

Original Article

Tirofiban plus emergency PCI in elderly MI patients complicated with DM

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Abstract: Objective: To explore the effects of tirofiban combined with emergency percutaneous coronary intervention (PCI) in the elderly patients with myocardial infarction (MI) complicated with diabetes mellitus (DM) and the improvement in serum leptin and BDNF levels. Methods: A total 100 ST-segment elevation myocardial infarction (STEMI) patients who underwent emergency PCI in our hospital from September 2015 to September 2019 were collected and divided into an observation group (OG, n=52) and a control group (CG, n=48) in accordance with different treatment methods. Patients in the OG received tirofiban in the early stage, while those in the CG were not treated with tirofiban. The curative effect, PCI related indexes, cardiac ultrasound indexes, complications and serum adiponectin and leptin levels before and after treatment were compared between the OG and CG. Results: After treatment, thrombolysis in myocardial infarction (TIMI) flow grade, and TIMI myocardial perfusion grading (TMPG) in the OG was better than that of the CG ($P<0.05$). The length of hospital stay of the OG was shorter than in the CG ($P<0.05$). Ninety days after operation, compared with the CG, the OG had notably higher left ventricular ejection fraction (LVEF), cardiac index (CI), and stroke volume index (SVI) (all $P<0.05$), while also having notably lower left ventricular end diastolic diameter (LVEDD) and Left ventricular end systolic diameter (LVESD) ($P<0.05$). There was no considerable difference in the incidence of hemorrhage complications between the OG and CG ($P>0.05$). After treatment, serum adiponectin level elevated ($P<0.05$) and leptin level reduced ($P<0.05$). The adiponectin level in the OG was higher than that in the CG ($P<0.05$), and the leptin level was lower than that of the CG ($P<0.05$). The ejection fraction (EF) of the OG was remarkably higher than that of the CG ($P<0.05$). Conclusion: Tirofiban combined with emergency PCI is helpful to improve the curative effect and serum leptin and BDNF levels in elderly patients with MI complicated with DM, which is worthy of clinical application.

Keywords: Myocardial infarction complicated with diabetes mellitus, percutaneous coronary intervention, tirofiban, curative effect

Introduction

Since living standards have improved and social aging trends continue, the incidence of acute myocardial infarction (AMI) complicated with diabetes mellitus (DM) has increased for the past few years, and it has become a cardiovascular disease that seriously threatens human health [1, 2]. Patients with AMI and DM have a heavy thrombotic load and often have slow or no reflow, which affects coronary reperfusion. Most patients have diffused and severe coronary artery lesions, and the incidence of asymptomatic myocardial ischemia and myocardial infarction (MI) is high, with extensive lesions and relatively poor prognosis [3-5].

Antithrombosis combined with percutaneous coronary intervention (PCI) can promote coronary perfusion reconstruction, which has been widely used in clinic in recent years and has greatly improved the survival rate of AMI patients with DM [6, 7]. However, the development of PCI may increase the risk of thrombus loss and the possibility of distal microcirculation embolism [8]. Abnormal glucose metabolism is one of the independent risk factors leading to arteriosclerosis. After emergency PCI, the incidence of complications such as no-reflow and slow blood flow was significantly increased in patients with AMI complicated with DM [9]. Platelet membrane glycoproteins IIb/IIIa receptor antagonist treatment can improve myocar-

dial microcirculation perfusion after PCI, evidently decrease the incidence of no-reflow phenomenon and enhance the clinical treatment effect of PCI [10-12]. Tirofiban is a kind of platelet membrane glycoprotein IIb/IIIa receptor antagonist, which has been shown to have a good effect in reducing thrombus load and preventing platelet aggregation during PCI [13-15]. However, the application of tirofiban combined with emergency PCI in elderly patients with MI and DM is less studied.

Here, 100 patients with AMI in our hospital were selected, and different treatment methods were applied. The effects of tirofiban in emergency PCI and its curative effect in patients with AMI and the improvement of serum leptin and BDNF were analyzed.

