Journal of Hainan Medical University

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Effect of intracoronary injection of tirofiban combined with anisodamine on myocardial perfusion in patients with STEMI after PCI

Xiao-Gang Zhu, Li-Yue Wang✉, Hao-Jin Ren, Jin-Hua Liu

Department of Cardiology, Puren Hospital of Wuhan City Hubei Province, Wuhan City, Hubei Province, 430081, China

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
STEMI
PCI
Tirofiban
Anisodamine
Myocardial perfusion

ABSTRACT

Objective: To analyze the effect of intracoronary injection of tirofiban combined with anisodamine on myocardial perfusion in patients with STEMI after PCI. **Methods:** A total of 78 patients with acute ST segment elevation myocardial infarction (STEMI) who received PCI therapy in our hospital were randomly divided into control group and observation group, control group accepted routine PCI treatment, observation group received intracoronary injection of tirofiban and anisodamine in PCI, and myocardial perfusion of two groups was compared. **Results:** QRS duration values of observation group the instant after PCI and 4h after PCI were less than those of control group (P<0.05); ^{99m}Tc-MIBI and ^{18}F-FDG intake of observation group after PCI were more than those of control group (P<0.05); serum MCP-1, sFas, Copeptin, OPN and vWF levels of observation group 4 h after PCI were lower than those of control group (P<0.05). **Conclusions:** Intracoronary injection of tirofiban combined with anisodamine can optimize myocardial perfusion in patients with STEMI after PCI, and has positive clinical significance.

1. Introduction

1.*Introduction*

Acute ST elevation myocardial infarction (STEMI) is a clinical common type of myocardial infarction, and percutaneous coronary intervention (PCI) within 12 hours after disease attack can achieve high success rate. At the same time of confirming the effect of PCI on restoring the infarcted myocardium function in patients with STEMI, many clinical researchers have also found that there is a certain probability of microcirculation dysfunction, no perfusion in infarcted myocardium and other circumstances after PCI, which is directly because that PCI damages coronary artery intima and leads to platelet aggregation and microthrombosis[1,2]. It is the hotspot of current clinical studies to effectively reduce the probability of thrombosis in PCI and increase myocardial perfusion in infarcted area. Intracoronary injection of anticoagulant drugs in PCI is a new method to optimize operation effect, but the drug choice for intracoronary injection remains controversial[3]. At present, there have been case reports about intracoronary injection of tirofiban and anisodamine for intervention of myocardial perfusion, intracoronary injection of tirofiban combined with anisodamine was the research focus of the study, and the effect of the compatibility therapy on improving the effect of PCI treatment and increasing myocardial perfusion was mainly stated.

2. Materials and methods

2.1. General information

A total of 78 patients with STEMI received emergency PCI therapy in our hospital from July 2013 to July 2015, and all patients were treated within 12 hours after onset. Patients were without PCI treatment-related contraindications, and not allergic to tirofiban and anisodamine. According to the random number table, the included patients were divided into observation group and control group (n=39). Control group included 22 male cases and 17 female cases, they were 56-70 years old and (64.18±5.93) years old in average,

✉Corresponding author: Li-Yue Wang, Department of Cardiology, Puren Hospital of Wuhan City, No.1, Benxi Street, Qingshan District, Wuhan City, Hubei Province, 430081, China.
Tel: 13507149955
Fund project: Project of Hubei Provincial Fund for Nature No: 2010CDB8701.

27 cases were with hypertension, 19 cases were with diabetes and 32 cases were with smoking history; observation group included 21 male cases and 18 female cases, they were 54-72 years old and (64.76±5.87) years old in average, 31 cases were with hypertension, 18 cases were with diabetes and 33 cases were with smoking history. The study had the informed consent form patients' families and was approved by the hospital ethics committee, the patients showed no statistically significant difference in gender, age or medical history distribution (P>0.05), and they could be compared in follow-up study.

2.2. Treatment methods

Both groups received emergency PCI, specifically as follows: aspirin, clopidogrel and other antiplatelet drugs were taken orally before operation, 300 mg respectively. Coronary angiography and PCI were performed via femoral artery, 10 000 U heparin was injected via artery before PCI started, a balloon was used to pre-expand the lesion, then stents was placed, pre-expansion pressure was appropriate when the balloon could fully open, and balloon expansion time was < 10 s. Stent diameter was selected (its ratio to vascular diameter 1:1), and stent release pressure was 14-18 atmospheres. Aspirin 100 mg/d was taken for a long time after operative, and clopidogrel 75 mg/d was taken for 9-12 months. Low-molecular-weight heparin sodium 0.5 mL was subcutaneously injected 4-6 d after operation, 2 times/d for consecutive 5 d. Statins were conventionally applied to regulate lipid, and patients with hypertension and diabetes patients received conventional antihypertensive and hypoglycemic therapy.

