Tropical Journal of Pharmaceutical Research January 2019; 18 (1): 145-149
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v18i1.22

Original Research Article

Effect of tirofiban on cardiac function, cardiomyocytes and inflammatory reaction in patients with acute myocardial infarction during emergency percutaneous coronary intervention

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Sent for review: 19 October 2018 *Revised accepted: 27 December 2018*

Abstract

Purpose: *To investigate the effect of tirofiban on cardiac function, cardiomyocytes and inflammatory reaction in acute myocardial infarction (AMI) patients during emergency percutaneous coronary intervention (PCI).*
Methods: *Ninety AMI patients who underwent PCI for two years in Hanchuan Hospital, Hanchuan People's Hospital/Wuhan University People's Hospital, Hanchuan, China, were involved in this retrospective studies. Two groups were used (46 patients per group). The study group was treated with tirofiban, while the control group was without tirofiban exposure. Changes in brain natriuretic peptide (BNP), left ventricular end systolic diameter (LVESD) and left ventricular end diastolic diameter (LVEDD) were determined using a biochemical analyzer, while the inflammatory cytokines i.e. interleukin -6 (IL-6), tumor necrosis factor (TNF-) and high sensitive C reactive protein (hs-CRP) were assayed with ELISA kits.*
Results: *One week after operation, a significantly lower level of BNP and a significantly higher level of LVEF were seen in the study group than in controls ($p < 0.05$). After the operation, the study group had significantly lower levels of CK, CK-MB and cTnI than the control group ($p < 0.01$). Pre-operative IL-6, TNF-α and hs-CRP levels were comparable between both groups ($p > 0.05$), but their post-operative values were significantly lower in the study group than in the control group ($p < 0.01$).*
Conclusion: *The use of tirofiban for AMI patients undergoing PCI significantly reduces BNP, increases LVEF, improves cardiac function, protects myocardial cells, reduces the level of inflammatory cytokines, and inhibits inflammatory reactions.*

Keywords: *Percutaneous coronary intervention, Acute myocardial infarction, Tirofiban, Cardiac function*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Acute myocardial infarction (AMI) is a frequent and critical cardiovascular problem seen in clinics. Acute decrease or stoppage of blood supply caused by coronary artery stenosis or obstruction gives rise to AMI, which leads to myocardial necrosis. The main clinical manifestations of AMI are severe and persistent chest tightness, palpitations, chest pain, and

arrhythmia or shock [1]. The disease is associated with high frequency of occurrence, unfavorable prognosis and high mortality, and poor quality of life. In recent years, with rapid advances in economy, the lifestyle of people has changed a lot in China, resulting in increasing incidence of AMI.

Emergency percutaneous coronary intervention (PCI) is currently the major therapy for AMI. It is the preferred option for AMI based on the guidelines for AMI. Emergency PCI restores vessel recanalization in a short time, effectively reduces mortality and relapse rate of infarction, improves microcirculatory blood flow and cardiac function, and shortens the length of hospital stay [2-4]. Some studies have revealed that the use of tirofiban in emergency PCI can enhance clinical outcomes and safety [5]. However, it is not clear whether it affects postoperative cardiac function, myocardial cells and inflammatory response of patients.

This study was aimed at investigating the influence of tirofiban on postoperative cardiac function, myocardial cells and inflammatory response in patients with AMI undergoing emergency PCI.

METHODS

General characteristics of the patients

A retrospective study was carried out on 90 AMI patients who underwent emergency PCI on admission to the Cardiology Department of Hanchuan Hospital, Hanchuan People's Hospital/Wuhan University People's Hospital, Hanchuan, China from January 2015 to December 2017. Diagnosis of AMI was in accordance with the *Diagnosis and Treatment Criteria of AMI* [6].

Inclusion criteria: The included patients were those diagnosed with AMI in the clinic, and who were aged from 45 to 68 years, with presentations consistent with emergency PCI indication, and with onset time < 4 h.

Exclusion criteria: Subjects with PCI intolerance, severe liver and kidney dysfunction, malignant tumors, severe anemia, poor compliance, and mental disorder, were excluded. Two classes of patients were studied: those exposed to tirofiban (observation group) and patients who were not treated with tirofiban (these served as controls), with 45 subjects/group. The observation group comprised 23 men and 22 women with mean age of 57.4 ± 5.2 years, and mean disease course of 115 ± 51 min. There were 17 patients with hypertension, 8 with diabetes, and 11 smokers. In the control group, there were 24 males and 21 females aged between 46 to 67 years (mean age = 58.6 ± 5.4 years), with mean disease course of 122 ± 57 min. The control group had 15 patients with hypertension, 9 with diabetes, and 13 smokers. There were no statistical differences in general clinical data/biodata i.e., sex, age, disease course, hypertension, diabetes and smoking between two groups ($p > 0.05$). All patients signed informed consent form. This study received approval from the Ethical Committee of Hanchuan Hospital, Hanchuan People's Hospital and Wuhan University People's Hospital, Hanchuan City, China. (approval no. = 201810292). The study was conducted in line with the provisions in Helsinki Declaration promulgated in 1964 as amended in 1996 [7].