Materials and methods

General data

One hundred ST segment elevation myocardial infarction (STEMI) patients who received emergency PCI in the First People's Hospital of Chun'an County from September 2015 to September 2019 were chosen to be research subjects, including 72 males and 28 females, aged from 60 to 69 years. Informed consent was signed by patients and their families, and the study was approved by the ethics committee. Inclusion criteria: Patients who met the relevant diagnostic criteria of AMI [16], with sustained chest pain >30 min, more than 2 adjacent electrocardiogram (ECG) leads showing ST segment elevation >0.2 mV, and the onset time <12 h. Patients who met the relevant standards of DM in the diagnostic criteria of American Diabetes Association [17]. Patients who underwent emergency PCI treatment. Exclusion criteria: Patients who were complicated with STEMI mechanical complications. Patients who had unstable hemodynamics. Patients who had liver or kidney dysfunction. Patients who had a recent history of trauma or surgery. Patients who were over 75 years old. Patients with cardiogenic shock, recent history of hemorrhagic diseases, or a history of ischemic stroke or cerebral hemorrhage within 12 months.

Treatment methods

Patients in the CG received ECG, blood lipid, blood glucose, myocardial enzyme, troponin and other related tests immediately after ad-

mission, and simultaneously chewed aspirin (JQC pharmaceutical Co., Ltd., Huayin, H200-46739) 300 mg and clopidogrel (Wuyao Pharmaceutical Co., Ltd., Wuhan, 20123155) 600 mg. The Judksin method was used in coronary angiography. Before angiography, 3000 U heparin was injected through a sheath tube, and after angiography, 7000 U heparin was added. Then the catheter was guided to the opening of coronary artery. The visible thrombus was removed by thrombus suction catheter, and the guide wire was guided to pass through the occlusion of the diseased blood vessel. On this basis, the OG was also given tirofiban (Xinshidai Pharmaceutical Co., Ltd., Shandong, H20090227) 10 µg/kg in coronary artery, and the injection was completed within 3 minutes. Then, the administration was pumped continuously for 24 h with 0.15 µg·kg⁻¹·min⁻¹ as the maintenance dose, and the CG was not administered tirofiban. Coronary angiography was rechecked and PCI was performed according to the lesion. After the operation, all the related indexes were reexamined, and aspirin, clopidogrel and β receptor antagonist were taken continuously. It should be noted that the diseased blood vessels were treated by emergency PCI. If other blood vessels needed to be treated, the second operation was performed after 7-14 days.

Evaluation indexes

Curative effect: including thrombolysis in myocardial infarction (TIMI) blood flow grade [18] and TIMI myocardial perfusion grading (TMPG) of related vessels after PCI [19]. The platelet aggregation rate before and after treatment was compared between the OG and the CG. The related indexes of PCI were compared between the OG and CG: the time from admission to balloon dilatation, number of patients with more than 2 implanted stents, selective second operation, and length of hospital stay. At 90 days after PCI, the cardiac function was evaluated by cardiac color ultrasound imaging, including the left ventricular ejection fraction (LVEF), cardiac index (CI), stroke volume index (SVI), left ventricular end diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD). The complications of the two groups were compared: including thrombocytopenia, massive hemorrhage of gastrointestinal tract, intracranial hemorrhage, mucocutaneous hemorrhage, puncture site hemorrhage.

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Table 1. Basic information of both groups

Group	Observation group (n=52)	Control group (n=48)	t/ χ^2	P
Male/female (n/n)	39/13	33/15	0.484	0.487
Average age (years)	61.88±1.29	62.47±1.54	1.024	0.309
BMI (kg/m ²)	24.68±3.27	24.42±2.87	0.421	0.675
Hypertension (n, %)	37 (66.07)	33 (58.93)	0.689	0.793
Duration of DM (years)	5.64±9.46	5.89±9.33	0.133	0.895
Hyperlipidemia (n, %)	13 (23.21)	15 (31.25)	0.484	0.487
Smoking (n, %)	35 (62.5)	31 (64.58)	0.826	0.774
History of MI (n, %)	3 (5.36)	2 (4.17)	0.135	0.713
Blood-glucose on admission (mmol/L)	8.43±2.51	8.66±2.48	0.460	0.646
Time of MI (h)	5.77±4.28	5.69±4.46	0.092	0.927
Troponin I before operation (ng/L)	7.78±3.40	7.82±4.37	0.051	0.959
EF (%)	44.61±12.94	43.87±13.19	0.283	0.778
Creatinine (μ mol)	68.54±13.28	69.41±14.08	0.318	0.751

Table 2. Comparison of curative effect between the two groups [n (%)]

Group	TIMI blood flow grade		TMPG	
	Grade 0-2	Grade 3	Grade 0-2	Grade 3
Observation group (n=52)	2 (3.85)	50 (96.15)	4 (7.69)	48 (92.31)
Control group (n=48)	9 (18.75)	39 (81.25)	12 (25)	36 (75)
t value		5.663		5.563
P value		0.017		0.018

and CG in gender, age, body mass index (BMI), hypertension, duration of DM, hyperlipidemia, smoking, previous history of MI, blood glucose at admission, time of AMI, troponin I at admission and creatinine (all $P > 0.05$). See **Table 1** for more details.

