

Research Article

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Analysis of the Best Timing for Applying Tirofiban in PCI Operation for the Patients with ST Segment Elevation Myocardial Infarction

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Abstract: This study is a comparative analysis of the best timing for applying tirofiban in the PCI emergency treatment for STEMI patients. We selected 109 patients with ST-segment elevation myocardial infarction from October 2013 to October 2014 and divided them into two groups, the early treatment group (53 cases) received tirofiban during the operation and the later treatment group (56 cases) received tirofiban after operation. The analysis was then conducted. Results: The proportion of IRA forward flow in TIMI2-3 for the 1st group during the radiography was higher than 2nd group, 50 cases with TIMI3 blood flow and 52 cases with TIMI3 blood flow in later treatment group. Comparing the TIMI3 flow of both groups, the difference was not statistically significant; for the CK-MB 4h and 8h after operation as well as the LVEF after operation, the differences are were not statistically significant. The occurrence rate of hemorrhage complication was low for both groups. The early use of tirofiban can make the thrombus fully dissolve and coronary blood flow remains in a good state, which is not only beneficial for myocardial perfusion but also helpful for deciding the length and side branch situation of coronary artery pathological changes.

Keywords: PCI, MI, tirofiban, treatment timing

1 Introduction

ST segment elevation myocardial infarction (STEMI) results from a coronary atherosclerotic plaque rupture caused by the joint effect of blood flow shearing force and

nervous-humoral regulation, which produces a series of subsequent effects and finally blocks the coronary vessels completely [1]. The first goals of STEMI treatment are to effectively, reasonably, and quickly open up the infarct vessels, improve myocardial microcirculation, realize reperfusion of infarct myocardium as early as possible, and remedy the nearly necrotic myocardium as well as to improve the cardiac function [2]. Intravenous thrombolysis and direct percutaneous coronary intervention (PCI) are the main treatment means for reperfusion [3]. A recent (2010) study has shown that early use of tirofiban facilitates the direct PCI effect on STEMI. However, there are no definite research conclusions on when to apply tirofiban in the emergency PCI for maximum safety [4]. For this reason, the authors of the present study conducted analysis of the efficacy and safety of using tirofiban in emergency PCI for STEMI patients at different times and further confirmed the curative effects.

2 Data and methods

2.1 General data

109 acute STEMI patients who received PCI during October 2013 to October 2014 were selected and divided into an early treatment group (53 cases) and a later treatment group (56 cases). The early treatment group included 38 males and 15 females, aged from 36 to 78 and on average 56.2±8.1 years old; the later treatment group included 40 males and 16 females, aged from 35 to 81 and on average 55.4±7.7 years old.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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Informed consent: Informed consent has been obtained from all individuals included in this study.

2.2 Inclusion criteria

Treatment conformed to the Diagnosis and Treatment Guidelines for Acute ST-segment Elevation Myocardial Infarction formulated by the Chinese Society of Cardiology in 2010. The treatment time of patients is no more than 12 h after the disease onset. Patients were informed and signed the letter of consent.

2.3 Exclusion criteria

Excluded were the following patients: those having a past medical history of intracranial malignant tumor, cerebral hemorrhage, arterial aneurysm or arteriovenous malformation, transient cerebral ischemia, or ischemic stroke within 6 months; those suffering from a severe facial wound, closed head trauma, peptic ulcer, or suspected aortic dissection; those who have received CPR for over 10 min or have suffered trauma, a visceral hemorrhage, or had major surgery or major vascular access within 2–5 weeks.

2.4 Treatment and medication method

All patients received 300 mg aspirin immediately after being hospitalized and later received 100 mg orally daily (they should take this medicine lifelong). In addition, they immediately took 300–600 mg clopidogrel orally and later, took 75 mg daily. The time of taking the medication shall be no less than 18 months after the operation. In addition, the patients received subcutaneous injection of 0.4 ml low molecular heparin every 12 hours for 7 days after the surgery.

