

Original Article

Impact of high-dose statin on the PCI prognosis of patients with acute coronary syndromes

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Abstract: Percutaneous coronary intervention (PCI) has become an important means of vascular remodeling in patients with acute coronary syndrome (ACS). Statins is important in the treatment of ACS by improving endothelial function, anti-inflammation, and protecting myocardial function. This study observed its impact on prognosis by using different doses of statins on ACS patients received PCI treatment. ACS patients receiving PCI in our hospital were divided into three groups according to different doses of atorvastatin, including high-dose group (40 mg/d), normal dose group (10 mg/d), and the control group (without atorvastatin). TIMI, TMPG grade, cTnl, CK-MB, CRP, MACE rate, and adverse reactions were compared. TIMI (1.3 ± 0.8) and TMPG (2.7 ± 0.7) in high-dose group at 6 months after treatment were higher than that in normal dose group (1.2 ± 0.6 and 2.5 ± 0.4 , respectively) and control group (1.1 ± 0.7 and 2.0 ± 0.2 , respectively). While cTnl (0.252 ± 0.013), CK-MB (26.93 ± 0.57), and CRP (4.65 ± 0.14) were lower than the normal dose group (0.298 ± 0.014 , 27.98 ± 0.58 , and 5.67 ± 0.21 , respectively) and control group (0.415 ± 0.021 , 30.05 ± 0.64 , and 6.26 ± 0.12 , respectively). High-dose group showed significantly lower MACE rate (6.7%) than normal dose group (10%) and control (33%). The adverse reaction rate showed no statistical difference ($P > 0.05$). High-dose atorvastatin application on ACS patients before PCI can restore coronary artery perfusion, inhibit inflammation, and reduce cardiovascular event incidence with few adverse reaction.

Keywords: Atorvastatin, acute coronary syndrome, PCI, high-dose

Introduction

For patients with acute coronary syndrome (ACS), percutaneous coronary intervention (PCI) can effectively dredge the infarction related artery (IRA) in early stage and restore the blood flow perfusion. However, PCI may damage the structure and function of vascular endothelial cells, induce inflammatory reaction and increase the production of oxygen free radicals [1]. Statin, a type of reductase inhibitor of 3-hydroxy-3-methyl-glutaric acyl coenzyme A (HMG-CoA), has many kinds of biological functions, such as regulating lipid, improving endothelial cell function, reducing oxidative stress reaction, declining platelet adhesion ability, protecting myocardial cells and inhibiting inflammatory reaction development [2, 3]. This study evaluated the impact of statin on the prognosis by using high-dose statin on ACS patients in our hospital before PCI treatment.

Materials and methods

General information

Ninety ACS patients received PCI from January 2014 to January 2015 in our hospital were enrolled, including 50 males and 40 females. 45 patients had acute myocardial infarction, including 23 cases of acute ST segment elevation myocardial infarction and 22 cases of acute non ST segment elevation myocardial infarction, while the other 45 cases had unstable angina. All enrolled subjects were diagnosed based on the criteria published by European society of cardiology.

Inclusion criteria: PCI indication; TIMI grade ≤ 2 ; TIMI at third grade but residual stenosis $\geq 75\%$

Exclusion criteria: PCI history; restenosis lesions; with malignant tumor or hepatic and

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Table 1. General information

Item	High-dose group	Normal-dose group	Control
Male/female (n)	16/14	15/15	11/19
Age (years old)	54.82 ± 7.24	55.71 ± 6.58	54.93 ± 7.05
BMI (kg/m ²)	23.7 ± 2.4	23.6 ± 2.8	24.1 ± 2.2
Hypertension	14 (46.7)	14 (46.7)	15 (50)
Diabetes	11 (36.7)	12 (40%)	12 (40%)
Hyperlipemia	21 (70)	22 (73.3)	23 (76.7)
PCI history	1 (3.33)	1 (3.33)	1 (3.33)

Table 2. TIMI and TMPG grading comparison

Group	Cases	TIMI grading		TMPG grading	
		Before PCI	6 months after PCI	Before PCI	6 months after PCI
High-dose group	30	1.1 ± 0.9	1.3 ± 0.8*	1.5 ± 0.7	2.7 ± 0.7*,&#
Normal dose group	30	1.1 ± 0.8	1.2 ± 0.6*	1.5 ± 0.5	2.5 ± 0.4*,&#
Control	30	1.0 ± 0.1	1.1 ± 0.7*	1.4 ± 0.9	2.0 ± 0.2*

*P < 0.05, compared with before PCI; #P < 0.05, compared with control; &P < 0.05, compared with normal dose group.

renal insufficiency; bleeding tendency and cannot controlled by anticoagulant therapy; systolic blood pressure > 180 mmHg, diastolic blood pressure > 110 mmHg.

The patients were randomly divided into three groups: high-dose group (atorvastatin 40 mg/d), 30 cases including 16 males and 14 females, with mean age 54.82 ± 7.24 (31-82) years old; normal dose group (atorvastatin 10 mg/d), 30 cases including 15 males and 15 females with mean age 55.71 ± 6.58 years old; control group (without atorvastatin), 30 cases including 11 males and 19 females with mean age 54.93 ± 7.05 (32-81) years old. Patients in different groups showed no statistical differences on gender, age, and BMI ($P > 0.05$) (**Table 1**).

Treatment method

The patients received conventional treatment after admission, including nitrate esters, β receptor blockers, calcium antagonists, angiotensin converting enzyme inhibitors, anticoagulation and antiplatelet agents, etc.