Observation group received intracoronary injection of tirofiban and anisodamine in PCI, specifically as follows: after guide wire or balloon passed through the lesions, patients received intracoronary injection of loading dose of tirofiban 0.5 mg (10 mL), which was completed within 1-3 minutes; anisodamine, according to the patients' heart rate, blood pressure and hemodynamic parameters, was fractionally injected into coronary artery with 200 μg/mL concentration, 200 μg for the first time and 200 μg again after 2 min interval. Then intravenous pumping was maintained at 0.15 μg/(kg • min) for 24-36 h.

2.3. Observation indexes

Infarction-related lead QRS duration was measured in perioperative stage of PCI, and the average of all lead QRS duration was calculated.

Before and 4h after PCI, ^{99m}Tc-MIBI and ^{18}F-FDG dual-isotopic myocardial perfusion imaging was performed in patients under resting state. Short-axis slices cardiac apex, midpiece and cardiac base were semi-quantitatively analyzed, the highest segment of ^{99m}Tc-MIBI radioactive counting was set to 100, ^{18}F-FDG counting of the section was also set to 100, they were used as the standard to calculate the relative counting of the radioactive counting of other segments to the counting of highest segment, and myocardial intake 75% indicated decreased perfusion.

Monocyte chemotactic factor-1 (MCP-1), apoptosis-inhibiting factor (sFas), Copeptin, osteopontin (OPN) and vascular willebrand factor (vWF) were determined.

2.4. Statistical methods

SPSS23.0 software was used to input and analyze data, measurement data comparison between groups was performed by t test, count data was by chi-square test and P<0.05 indicated statistical significant differences.

3. Results

3.1.QRS duration

Differences in QRS duration of two groups on admission were not statistically significant (P>0.05); the instant after PCI and 4 h after PCI, QRS duration values of observation group were significantly less than those of control group, and differences in QRS duration values of two groups the instant after PCI and 4 h after PCI were statistically significant (P<0.05), shown in Table 1.

3.2. Myocardial perfusion

Differences in ^{99m}Tc-MIBI and ^{18}F-FDG myocardial intake of two groups were not statistically significant before PCI (P>0.05), 99mTc-MIBI and 18F-FDG myocardial intake of both groups increased after PCI, the myocardial intake increase of observation group was more significant (P<0.05), and ^{99m}Tc-MIBI and ^{18}F-FDG intake of observation group after PCI were more than those of control group (P<0.05), shown in Table 2.

Table 1

Comparison of peri-PCI QRS duration values (ms).

Groups	Case No.	On admission	Instant after PCI	4 h after PCI
Observation group	39	93.29±5.32	83.25±6.82	81.27±4.93
Control group	39	94.61±6.39	92.14±8.69	90.59±8.47
t		0.281	8.293	7.384
P		>0.05	<0.05	<0.05

3.3. Serum myocardial function–related indexes

Serum MCP-1, sFas, Copeptin, OPN and vWF levels of observation group 4 h after PCI were significantly lower than those of control group, and differences in serum MCP-1, sFas, Copeptin, OPN and vWF levels of two groups 4 h after PCI were statistically significant (P<0.05), shown in Table 3.

4. Discussion

Latest studies have shown that the success rate of emergency PCI is above 90% for patients with acute STEMI, confirming that PCI is the preferred way for STEMI. But there is still around 10% failure rate in PCI, the main reasons are that coronary microthrombus is formed, the plaque falls off in the process of intervention and obstructs distal vessels, the opened infarction-related artery cannot effectively perfuse myocardial tissue, *etc*., and the myocardial perfusion deficiency in the opened infarction-related artery is the main cause of failure and has received extensive clinical attention[4,5]. Related studies[6–8] believe that invalid perfusion in infracted myocardium can lead to continuous ischemia state in circulation of infarction area, cause further arrhythmia and cardiac hypofunction, and reduce the overall treatment and prognosis. Some scholars have put forward that intracoronary injection of related drugs in PCI can increase the complete patent rate of infarction-related artery so as to increase the myocardial perfusion in infarction area. Intracoronary injection of drugs in PCI is expected to increase PCI treatment success rate, intracoronary injection of tirofiban combined with anisodamine was used in PCI of patients with STEMI in the study, and the myocardial perfusion in infarction area was mainly observed.

