



Effect of loading–dose ticagrelor on coronary blood flow, left ventricular remodeling and myocardial enzyme spectrum in patients with acute myocardial infarction after interventional therapy

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ABSTRACT

Objective: To study the effect of loading-dose ticagrelor on coronary blood flow, left ventricular remodeling and myocardial enzyme spectrum in patients with acute myocardial infarction after interventional therapy. **Methods:** A total of 86 patients with acute myocardial infarction who received emergency PCI in our hospital between May 2013 and May 2016 were selected and randomly divided into two groups, ticagrelor group received perioperative ticagrelor therapy and clopidogrel group received perioperative clopidogrel therapy. After PCI, coronary blood flow reperfusion was evaluated, serum myocardial remodeling indexes and myocardial enzymes were determined, and cardiac color Doppler ultrasonography was conducted to determine the cardiac function indexes. **Results:** TIMI grading and TMPG grading of ticagrelor group after PCI were significantly higher than those of clopidogrel group; serum MMP9, BNP, C1TP, PICP, PIIINP, CK, CK-MB, cTnI and cTnT content of ticagrelor group 24h after operation were significantly lower than those of clopidogrel group; LVEDD, LVSED and LVMI of ticagrelor group 2 weeks after operation were significantly lower than those of clopidogrel group while LVEF was significantly higher than that of clopidogrel group. **Conclusion:** Peri-PCI loading-dose ticagrelor can improve coronary blood perfusion and reduce ventricular remodeling and myocardial injury in patients with acute myocardial infarction.

1. Introduction

Acute myocardial infarction is a common disease of cardiovascular system, and the pathological physiological basis of the disease is the arterial lumen obstruction and myocardial blood flow interruption caused by coronary atherosclerosis, plaque rupture as well as platelet activation and aggregation. Percutaneous coronary intervention (PCI) is the preferred method for emergency treatment of acute myocardial infarction, and can effectively recanalize coronary artery and restore myocardial perfusion, which will alleviate myocardial damage caused by ischemia hypoxia. PCI treatment can directly recanalize the coronary artery, but under the influence of perioperative platelet activation, there is the risk of stent thrombosis and myocardial no reflow after PCI, which will affect

the curative effect of PCI for myocardial infarction[1,2]. Antiplatelet drug clopidogrel is the conventional peri-PCI drug for patients with myocardial infarction, and it can inhibit platelet activation and aggregation, and reduce the incidence of no reflow after PCI[3]. But after entering the body, clopidogrel can not have the antiplatelet activity until the catalysis of cytochrome P450 isoenzyme, so it takes effect slowly, and its antiplatelet effect is limited for perioperative treatment of the emergency PCI[4]. Ticagrelor is a new type of antiplatelet agent that can exert antiplatelet effect without the bioconversion of catalyzing enzyme and takes effect more quickly, so it is more suitable for the emergency treatment[5]. In the following study, the effect of loading-dose ticagrelor on coronary blood flow, left ventricular remodeling and myocardial enzyme spectrum in patients with acute myocardial infarction after interventional therapy was analyzed.

2. Subjects and methods

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2.1 Research subjects

A total of 86 patients with acute myocardial infarction who received emergency PCI in our hospital between May 2013 and May 2016 were selected as the research subjects, all patients had the clinical symptom of persistent retrosternal pain that lasted for more than 30 min, the electrocardiogram after admission showed ST-segment elevation of 2 leads by more than 0.2 mV, and myocardial enzyme spectrum indicated elevated cTnI and CK-MB. Random number table was used to divide the included patients into ticagrelor group and clopidogrel group, 43 cases in each group. Ticagrelor group received emergency PCI combined with perioperative ticagrelor therapy, including 28 male cases and 15 female cases that were (56.4±7.3) years old; clopidogrel group received emergency PCI combined with perioperative clopidogrel therapy, including 26 male cases and 17 female cases that were (57.1±7.6) years old. The two groups of patients were not significantly different in general information ($P>0.05$).