The venous blood of patients was extracted, and detection of serum adiponectin and leptin levels was conducted using enzyme-linked immunosorbent assay (ELISA) according to kit instructions (Shanghai Chuanqiu Biotechnology Co., Ltd., HH-71, HH-73-1). Ejection fraction (EF) and platelet count were compared between the OG and CG.

Statistical analysis

All the data was analyzed by SPSS 22.0. GraphPad Prism 7 was used to illustrate the collected data. Measurement data was expressed in the form of mean \pm standard deviation ($\bar{x} \pm s$), and t test was adopted. Enumeration data adopted χ^2 . $P < 0.05$ indicated a statistical significance.

Results

Basic information

According to the treatment methods, patients were divided into a control group (CG, n=48) and an observation group (OG, n=52). There was no significant difference between the OG

Effects

TIMI blood flow grade and TMPG of patients in the OG were better than those in the CG after treatment, with statistical significant difference ($P < 0.05$), as shown in **Table 2**.

Comparison of platelet aggregation rate

Before treatment, there was no considerable difference in platelet aggregation rate between the OG and the CG (all $P > 0.05$). After 24 hours of treatment, the platelet aggregation rate reduced notably in both groups, and the rate was remarkably lower in the OG than in the CG ($P < 0.05$). As shown in **Figure 1**.

Comparison of PCI related indexes

There was no remarkable difference between the OG and CG in time from admission to balloon dilatation, ratio of number of patients with more than 2 implanted stents, ratio of selective second operation ($P > 0.05$). The OG had a shorter average length of hospital stay than the CG. All the differences were statistically significant ($P < 0.05$), as shown in **Table 3**.

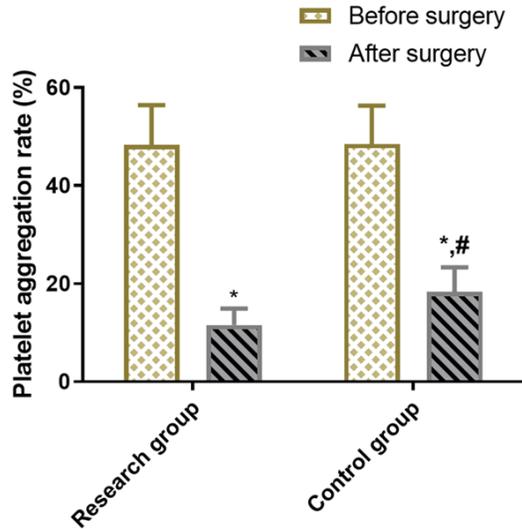


Figure 1. Comparison of platelet aggregation rate between the two groups. There was no significant difference in platelet aggregation rate between the two groups before treatment (all $P > 0.05$). After 24 hours of treatment, the platelet aggregation rate of the two groups decreased significantly, and the platelet aggregation rate of the observation group decreased significantly compared with that of the control group ($P < 0.05$). See **Figure 1**.

Comparison of cardiac ultrasound indexes ($x \pm s$)

Compared with the CG, the LVEF, CI, and SVI in the OG were evidently higher at 90 d after operation (all $P < 0.05$), while LVEDD and LVESD were evidently lower at 90 d after operation ($P < 0.05$), as shown in **Table 4**.

Comparison of incidence of complications

There was no statistically significant difference in the incidence of hemorrhage complications between the OG and CG ($P > 0.05$), as shown in **Table 5**.

Comparison of serum adiponectin and leptin levels between the two groups before and after treatment

Before treatment, there was no remarkable difference in serum adiponectin and leptin levels between the OG and CG ($P > 0.05$), but serum adiponectin level increased in both groups after treatment ($P < 0.05$), and was higher in the OG than in the CG ($P < 0.05$). Serum leptin level decreased ($P < 0.05$), and was lower in the OG than CG ($P < 0.05$). As shown in **Figure 2**.