Electrocardiogram is the most common cardiac function state examination way in patients with myocardial infarction, and it can macroscopically and early detect myocardial infarction, cardiac functional recovery and other states in patients. For patients with STEMI, the degree of ST-segment resolution in electrocardiogram has been widely used in clinic and can reflect the effectiveness of myocardial reperfusion. Given that the change in ventricular myocyte function in patients with STEMI is the most significant, detecting ventricular electrical activity state in patients is a more reasonable indicator to judge myocardial reperfusion, but this way is less reported[9]. In the study, perioperative electrocardiogram QRS duration in patients with STEMI was monitored, and it was found that QRS duration of both groups were shortened after PCI, and QRS duration values of observation group the instant after PCI and 4h after PCI were shorter than those of control group, indicating that intracoronary injection of tirofiban and anisodamine in PCI is a reliable way to improve the electrical activity of ventricular muscle in infarction area, and indirectly indicating that intracoronary injection of above drugs has increased myocardial perfusion. Tirofiban is platelet glycoprotein GP Ⅱb/Ⅲa receptor antagonist that can resist platelet aggregation and prevent coronary microangiogenesis; anisodamine is M-receptor blocker that can relieve microvascular spasm and improve microcirculation[10,11]. The roles of tirofiban combined with anisodamine in increasing coronary blood flow and reducing infracted vessel reocclusion have both increased the blood supply to infarction-related myocardial cell and played a positive role in restoring their normal function.

In order to better determine the recovery of myocardial viability and ventricular wall motion after revascularization, radionuclide imaging is introduced into the judgment of treatment effect of patients with myocardial infarction. PET myocardial metabolic imaging is the gold standard for noninvasive evaluation of survival myocardium after ischemic injury, but it costs a lot and is difficult to be popularized, myocardial perfusion imaging can better locate ischemia area and judge survival myocardium, and its cost is relatively low, so it has been widely used in clinic at present[12]. Many nuclides can be used for the myocardial perfusion imaging, and because of their good consistency, ^{99m}Tc-MIBI combined with ^{18}F-FDG is recommended by foreign scholars for the survival myocardial perfusion imaging examination of patients with myocardial infarction[13]. The study results showed that ^{99m}Tc-MIBI and ^{18}F-FDG intake of observation group after PCI were more,

Table 2

Comparison of dual–isotopic imaging myocardial perfusion parameter values0

Groups	Case No.	^{99m}Tc–MIBI		^{18}F–FDG	
		Before PCI	4 h after PCI	Before PCI	4h after PCI
Observation group	39	34.28±4.59	87.63±9.12	39.84±5.37	83.29±9.04
Control group	39	35.71±4.73	71.92±8.02	41.29±4.97	72.66±8.15
t		0.183	8.495	0.251	7.892
P		>0.05	<0.05	>0.05	<0.05

Table 3

Comparison of serum myocardial function–related index levels.

Groups	Case No.	MCP–1 (ng/L)	sFas (ng/L)	Copeptin (pmol/L)	OPN (μg/L)	vWF (μg/L)
Observation group	39	493.75±57.39	512.83±63.29	5.32±0.61	3.02±0.41	132.42±15.98
Control group	39	871.25±90.47	1021.79±132.55	5.98±0.67	4.89±0.53	150.35±17.84
t		12.482	14.367	5.184	6.094	7.336
P		<0.05	<0.05	<0.05	<0.05	<0.05

indicating that there are more survival and well-behaved myocardial tissues in infarction area of observation group after treatment, in other words, the myocardial reperfusion in infarction area of observation group is better, and the results also directly verify the effectiveness of intracoronary injection of tirofiban and anisodamine in resisting thrombosis and improving microcirculation.

With the occurrence of myocardial infarction and the development of reperfusion therapy, the serum values of many parameters associated with cardiac function also change accordingly, and they can be used as the indirect criteria to judge the validity of blood reperfusion in infracted myocardium. MCP-1, sFas, Copeptin, OPN and vWF are the recognized serum factors directly related to myocardial infarction[14,15]. There is basic inflammatory state in patients with STEMI, it is one of the important internal causes of disease, and the serum levels of inflammation-related factors are directly related to patients' conditions. MCP-1 is secreted by mononuclear macrophages, and has chemotaxis and activation effect. sFas antigen expression increase-mediated smooth muscle cell apoptosis is the direct cause of STEMI. Copeptin is the strongest predictor of mortality in patients with Ⅱ-Ⅲ level cardiac function, and its level is positively correlated with the risk of heart failure in patients with myocardial infarction[16]. OPN, as an important functional protein of extracellular matrix, is the initial factor of vascular remodeling process after damage, and after vascular endothelial injury in PCI, OPN can be massively produced and lead to vascular remodeling[17]. vWF can be combined with Platelet GPⅡb/Ⅲa receptor and mediate platelet aggregation and thrombosis, and high levels of vWF mostly indicate high risk of microthrombus after PCI. It was found in the study that serum MCP-1, sFas, Copeptin, OPN and vWF levels of observation group were lower after treatment, indicating that intracoronary injection of tirofiban and anisodamine in PCI has exerted positive antithrombotic and cardioprotective effect.

To sum up, it is concluded as follows: intracoronary injection of tirofiban combined with anisodamine can optimize myocardial perfusion in patients with STEMI after PCI, and it is worth popularization and application in clinical practice in the future.

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