Treatment

At admission, all patients were given aspirin enteric-coated tablets (Sinopharm Shantou Jinshi Pharmaceutical Co. Ltd, H44025065), 300 mg *po*, and clopidogrel hydrogen sulfate tablets (Sinofi Pharmaceutical Co. Ltd, J20130083), 600 mg *po*. For the patients in the observation group, tirofiban (Hangzhou Zhongmei Huadong Medicine Co. Ltd, H20060265) was injected at 10 μg/kg into their coronary arteries during PCI, along with *i.v.* infusion of 0.15 μg/(kg/min) for 24 - 36 h. Both groups were treated with conventional drugs and β-blockers. Statins and angiotensin receptor antagonists were used depending on the patient's condition.

Therapeutic and biochemical indicators

The following indicators of patients were determined before, and one week after surgery using color Doppler echocardiography: cardiac function indicators i.e. BNP, LVESD, LVEDD and LVEF. Myocardial-related indicators (CK, CK-MB and cTnI) were determined with automatic biochemical analyzer. The inflammatory cytokines (IL-6, TNF-α and hs-CRP, LVESD, LVEDD and LVEF) were determined using ELISA kits.

Statistical analysis

All data were collected and then completely input into the research database after statistics. The data were analyzed using software SPSS 21.0. Enumeration data are presented as ratio, and were compared using χ^2 test. Measurement data are presented as mean ± standard deviation, and comparison between the two groups was done using *t*-test. Values of $p < 0.05$ were taken as statistically significant.

RESULTS

Cardiac function

As shown in Table 1, the pre-surgery levels of BNP, LVESD, LVEDD and LVEF in the two groups were comparable ($p > 0.05$). However, there were significant improvements in these cardiac function parameters after surgery: BNP was significantly lower in the tirofiban-treated patients than in controls, while the tirofiban treatment led to significant increase in LVEF, when compared with controls ($p < 0.05$). There were no significant differences in LVESD and LVEDD between the two groups ($p > 0.05$).

Table 1: Cardiac function indicators in the two groups (mean ± SD, n = 45)

Group	Time	BNP (pg/mL)	LVESD (mm)	LVEDD (mm)	LVEF (%)
Study	Before surgery	1261.4 ± 157.9	39.6 ± 5.2	56.7 ± 4.3	44.6 ± 5.3
	After surgery	352.7 ± 43.4*	33.9 ± 4.9*	52.8 ± 3.6*	51.2 ± 7.1*
Control	Before surgery	1485.7 ± 168.2	39.1 ± 5.3	56.9 ± 4.1	44.9 ± 5.4
	After surgery	551.6 ± 84.7#*	34.6 ± 5.4*	53.2 ± 3.7*	47.7 ± 6.8#*

*$p > 0.05$, relative to the preoperative value, #$p > 0.05$, relative to control group

Myocardium-related indicators

There were no significant differences in CK, CK-MB and cTnI in the two groups before surgery ($p > 0.05$). As shown in Table 2, the levels of myocardial-related indicators in the two groups were improved after surgery, with statistical differences between the preoperative and the postoperative values ($p > 0.05$). After surgery, CK, CK-MB and cTnI levels were significantly lower in the observation group than in the control group ($p > 0.05$).

Inflammatory cytokines

The pre-operation values of IL-6, TNF-α and hs-CRP were comparable between tirofiban-treated group and the control group ($p > 0.05$). In contrast, the levels of inflammatory cytokines were significantly improved after surgery ($p < 0.01$; Table 3). Moreover, IL-6, TNF-α and hs-CRP levels were significantly lower in the tirofiban-treated patients than in the controls ($p > 0.05$).

DISCUSSION

Acute myocardial infarction (AMI) is a cardiovascular disease resulting from acute myocardial ischemia due to coronary vascular occlusion caused by aggregation of platelet due to a variety of factors. The key in treating AMI is to lessen the area of vascular infarction and dredge the infarct-related artery as soon as possible, thereby restoring myocardial blood supply and reducing irreversible myocardial necrosis [8]. The sooner the dredging is effected, the better the outcome. In clinics, emergency PCI is the preferred therapy for AMI, and it has better effectiveness than thrombolysis or other conservative treatments [4].