Use of tirofiban (Lunan Better Pharmaceutical Co., Ltd.) solution: The tirofiban use time for early treatment group was 1–2 h before the radiography for coronary artery; ② The tirofiban use time for the later treatment group was just after the PCI operation and return to the ward. Both groups of patients received intravenous injection of tirofiban within 3 min of 10 µg/kg and then received continuous intravenous injection at the rate of 0.15 µg 0–1·min⁻¹ for 24–36 h. In addition, both groups of patients received conventional standard treatment for coronary heart disease (CHD).

2.5 PCI operation method and coronary artery angiography

Preoperative examinations such as routine blood tests, biochemical test, hepatitis B testing, blood coagulation testing, and examination for possible HIV were performed for the two groups of patients before the operation; the PCI operation were conducted after ascertaining that there was no surgical contraindication. After sending the patients to the conduit room, the patients' operation site was disinfected using iodophor; local anesthesia (lidocaine) was initiated, and the patients were connected to the pressure monitor and ECG devices. Upon the completion of those steps, the radial artery or femoral artery of the patient was punctured using the Seldinger method, a guide wire was placed along with an artery sheath catheter after successful puncture; the catheter of coronary artery angiography was then placed at the introitus of the coronary artery to conduct the contrast examination. Generally, the coronary artery angiography of 6 to 8 body positions were chosen to judge pathological vessels; specific judgment had to be made according to the condition of the pathological vessels and the degree of coronary artery stenosis shown by the coronary artery angiography. After the completion of coronary artery angiography, the proper guide wire and catheter were chosen to place into the pathological vessels according to the pathological changes shown by angiography in combination with the vessel arrangement. The sacculus of proper inner diameter in the vessels for pre-dilation was put in place, and finally, the stent was placed by the routine method.

2.6 Determination criterion of surgical effect

If the stent completely spanned the lesion site of stenosis, the vessels expanded sufficiently, the residual stenosis visible in angiography was less than 30%, the vessels before and back of the stenosis lesion are parallel to the vessels at the stent section, and the far-end blood flow of lesion vessels meets the TIMI3 standard, the operation is determined to be successful.

2.7 Observation indicators

2.7.1 The procedure used for determination of blood flow classification after the treatment of thrombolysis in myocardial infarction (TIMI) follow:

Class 0: No instillation, infarction related artery (IRA) is thoroughly occluded, and there is no contrast medium flowing at the occlusion site and far end of vessels. Class 1: Slight instillation. There is a small amount of contrast medium flowing at the occlusion site of the IRA. Class 2: Partial instillation. There is contrast medium flowing at the occlusion site of the IRA and its distal vessels; compared with its proximal vessels, the contrast medium of its occlusion site flows slowly. Class 3: Complete instillation. There is contrast medium rapidly and fully flowing at the occlusion site of the IRA and its distal vessels; the speed of the forward blood flow to the distal lesion vessel bed is equal to that to proximal lesion vessel bed.

2.7.2 Markers of myocardial damage

We determined the level of (creatinine kinase) CK and creatine kinase-MB (CK-sMB) 4 hours and 8 hours after the patients had the operation, and then determined the level of left ventricular ejection fraction (LVEF) 24 hours after the patients had the operation.

2.7.3 ST-segment resolution degree on ECG

We compared the ECG of different groups of patients after 90 min of recanalization with that of department entrance, taking the T-P segment as the equipotential line of ST segment elevation, and measured the voltage elevation range of ST segment of the later 20 ms at the J point. We calculated the total elevation (Σ ST elevation, Σ STE) of the elevation range of the ST segment lead according to the site of infarction. Here, the VI-V6 lead means anterior wall myocardial infarction, I and aVL lead means high lateral wall myocardial infarction, the VI-V4 lead means anterior septal myocardial infarction, the II, III and aVF lead means inferior wall myocardial infarction.

