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Clinical effects of treatment with Tirofiban on patients with high-risk NSTE-ACS after PCI

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Abstract. – OBJECTIVE: To explore clinical effects of Tirofiban treatment on patients with high-risk non-ST-segment elevation acute coronary syndrome (NSTE-ACS) after percutaneous coronary intervention (PCI).

PATIENTS AND METHODS: 107 patients with high-risk NSTE-ACS after PCI were selected and were divided into two groups. One group of 56 patients was treated with Tirofiban and a second group of 51 patients was taken as control. The occurrence conditions of creatine kinase-myoglobin (CK-MB), cardiac troponin1 (cTnI) level, hemorrhage incidents and major adverse cardiac events (MACE) incidents after treatments were compared.

RESULTS: After 24 h operation, CK-MB and cTnI level in Tirofiban group were both significantly lower than those in control group ($p < 0.05$), while the difference of hemorrhage incidents between two groups is of no statistical significance ($p < 0.05$); and the differences in overall occurrence rate of MACE incidents and the occurrence rate of angina pectoris after infarct between two groups were statistically significant ($p < 0.05$).

CONCLUSIONS: Tirofiban could improve the blood supply condition of hearts of patients with high-risk NSTE-ACS after emergent PCI, lower the occurrence rate of MACE incidents, and decrease the risk of hemorrhage.

Key Words:
ACS, NSTE, Tirofiban, PCI, MACE incidents.

Introduction

Non-ST-segment elevation acute coronary syndromes (NSTE-ACS) includes unstable angina pectoris (UA) and non-ST segment elevation myocardial infarction (NSTEMI). The cause of complications and high mortality is due to rupture of unstable atherosclerotic plaque in the coronary artery, which leads to the formation of incomplete obstructive thrombus and, therefore, acute cardiac ischemia syndrome. Since platelet aggregation is an important consequence and initiative factor of the formation of thrombus, antiplatelet therapy has of particular importance. Therefore, we discussed the impact of enhanced antithrombotic therapy on patients with high-risk NSTE-ACS treated by Tirofiban after emergent percutaneous coronary intervention (PCI).

Patients and Methods

Patients

The study was conducted on 107 patients with high-risk NSTE-ACS admitted in Xuzhou Central Hospital between January 2013 and January 2015. The study was started since from the appearance of the first symptom. There were 61 were male patients and 46 were female patients of age range between 35 to 75 years, and with an average age of 58.13 ± 14.70 years. All patients selected were confirmed to the diagnosis by the standard of high-risk patients GRACE score > 140 in NSTE-ACS diagnosis instruction which was formulated by Chinese Society of Cardiology of Chinese Medical Association in 2012.

The following patients were excluded: (1) Patients having the history of myocardial infarction disease, PCI and coronary artery bypass grafting; (2) Patients with chronic cardiac failure and liver and kidney function deficiency; (3) Allergic to aspirin, heparin, Tirofiban and contrast agent; (4) Unmanageable hypertension; (5) Patients having active hemorrhage and hematological system dis-

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eases within three months before being selected; (6) Patients having cerebrovascular disease and peripheral vascular disease.

There were 56 patients in Tirofiban group and 51 patients in control group according to whether they were treated by Tirofiban or not, and there were matched for gender, age, BMI, history of smoking, history of alcohol intake, history of hypertension, history of diabetes mellitus and the intakes of nitrate lipid, β-BRB, ACEI/ARB and statins ($p > 0.05$).

Therapeutic Methods

PCI operations were performed on patients in both groups within 24 h from the appearance of symptoms. 300 mg aspirin for chewing and 300 mg clopidogrel for oral intake were given before the operation. Coronary angiography was done through the right radial artery or femoral artery puncture path to determine the number of diseased coronary arteries and culprit's vessels, after which PCI was given. After the operation, it was shown by coronary angiogram that all residual stenosis were lower than 20%, and level 3 thrombolysis in myocardial infarction (TIMI) blood flow appeared (operation successfully completed). All patients were normally treated with aspirin, clopidogrel and enoxaparin sodium, and patients with indications were treated by β-BRB, nitrate lipid and ACEI/ARB simultaneously. Intravenous bolus injection was used to inject 10 μg/kg Tirofiban to patients in Tirofiban group, and the injection period was no less than 3 min, after which Tirofiban was continuously injected by intravenous route for 36 h at the rate of 0.15 μg/kg/min.

Detections of the Levels of CK-MB and cTnI

7600-020 automatic biochemical analyzer (produced by Hitachi Corporation, Tokyo, Japan) and its corresponding kits (produced by Shanghai Fosun Long March Medical Science Co. Ltd, China) were adopted to detect the levels of CK-MB of patients at the time of admission and was repeated after 24 hours of operations by the method of immunosuppression, and Centaur CP chemiluminescence apparatus (produced by Siemens Corporation, Munich, Germany). The corresponding kits (produced by Siemens Corporation, Munich, Germany) were adopted to detect the levels of cTnI of patients at the time of admission and 24 hours after operations by the method of chemiluminescence.

Definitions of Hemorrhage and MACE Incidents

(1) Hemorrhage Incidents: Hemoglobin declined more than 50 g/L or red blood cell hematocrit declined more than 15% caused by intracranial hemorrhage and alimentary tract hemorrhage were considered as massive hemorrhage; while hemoglobin declined more than 30 g/L or red blood cell hematocrit declined more than 10% caused by spontaneous hematuria and hematemesis were considered as slight hemorrhage. Blood loss did not reach the criteria above was considered as non-obvious hemorrhage. (2) MACE Incidents: The occurrence conditions of cardiac incidents such as secondary heart failure, severe arrhythmia (ventricular tachycardia, ventricular fibrillation and atrioventricular block of level II, level III or above), post-infarction angina pectoris, recurrence of myocardial infarction, cardiac death and so on of patients were recorded within 6 months since showing symptoms (including the period of hospitalization).