2.2 Treatment methods

Two groups of patients received antiplatelet therapy immediately after admission, ticagrelor group received ticagrelor 180 mg and aspirin enteric-coated tablet 300 mg, by chewing; clopidogrel group received clopidogrel 300 ng and aspirin enteric-coated tablet 300 mg, by chewing. PCI treatment was performed as follows: inserting arterial sheath after arterial puncture, conducting coronary angiography according to Judkins method, making clear the site of infarction-related arteries, then conducting thrombus aspiration or intracoronary injection of tirofiban, and then inserting coronary artery stent. Patients continued to received antiplatelet therapy after PCI, and ticagrelor group received aspirin enteric-coated tablet 100 mg, oral administration, 1 time/d as well as ticagrelor 90 mg, oral administration, 2 times/d; clopidogrel group received aspirin enteric-coated tablet 100 mg, oral administration, 1 time/d as well as clopidogrel 75 mg, oral administration, 2 times/d.

2.3 Postoperative coronary blood flow evaluation methods

After PCI, TIMI grading and TMPG grading were followed to judge myocardial perfusion, and TIMI blood flow grading standard was as follows: that there was no contrast agent transit in infarction-related blood vessels was grade 0, that there was contrast agent transit, but it couldn't fill peripheral blood vessels was grade 1, that there was complete contrast agent filling, but the speed was lower than that in non-infarction vessels was grade 2, and that there was normal contrast agent filling and perfusion was grade 3. TMPG myocardial perfusion grading standard was as follows: that there was no contrast agent in myocardium of infarction-related arterial blood-supply area was grade 0, that the contrast agent appeared slowly and the color was lighter was grade 1, that the contrast agent appeared rapidly and couldn't be cleared in three cardiac cycles was grade 2, and that the contrast agent appeared rapidly and could be cleared within 3 cardiac cycles was grade 3.

2.4 Serum sample collection and detection methods

24 h after operation, 5 mL of peripheral blood was collected from two groups of patients and centrifuged to get serum, and then

enzyme-linked immunosorbent assay kits were used to determine matrix metalloproteinase 9 (MMP9), B-type natriuretic peptide (BNP), C-terminal telopeptide of collagen type I (CITP), C-terminal propeptide of procollagen type I (PICP) and N-terminal propeptide of procollagen type III (PIIINP) as well as creatine kinase (CK), creatine kinase isoenzyme (CK-MB), troponin I (cTnI) and troponin T (cTnT) content.

2.5 Left ventricular remodeling ultrasonography

Two weeks after PCI, both groups of patients received cardiac color Doppler ultrasonography, the probe frequency was 3.0 MHz, the clear cardiac section image was obtained and then the left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVSED) as well as left ventricular ejection fraction (LVEF) and left ventricular mass index (LVMI) were measured.

2.6 Statistical methods

SPSS 20.0 software was used to input and analyze data, measurement data analysis between two groups was by t test and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1 TIMI grading and TMPG grading of coronary blood flow

Analysis of TIMI grading and TMPG grading of coronary blood flow between two groups of patients after PCI was as follows: TIMI grading and TMPG grading of ticagrelor group were significantly higher than those of clopidogrel group. Differences in TIMI grading and TMPG grading of coronary blood flow after PCI were statistically significant between two groups of patients ($P<0.05$).

3.2 Serum indexes of left ventricular remodeling

24 h after PCI, analysis of serum left ventricular remodeling indexes MMP9, BNP, CITP, PICP and PIIINP between two groups of patients was as follows: serum MMP9, BNP, CITP, PICP and PIIINP content of ticagrelor group were significantly lower than those of clopidogrel group. Differences in serum MMP9, BNP, CITP, PICP and PIIINP content 24 h after PCI were statistically significant between two groups of patients ($P<0.05$).

3.3 Ultrasound indexes of left ventricular remodeling

2 weeks after PCI, analysis of left ventricular remodeling ultrasound indexes LVEDD, LVSED, LVEF and LVMI was as follows: LVEDD, LVSED and LVMI of ticagrelor group were

Table 1.

Comparison of TIMI grading and TMPG grading of coronary blood flow after PCI between two groups of patients.