2.7.4 Major adverse cardiovascular events (MACE)

These events include death by any cause, including: Infarction angina with ST-T ischemic change (ST segment

depression or elevation of 0.1 mV). New-onset myocardial infarction. Myocardial revascularization.

2.7.5 Safety indicators

Safety indicators were as follows. Severe hemorrhage mainly refers to intracranial hemorrhage or if the decrease of hemoglobin of the patients before and after operation is $>50\text{g/L}$, Slight hemorrhage mainly refers to hemoptysis, hematuria, and alimentary tract hemorrhage, or the decrease of hemoglobin of the patients before and after operation is $(30\sim50)\text{g/L}$; Thrombocytopenia, wherein the number of platelet before operation is normal, whereas that after operation is $<100\times 10^9/\text{L}$.

2.8 Statistical treatment

The statistical analysis of research data was conducted via statistical analysis software SPSS17.0. The enumeration data was compared and analyzed via a chi-square test, and the difference between measurement data is compared and analyzed via a Student's *t*-test. Ranked data and abnormal measurement data are conducted by non-parametric tests. A significant difference between these statistical results is indicated by $P<0.05$.

3 Conclusions

The following comparisons were made to come to our conclusions:

- 3.1 Comparison of flood flow condition of coronary artery TIMI of two groups of patients before and after operation and no reflow during operation: The proportion of the forward flood flow of IRA of the patients in the early-stage group to TIMI2-3 level was higher than that of the patients in the later-stage group, and the difference was statistically significant. Among the patients in the early-stage group, there were 3 patients who have no reflow and 50 patients had TIMI3 blood flow. Among the patients in the later-stage group, there were 4 patients who had no reflow and 52 patients who had TIMI3 blood flow. The comparison between the TIMI3 level blood flow of patients in two groups was not statistically significant. See details in Table 1.
- 3.2 Comparison of microcirculation perfusion of CK-MB, LVEF indicators and postoperative reaction of

Table 1: Comparison of flood flow condition of coronary artery TIMI of patients in two groups before and after PCI operation [%].

Group	TIMI blood flow classification before operation				TIMI blood flow classification after operation		
	Class 0	Class 1	Class 2	Class 3	Class 1	Class 2	Class 3
Early-stage group	29 (51.72)	7 (13.21)	7 (13.21)	10 (18.87)	0 (0)	3 (5.67)	50 (94.34)
Later-stage group	37 (66.07)	10 (17.86)	4 (7.14)	5 (8.93)	1 (1.79)	4 (7.14)	52 (92.86)
P value	0.763	0.656	0.036	0.0033	0.002	0.020	0.972

Table 2: Comparison of microcirculation perfusion of CK-MB, LVEF indicators and postoperative reaction of patients in two groups ($\bar{x} \pm s$).

Group	CK-MB (U/L)		LVEF 2 days after operation (%)	Related ST segment resolution 90min after operation (mm)
	4 hours after operation	8 hours after operation		
Early-stage group	164.3±10.4	57.3±6.4	56.7±10.6	1.922±0.563
Later-stage group	168.3±9.3	56.3±4.8	55.6±10.2	1.064±0.286
P value	0.372	0.262	0.867	0.016

Table 3: Comparison of MACE condition during hospitalization and safety indicators of the patients in two groups.

Group	MACE during hospitalization				Safety indicators		
	Death	Myocardial revascularization	New-onset myocardial infarction	Infarction angina	severe hemorrhage	Slight hemorrhage	Thrombocytopenia
Early-stage group	2	0	0	0	0	4	0
Later-stage group	1	0	0	1	0	2	0
P value	0.572	0.262	0.867	0.916	0.742	0.372	0.262

patients in the two groups: The comparison of CK-MB 4 hours and 8 hours after operation and LVEF condition after operation of patients in two groups was not statistically significant; the ECG-related lead ST segment after the revascularization of patients in the early-stage group for 90 min was higher than that of patients in the later-stage group, and the difference was statistically significant. See details in Table 2.