Table 2: Myocardium-related indicators for the two groups (mean ± SD, N = 45)

Group	CK (μg/mL)		CK-MB (μg/mL)		cTnI (μg/mL)	
	Before surgery	*After surgery*	*Before surgery*	*After surgery*	*Before surgery*	*After surgery*
Study	257.61±28.43	131.62±16.58*	34.73±6.45	18.61±5.32*	31.52±5.21	19.84±3.47*
Control	259.73±26.39	172.24±19.67*	36.64±6.29	22.74±5.87*	32.74±5.11	27.62±3.85*
T	0.366	10.592	1.422	3.497	1.122	10.069
P	0.715	0.001	0.159	0.001	0.265	0.001

*$p > 0.01$, relative to value before surgery

Table 3: Levels of inflammatory cytokines in the two groups (mean ± SD, N = 45)

Group	IL-6 (μg/mL)		TNF-α (pg/mL)		hs-CRP (μg/mL)	
	Before surgery	*After surgery*	*Before surgery*	*After surgery*	*Before surgery*	*After surgery*
Study	47.61 ± 8.42	31.21 ± 6.57*	49.73 ± 6.34	38.86 ± 5.14*	15.73 ± 3.36	9.58 ± 2.15*
Control	48.94 ± 8.37	37.16 ± 6.92*	48.61 ± 6.29	43.54 ± 6.51*	15.87 ± 3.42	11.74 ± 2.86*
T	0.752	4.183	0.841	3.785	0.196	4.050
P	0.454	0.001	0.403	0.001	0.845	0.001

*$P > 0.01$, compared with the preoperative value

However, small amounts of thrombus may be detached during PCI, leading to microcirculation embolization; at the same time, surgical instruments may cause vascular endothelial injury which aggravates inflammatory reactions and affects myocardial cell reperfusion [9-11].

These issues can be mitigated through antithrombotic or intensive anticoagulant therapy, thereby enhancing the effectiveness of emergency PCI [5]. Tirofiban, a platelet GPIIb/IIIa receptor antagonist, inhibits platelet aggregation and prevents thrombosis [12]. It has been revealed that the use of tirofiban in AMI (involving ST-segment elevation) prior to emergency PCI resulted in improvement of cardiac function, with good safety [13]. In addition, using tirofiban before PCI can enhance cardiac function in patients with AMI, and it has been shown to protect vascular endothelium and restore coronary blood flow [14]. It has also been demonstrated that the use of tirofiban in AMI patients undergoing emergency PCI can ameliorate distal embolism and micro-circulatory disorder.

Brain natriuretic peptide (BNP) is generated from myocardial cells. The synthesis and secretion of BNP rise with increase in chamber wall tension, resulting in elevation of serum BNP levels. Thus, BNP reflects the severity of myocardial ischemia in patients, and so it is one of the indicators of cardiac function. The findings in this study reveal that BNP and LVEF were comparable between both groups one week after surgery, and the level of BNB was much lower in the tirofiban-treated patients than in patients who were not exposed to the drug. However, LVEF was much higher in the tirofiban-treated group than in the controls. There were no significant differences in LVESD and LVEDD between both groups one week after surgery. This indicates that the use of tirofiban in emergency PCI improves the cardiac function of AMI patients. These results are consistent with those reported by other investigators [15].

Creatine kinase (CK) and CK-MB are important myocardial enzymes, and CK is involved in the regeneration of adenosine triphosphate (ATP) which can regulate intracellular ATP concentrations. The CK-MB is found mainly in myocardial cells. To some extent, it is an important indicator of myocardial damage, and so it used for the diagnosis of AMI. The cTnI is used to assess the area of myocardial infarction due to the fact that it is specific to the myocardium, and it is also very sensitive. Thus, it is an ideal myocardial infarction indicator. Prior to surgery, the levels of CK, CK-MB and cTnI were comparable between the tirofiban-treated patients and controls, suggesting that the severity of myocardial damage in both groups were similar. In contrast, one week after surgery, these parameters were much lower in the tirofiban-treated group, showing significant decreases in the number of apoptotic myocardial cells.

It has been revealed that patients with acute coronary syndrome have significant inflammatory response, suggesting an association with arrhythmia [16]. Some studies have shown that tirofiban inhibits inflammatory cytokines and reduces inflammatory response [17]. The results of this study revealed no significant differences in TNF-α, Il-6 and hs-CRP between two groups before surgery. However, one week after surgery, the levels of inflammatory cytokines were significantly reduced in the two groups, relative to preoperative values, and the levels of TNF-α, IL-6 and hs-CRP were much lower in the tirofiban-treated patients than in controls. These results indicate that tirofiban markedly ameliorated inflammatory response in AMI patients after emergency PCI.

CONCLUSION

The application of tirofiban for AMI patients during emergency PCI significantly reduces BNP level, elevates LVEF level, enhances cardiac function, protects myocardial cells, reduces inflammatory cytokines, and inhibits inflammatory responses.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors read and approved the manuscript for publication. Zou Li-jun conceived and designed the study; Wang Qi-sheng, Zou Li-jun collected and analysed the data, while Wang Qi-sheng wrote the manuscript.

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