Statistical Analysis

SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was adopted, and the measured data were represented by mean ± standard deviation. The independent sample *t*-test was adopted for comparison between groups; rates were represented by percentages, and χ^2-test or Fisher exact test was adopted for comparison between groups. $p < 0.05$ means the difference was of statistical significance.

Results

Comparison of CK-MB and cTnI Levels Between Two Groups

The differences of CK-MB and cTnI levels between two groups at the time of admission to hospital are of no statistical significance ($p < 0.05$); while 24 hrs after the operation, CK-MB and cTnI levels of Tirofiban group are both significantly lower than those of control group ($p < 0.05$) (Table I).

Comparison of Occurrence Conditions of Hemorrhage Incidents Between Two Groups

There was one case of massive hemorrhage (1.8%), one case of slight hemorrhage (1.8%) and one case of non-obvious hemorrhage (1.8%) in the Tirofiban group. There were no cases of

Table I. Comparison of CK-MB and cTnI levels.

Groups	n	CK-MB (u/L)	cTnI (ng/ml)
Tirofiban group	56		
Before treatment		50.78 ± 9.62	1.25 ± 0.65
After treatment		216.88 ± 35.26*	4.18 ± 1.03*
Control group	51		
Before treatment		50.71 ± 10.10	1.40 ± 0.61
After treatment		244.64 ± 18.83	4.71 ± 1.08

Note: Compared with control group after treatment, *$p < 0.05$.

massive hemorrhage (0%), one case of slight hemorrhage (1.9%) and one case of non-obvious hemorrhage (1.9%) in the control group. The difference of occurrence rates of overall hemorrhage incidents between the two groups is of no statistical significance ($p > 0.05$).

Comparison of Occurrence Conditions of MACE Incidents between Two Groups

The difference of overall occurrence rates of MACE incidents between two groups was of statistical significance ($p < 0.05$), among which the difference in the occurrence rate of post-infarction angina pectoris between the two groups was of statistical significance ($p < 0.05$) (Table II).

Discussion

In recent years, the occurrence rate of acute coronary syndrome (ACS) is increasing year by year for patients with NSTE-ACS, and especially for those high-risk patients NSTE-ACS would develop into STE-ACS or even sudden cardiac death without treatment in a timely and effective manner[1,2,9]. Currently, PCI operation is considered as the primary method for high-risk NSTE-ACS myocardial reperfusion therapy, and at the same time anti-thrombotic drugs enhancement has become particularly important. The regularly used anti-thrombotic drugs clinically include aspirin, clopidogrel, and heparins. By the inhibition of epoxidase, aspirin could inhibit the synthesis of blood platelet thromboxane A2 (TXA2) and release or reduce the platelet aggregation. Clopidogrel could block platelet aggregation through ADP pathway, and both of them are invalid for platelet aggregation induced by other activators. However, the common pathway of inducing platelet aggregation is GPIIb/IIIa receptor on the surface of blood platelet, thus blocking its function is sure to eliminate platelet aggregation induced by activators.

Tirofiban belongs to non-peptide blood platelet glycoprotein IIb/IIIa (GPIIb/IIIa) receptor antagonist, which has high degree of specificity and can block the conjunction of fibrinogen and receptor and, therefore, inhibit the final pathway of platelet aggregation, which competitively inhibit platelet crosslinking and aggregation caused by various reasons including adrenaline, 5-hydroxytryptamine, adenosine 5'-diphosphate (ADP), collagen, thrombin, etc. The addition of Tirofiban to the conventional anti-platelet drug treatments can provide more powerful, comprehensive and thorough anti-thrombotic effects, which are beneficial for cardiac blood supply and cardiac function[3]. We showed that 24 h after PCI operation, CK-MB and cTnI levels in the Tirofiban group were both significantly lower

Table II. Comparison of occurrence conditions of MACE incidents [cases (%)].

Groups	N	Secondary heart failure	Severe arrhythmia	Post-infarction angina pectoris	Recurrence of myocardial infarction	Cardiac death
Tirofiban group	55	2 (3.6%)	4 (7.3%)	1 (1.8%)*	1 (1.8%)	1 (1.9%)
Control group	52	4 (7.7%)	6 (11.5%)	8 (15.4%)	3 (5.8%)	2 (3.8%)
χ^2		0.241	0.181	4.746	0.321	0.000
p		0.623	0.671	0.029	0.571	0.987

than those in the control group, which directly demonstrates the anti-thrombotic treatment effects of Tirofiban.

The studies have shown by using Tirofiban as the basis of aspirin, clopidogrel and heparin treatments for the treatment of high-risk ACS patients. The patients have received emergent PCI treatment has better clinical effects, but there were some adverse reactions such as hemorrhage and thrombocytopenia[4,5]. The results of this research showed that patients in Tirofiban group have no obvious increase in terms of overall hemorrhage incidents. In the recent years, it has been also shown that GPIIB/IIIA receptor antagonists (Tirofiban) can significantly reduce the occurrence rate and morbidity rate of myocardial infarction in patients with acute coronary syndrome[6-10]. The two groups have no significant differences in cardiac incidents such as secondary heart failure, severe arrhythmia, recurrence of myocardial infarction and cardiac death, while occurrence rates of post-infarction angina pectoris and overall MACE incidents in Tirofiban group were significantly lower.

Conclusions

Tirofiban improves cardiac blood supply, lowers the levels of myocardial enzymes and troponin and occurrence rate of MACE incidents in enhanced anti-thrombotic treatments of patients with high-risk NSTE-ACS after emergent PCI operation, and also reduces the risk of hemorrhage.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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