- 3.3 Comparison of MACE condition during hospitalization and safety indicators of the patients in two groups: The comparison of MACE condition during hospitalization of patients in two groups was not statistically significant, and there was no new-onset myocardial infarction and myocardial revascularization. See details in Table 3. The patients in two groups had no severe intracranial hemorrhage or thrombocytopenia. The difference of the comparison with the occurrence rate of hemorrhage complication was not statistically significant. See details in Table 3.

4 Discussion

In recent years, tirofiban has been gradually applied in clinical treatment in China; it is the only receptor antagonist of platelet membrane glycoprotein used in China [5]. By binding to the specific receptor GPIIb/IIIa, competitive inhibition will be aroused to its binding to the fibrinogen, the platelet aggregation effect will be weakened and the final access for thrombosis will be blocked, thus realizing the antiplatelet effect. According to relevant meta-analyses, the early use of antagonist of receptor GPIIb/IIIa could more significantly improve the TIMI blood flow III of STEMI patient before operation rather than using it in a later time [6,7]. Because of this, tirofiban is more suitable for the AMI patient; it can increase the success rate of PCI.

In the present study, by comparing the TIMI blood flow grade before operation of the two groups of patients, it can be seen that the patients' conditions when using antagonist of receptor GPIIb/IIIa in an early period are much better than that of the patients using it in later

period; that indicates that pre-operation use of tirofiban could remarkably improve the IRA coronary blood flow and myocardial perfusion in the corresponding area before PCI, bring down platelet aggregation and adhesion and increase the reperfusion rate of occluded blood vessel for quick passing of the guide wire, decrease operation time and increase the success rate of PCI. However, the TIMI blood flow grade after PCI of the two groups of patients shows no significant difference. The possible reasons may be the short interval between medication time, too small a number of samples, and the short interval between attack and PCI, and other relevant factors [8,9].

ST segment resolution by an electrocardiogram is the easiest and most effective way for myocardial microcirculation evaluation. Some studies have indicated that the ST segment resolution of electrocardiogram is an important independent indicator that can predict the ratio of adverse events occurring during hospitalization [10,11]. The result of this study shows that by comparing the electrocardiographic lead ST segment resolution of the early-treated patients and the late-treated patients after 90 min recanalization, the ST segment resolution of the former is remarkably higher than that of the later. The possible reasons may be that there is a small difference between the time of using tirofiban to the early-treated patients before operation and the late-treated patients and the relevant related artery gets infarcted in time, thus causing no statistical difference in evolution of myocardial enzyme and LEVF determination [12,13].

IRA coronary blood flow and myocardial perfusion in the corresponding area of early-treated patients before operation was remarkably improved. Regarding the comparison with the ST segment resolution, the electrocardiographic lead ST segment resolution of the early-treated patients after 90 min recanalization is much higher than that of the late-treated patients; the difference was statistically significant. However, due to the unobvious MACE difference between both groups, the difference is not statistically significant. The possible reason is that the tirofiban was allowed to be applied after emergent PCI in all cases, thus there is a small difference between the pre-operation application time and post-operation application time.

In addition, no patients in either group had a serious intracranial hemorrhage during hospitalization. There is one other important issue that requires attention: at present, tirofiban is often used in combination with clopidogrel, aspirin, and heparin. However, the combination of these three medicines may increase the incidence of bleeding. Therefore, patients need to be closely observed for early detection and treatment [15,16].

In conclusion, early application of tirofiban can fully dissolve a thrombus and keep the coronary blood flow in a good state; not only is that important for myocardial perfusion, but also conducive to judging the coronary artery lesions length, distal lesion, and side branch; significantly increase the success rate of PCI; make revascularization fuller; delay thrombosis in the stent; and effectively the lower incidence rate of MACE.

Conflict of interest statement: Authors state no conflict of interest

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