Groups	n	TIMI grading	TMPG grading
Ticagrelor	43	3.48±0.38	3.29±0.41
Clopidogrel	43	2.84±0.27	2.66±0.29
T value		7.137	6.642
P value		<0.05	<0.05

significantly lower than those of clopidogrel group while LVEF was significantly higher than that of clopidogrel group. Differences in LVEDD, LVESD, LVEF and LVMI levels 2 weeks after PCI were statistically significant between two groups of patients ($P<0.05$).

3.4 Serum myocardial enzyme spectrum content

24 h after PCI, analysis of serum CK, CK-MB, cTnI and cTnT content between two groups of patients was as follows: serum CK, CK-MB, cTnI and cTnT content of ticagrelor group were significantly lower than those of clopidogrel group. Differences in serum CK, CK-MB, cTnI and cTnT content 24 h after PCI were statistically significant between two groups of patients ($P<0.05$).

4. Discussion

Emergency PCI is an effective method for clinical treatment of acute myocardial infarction, and it can recanalize coronary artery and restore blood perfusion to the ischemic myocardial tissue in a short time, and reduce ischemia hypoxia damage to the myocardium. All pathological links of acute myocardial infarction involve the platelet activation and aggregation. In the start and development of myocardial infarction, the ruptured atheromatous plaque will cause platelet activation, and the local platelet adhesion and aggregation can activate blood coagulation system, and cause intravascular thrombosis; after PCI treatment of myocardial infarction, persistently activated platelets will adhere and aggregate in coronary stent, which increase the risk of stent thrombosis. Related studies confirm that stent thrombosis is an important factor causing no reflow after PCI, which will affect myocardial blood reperfusion and the curative effect of PCI[6,7]. Because the platelet activation and aggregation are closely associated with no reflow after PCI, it is mostly clinically proposed to use antiplatelet drugs for adjuvant therapy in the perioperative process of PCI. Clopidogrel is a common antiplatelet

drug that has definite antiplatelet effect, but after orally entering the body, it needs the catalysis of cytochrome P450 isoenzyme before it becomes bioactive, and it is hard to take effect shortly when used for emergency treatment, which affects its antiplatelet effect[8,9].

Ticagrelor is a new antiplatelet drug used for the cardiovascular system diseases in recent years, the drug itself is an active precursor and can enter the body and then be directly transformed into the active form with antiplatelet effect, the process does not depend on the bioconversion effect of cytochrome P450 isoenzyme, so it takes effect quickly after taken orally, can exert antiplatelet effect in a short time, and is more suitable for emergency treatment[10,11]. In the study, loading-dose ticagrelor was used in perioperative process of PCI treatment of acute myocardial infarction, and in order to determine the differences between the drug and clopidogrel for emergency PCI, the recovery of coronary blood perfusion after PCI was compared at first. TIMI grading and TMPG grading are the common methods to evaluate blood perfusion in the process of coronary angiography, the former mainly reflects the intravascular blood perfusion, and the latter mainly reflects the myocardial perfusion corresponding to coronary artery. The analysis of the TIMI grading and TMPG grading showed that TIMI grading and TMPG grading of ticagrelor group were significantly higher than those of clopidogrel group. This means that ticagrelor for peri-PCI treatment can more effectively improve the blood perfusion of coronary artery and ischemic myocardium.

There is significant hypoxic-ischemic myocyte injury in patients with acute myocardial infarction, and the emergency PCI therapy can restore myocardial perfusion and reduce the myocyte damage caused by hypoxia. However, the coronary no reflow after PCI caused by platelet activation and aggregation will affect myocardial blood reperfusion, which causes the continuous myocyte injury after PCI. The maximum value of ticagrelor for peri-PCI antiplatelet therapy is that it takes effect rapidly and its bioactivity does not rely on liver enzyme catalysis, so it can exert anti-platelet aggregation effect in a short time, reduce the risk of no reflow after PCI caused by platelet

Table 2.

Comparison of serum left ventricular remodeling indexes after PCI between two groups of patients.

