metrics such as left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) were significantly reduced in study group compared to control group, while left ventricular ejection fraction (LVEF) was significantly increased, buttressing the premise that pre-procedural medication improves cardiac function more effectively. Utilizing the ST-segment resolution as a robust surrogate for myocardial microcirculatory health, study group manifested higher ST-segment resolution and greater incidence of complete resolution 90 min post-PCI. Myocardial perfusion grades in study group superseded those in control group. This improvement emanates from an augmented nitric oxide (NO) activity in the circulatory system, induced by pre-procedural tirofiban, which facilitates restoration of endothelial functionality within microvessels [16]. Also, tirofiban limits secretion of bioactive compounds and chemo-attractants from platelets, thereby mitigating microvascular spasm and subsequently enriching coronary blood flow, a phenomenon corroborated by improved blood flow grades [17]. Furthermore, there was no significant difference in incidence of adverse effects such as bleeding between the two groups. Incidence of reperfusion arrhythmias was less frequent in study group, while rates of recurrent angina or myocardial infarction and other untoward cardiovascular effects did not differ significantly between study and control group. This suggests that pre-procedural tirofiban administration does not increase the risk profile for surgical or cardiovascular complications, corroborating its safety.

Limitations of this study

This study has some limitations. The relatively small sample size may limit generalizability of the findings to broader population. Also, the study was conducted at a single center, potentially limiting its external validity. The short follow-up duration of 6 months may not capture long-term outcomes and complications. Furthermore, while efforts were made to randomize patients, possibility of selection bias were not completely ruled out. This study did not assess the impact of different dosages or durations of tirofiban infusion, which may affect outcomes. Finally, although no severe bleeding complications were observed, the study may not have identified rare adverse effects.

CONCLUSION

Tirofiban administration minimizes myocardial damage, augments myocardial perfusion, enhances microcirculatory integrity, and did not compromise postoperative safety or initiate adverse cardiovascular sequelae. Further larger-scale, multicenter studies with longer follow-up periods are required to confirm these findings and evaluate the safety and efficacy of different administration times for tirofiban infusion in patients with acute myocardial infarction undergoing percutaneous coronary intervention.

DECLARATIONS

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Ethical approval

Ethical clearance for this study was granted by The First People's Hospital of Tianshui Ethics Committee (approval no. 2024017).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Yawei Jia and Yunjin Zhang contributed equally to this work.

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