Comparison of EF and platelet count between the two groups

After treatment, EF of patients in the OG was notably higher than that in the CG ($P < 0.05$), with statistically significant difference. Comparison of platelet count showed that there was no statistical difference in it between the OG and CG ($P > 0.05$), as shown in **Table 6**.

Discussion

The key to AMI treatment lies in revascularization. At present, emergency PCI treatment is widely used, which can promote myocardial blood flow reconstruction, restore occluded coronary blood flow, save dying myocardium, promote the narrowing of necrotic myocardium, and improve myocardial remodeling and patient prognosis [20, 21]. However, simple emergency PCI treatment is prone to no-reflow and reperfusion, which affects the prognosis, and needs to be supplemented with certain medication [22].

Tirofiban is a kind of platelet membrane protein IIb/IIIa receptor antagonist, which has a strong blocking effect on the combination of fibrinogen and platelet glycoprotein receptors, it inhibits platelet activity to the greatest extent, and quickly reaches the best state of inhibiting platelets after use [23, 24]. Therefore, when PCI is performed in elderly patients with MI and DM, the combination of tirofiban therapy is beneficial to restore the perfusion of coronary microcirculation and reduce the incidence of no-reflow phenomenon. At 90 d after operation, compared with the CG, the LVEF, CI, and SVI in the OG were notably higher (all $P < 0.05$), LVEDD and LVESD were notably lower ($P < 0.05$).

Patients with DM complicated with AMI have remarkably increasing incidence of slow blood flow and no-reflow events after PCI. Construction of PCI with increasing cardiovascular event for DM patients can induce thrombus shedding and distal microcirculation embolism [25], and a few patients will still have no-reflow phenomenon even if the TIMI blood flow grade recovers to grade 3 after operation [26]. According to the results of this study, TMPG II and TIMI grade III blood flow after operation in the OG was notably higher than that in the CG. Compared with the CG on 90 d after surgery, LVEF, CI and SVI in the OG were notably higher

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Table 3. Comparison of PCI related indexes between two groups

	Time from admission to balloon dilatation ($\bar{x} \pm s$, min)	Implanted stents >2 [n (%)]	Elective second operation [n (%)]	Hospital stay ($\bar{x} \pm s$, min)
Observation group (n=52)	85.63±20.68	23	28	11.46±3.81
Control group (n=48)	86.24±21.57	19	25	15.44±3.72
t/ χ^2 value	0.293	0.221	0.031	5.91
P value	0.770	0.638	0.860	<0.01

Table 4. Comparison of cardiac ultrasound indexes at 90 days after PCI between the two groups ($\bar{x} \pm s$)

Type	CI (L·min ⁻¹ ·m ⁻²)	SVI [SV (ml/m ²)]	LVEDD (mm)	LVESD (mm)
Observation group (n=52)	3.64±0.51	59.6±9.69	42.37±4.12	33.52±3.77
Control group (n=48)	2.88±0.37	54.31±7.89	48.18±5.48	38.65±4.31
t value	8.469	2.979	6.022	6.347
P value	<0.01	<0.01	<0.01	<0.01

Table 5. Comparison of incidence of complications in the two groups

	Thrombocytopenia	Massive hemorrhage of gastrointestinal tract	Intracranial hemorrhage	Mucocutaneous hemorrhage	Puncture site hemorrhage
Observation group (n=52)	0 (0)	1 (1.79)	1 (1.79)	7 (12.5)	5 (8.93)
Control group (n=48)	2 (4.17)	2 (4.17)	2 (4.17)	10 (20.83)	6 (12.5)
t value	2.211	0.657	0.657	0.961	0.212
P value	0.137	0.5111	0.5111	0.3269	0.6451