Groups	n	MMP9 (pg/mL)	BNP (pg/mL)	CITP (ng/mL)	PICP (ng/mL)	PIINP (ng/mL)
Ticagrelor	43	26.58±3.52	9.35±1.03	19.32±2.77	46.41±6.69	3.28±0.56
Clopidogrel	43	44.28±5.93	16.78±2.25	30.15±4.63	79.16±9.36	5.68±0.77
T value		8.182	8.945	7.668	9.117	8.342
P value		<0.05	<0.05	<0.05	<0.05	<0.05

Table 3.

Comparison of left ventricular remodeling ultrasound indexes after PCI between two groups of patients.

Groups	n	LVEDD (mm)	LVESD (mm)	LVEF	LVMI (g/m ²)
Ticagrelor	43	44.59±5.82	34.28±4.58	56.41±7.14	110.33±12.37
Clopidogrel	43	52.15±6.74	41.24±5.31	45.25±5.73	124.52±15.52
T value		6.810	6.483	7.577	6.926
P value		<0.05	<0.05	<0.05	<0.05

Table 4.

Comparison of serum myocardial enzyme spectrum after PCI between two groups of patients.

Groups	n	CK (U/L)	CK-MB (U/L)	cTnI (μg/L)	cTnT (μg/L)
Ticagrelor	43	93.14±10.17	22.64±3.34	74.56±8.85	1.67±0.19
Clopidogrel	43	158.52±17.24	36.58±4.76	132.14±16.44	2.85±0.36
T value		7.583	8.381	9.228	7.384
P value		<0.05	<0.05	<0.05	<0.05

aggregation, improve myocardial perfusion after PCI and reduce the myocyte injury[12]. Myocardial enzyme spectrum CK, CK-MB, cTnI and cTnT are the common biochemical indexes used to evaluate myocardial cell damage, and ischemic injury can lead to myocardial cell rupture and the release of myocardial enzymes from cytoplasm into the blood circulation, which is characterized by the significant rise in serum myocardial enzyme spectrum. In order to further clarify the differences in the effect of clopidogrel and ticagrelor for peri-PCI treatment on myocardial injury, the serum myocardial enzyme spectrum were analyzed in the study, and the results showed that serum CK, CK-MB, cTnI and cTnT content of ticagrelor group after PCI were significantly lower than those of clopidogrel group. This means that ticagrelor for peri-PCI treatment can more effectively reduce the myocyte injury.

Poor perfusion recovery after myocardial infarction can cause ventricular remodeling and affect long-term recovery of cardiac function. After infarction, the characteristics of ventricular remodeling are interstitial fibrosis and collagen deposition as well as the resulting secondary cardiac systolic and diastolic dysfunction. MMP-9 and BNP are the common marker molecules reflecting ventricular remodeling, the former participates in the extracellular matrix remodeling and collagen deposition[13,14], and the latter is closely related to the degree of ventricular diastolic dysfunction[15]. In the process of ventricular remodeling, besides the change of MMP9 and BNP, type I and type III collagen deposition in myocardial tissue can directly cause interstitial remodeling and myocardial compliance reduction, and can also cause increased generation of collagen metabolites C1P, PICP and PIIINP in serum[16,17]. In the study, analysis of the content of these ventricular remodeling molecules in serum showed that serum MMP9, BNP, C1P, PICP and PIIINP content of ticagrelor were significantly lower than those of clopidogrel group. Ventricular remodeling will also affect the ventricular diastolic function in patients with myocardial infarction, cardiac color Doppler ultrasound was used in the study to evaluate the degree of ventricular remodeling, and the results showed that LVEDD, LVSED and LVMI of ticagrelor group were significantly lower than those of clopidogrel group while LVEF was significantly higher than that of clopidogrel group. The above results show that ticagrelor for peri-PCI treatment can more effectively reduce the postoperative left ventricular remodeling.

To sum up, it is believed that peri-PCI loading-dose ticagrelor can better improve the coronary blood perfusion in patients with acute myocardial infarction than clopidogrel, and can reduce the ventricular remodeling and myocardial injury caused by ischemia hypoxia.

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