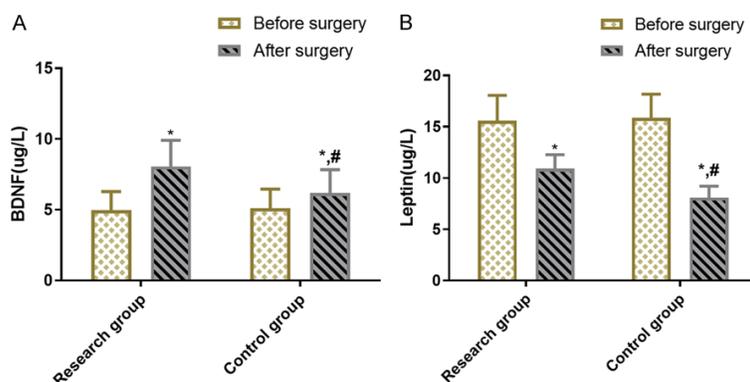


Figure 2. Comparison of serum leptin levels between the two groups before and after treatment. Comparison of serum adiponectin levels between the two groups before and after treatment. A: Before treatment, there was no significant difference in serum adiponectin levels between the two groups ($P>0.05$). After treatment, the serum adiponectin levels increased in both groups ($P<0.05$), and that of the observation group was higher than the control group ($P<0.05$). Comparison of serum leptin levels between the two groups before and after treatment. B: Before treatment, there was no significant difference in serum leptin levels between the two groups ($P>0.05$). After treatment, the leptin levels decreased in both groups ($P<0.05$), and that of the observation group was lower than the control group ($P<0.05$).

than those in the CG (all $P<0.05$), while LVEDD and LVESD were notably lower than those in the CG ($P<0.05$). The above results indicated that tirofiban can improve microvascular endo-

thelial function of coronary heart disease (CHD). Here, the incidence of platelet aggregation rate was evidently reduced ($P<0.05$), and EF of patients in the OG was considerably better than that in the CG after treatment ($P<0.05$). Tirofiban has a relatively strong antiplatelet effect, which can further shorten the time to effectively inhibit platelet aggregation, inhibit the damage of vascular endothelial cells and myocardial cells caused by platelets, reduce the occurrence of slow blood flow, and effectively improve the level of reperfusion. As the half-life of tirofiban is short, its effect disappears 3-5 h after stopping the drug and platelet function can be restored [27, 28], which is

beneficial to the clinical drug adjustment. Once the patient is found to have bleeding symptoms, the drug can be stopped in time to prevent the bleeding from being further aggravated.

Table 6. Comparison of EF and platelet count between the two groups

	EF	Platelet count
Observation group (n=52)	57.54±6.96	212.38±61.24
Control group (n=48)	51.25±11.37	210.11±64.37
t value	3.365	0.181
P value	0.001	0.857

ed. By comparing the complications between the two groups, it was found that there was no remarkable difference in the incidence of hemorrhage complications between the OG and CG ($P>0.05$). The team of Liu [29] also revealed that tirofiban is effective in improving TIMI flow grade and TMPG in elderly patients with DM complicated with AMI, and reducing serious complications without increasing the incidence of severe bleeding.

Previous studies have found that a variety of serological indicators are related to the prognosis of PCI, among which adiponectin and leptin are the focus of attention at present [30]. Adiponectin is a specific protein produced and secreted by adipocytes, which can inhibit the proliferation, differentiation and migration of vascular endothelial smooth muscle cells, and alleviate inflammatory reactions. Its level is significantly reduced in patients with AMI, and its low level is bound up with the occurrence of cardiovascular adverse events after PCI [31]. Leptin is a protein hormone produced and secreted by adipose tissue, which is an independent risk factor of CHD [32]. When AMI occurs, the level of leptin is obviously increased, which can promote inflammatory reactions and myocardial ischemia-reperfusion injury and other pathological processes, and it is bound up with the prognosis of PCI [33]. Therefore, improvement of serum adiponectin and leptin levels in patients with AMI complicated with DM have important clinical significance. In this study, the two levels improved in both groups after treatment. Compared with the CG, however, the serum adiponectin level increased and leptin level decreased in AMI patients with DM. The results showed that tirofiban played a significant role in improving serum adiponectin and leptin levels, which also indicated that the use of tirofiban before PCI could improve the prognosis of diseases more effectively.

Although this study proved the safety and efficacy of tirofiban combined with emergency

PCI, the long-term efficacy of the two combined and its effect on patient prognosis were not observed, leaving certain shortcomings.

To sum up, tirofiban combined with emergency PCI is helpful to improve the curative effect of elderly patients with MI and DM, improve serum leptin and BDNF levels, without increasing the incidence of complications of patients, which is a safe and reliable treatment scheme.

Disclosure of conflict of interest

None.

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