At 1 week before PCI treatment, patients in high-dose group were given atorvastatin (Honghui Medicine co., LTD., 10 mg/tablet) for 40 mg/day; patients in normal dose group were given atorvastatin 10 mg/day. The control group only received conventional treatment without statins. After PCI treatment, each group

received atorvastatin 10 mg for 1 week.

PHILIPS Cardiovascular angiographic system and coronary angiography quantitative analysis system was applied to perform coronary angiography and PCI therapy. The catheter was put into the distal end of IRA by 0.36 mm coronary guidewire, and then rapamycin eluting stents was placed. After giving 100-150 U/kg heparin, 200 μ g tirofiban was injected to the coronary artery. Angiography was performed at 3 min after injection, and the operation ended when reaching TMPG level 3.

Observational index

TIMI grading was used for coronary artery blood flow evaluation [4]. Level 0: vascular complete occlusion; Level 1: blood flow in distal lesions cannot fill vascular bed; Level 2: distal vessel filled in three cardiac cycles; Level 3: distal vessel complete filled in three cardiac cycles.

TMPG grading was applied for microvascular perfusion evaluation [5]. Level 0: contrast agent cannot enter the myocardial capillary bed; Level 1: contrast agent enters the myocardial capillary bed slowly and cannot discharge; Level 2: contrast agent enters the capillary bed but delay emptying; Level 3: contrast agent enters the capillary bed quickly and rapidly emptying.

The blood was extracted from subjects before PCI and at 6 months after PCI to test cTnI, CK-MB, and CRP levels.

Major adverse cardiac events (MACE) rate including angina, heart failure, arrhythmia, and cardiac shock in 30 days was recorded.

Adverse reaction in treatment group was observed, including dizziness headache, gastrointestinal reaction, myasthenia, urea nitrogen elevation, and ALT increase.

ELISA detection of cTnI, CK-MB, and CRP

The ELISA kits were placed at room temperature for 30 min before use. The standard sub-

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Table 3. cTnI, CK-MB, and CRP before and after PCI comparison

Group	Cases	cTnI	CK-MB	CRP
High-dose group	30			
Before PCI		0.012 ± 0.008	18.92 ± 0.69	3.54 ± 0.12
6 months after PCI		0.252 ± 0.013 ^{*,#,&}	26.93 ± 0.57 ^{*,#,&}	4.65 ± 0.14 ^{*,#,&}
Normal dose group	30			
Before PCI		0.010 ± 0.009	19.05 ± 0.70	3.51 ± 0.11
6 months after PCI		0.298 ± 0.014 ^{*,#}	27.98 ± 0.58 ^{*,#}	5.67 ± 0.21 ^{*,#}
Control	30			
Before PCI		0.009 ± 0.012	19.01 ± 0.81	3.41 ± 0.09
6 months after PCI		0.415 ± 0.021	30.05 ± 0.64	6.26 ± 0.12

*P < 0.05, compared with before PCI; #P < 0.05, compared with control; &P < 0.05, compared with normal dose group.

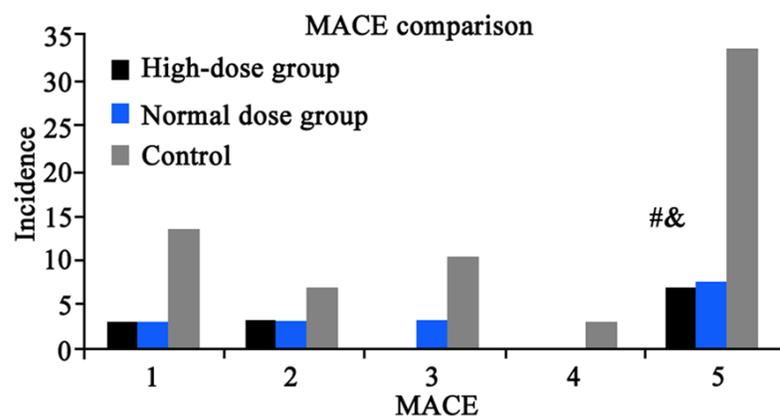


Figure 1. A. Angina; B. Heart failure; C. Arrhythmia; D. Cardiogenic shock; E. MACE rate. #P < 0.05, compared with control; *P < 0.05, compared with normal dose group.

stance was diluted. Each concentration had five replications. After sampling, dosing, washing, coloration, and termination, the plate was read at 450 nm to calculate the sample concentration.

Statistical analysis

All the statistical analysis was performed on SPSS17.0 software. The measurement data was presented as mean ± standard deviation. ANOVA were used for mean comparison. Chi-square test was used for comparison of categorical data, such as gender. P < 0.05 was considered as statistically significant.

Results

TIMI and TMPG grading comparison

TIMI and TMPG grading before and after PCI treatment in each group were compared. Three groups showed no significant difference in TIMI

and TMPG grading before PCI (P > 0.05). TIMI and TMPG grading increased obviously in all of the three groups after PCI treatment (P < 0.05). TIMI and TMPG grading after PCI were highest in high-dose group, followed by normal dose group and control group (P < 0.05) (Table 2).

cTnI, CK-MB, and CRP before and after PCI comparison

cTnI, CK-MB, and CRP levels before and after PCI in each group were compared.

It was found that they showed no statistical differences before treatment (P > 0.05), while increased at 6 months after PCI. Control group elevated more obviously, whereas high-dose group presented lowest cTnI, CK-MB, and CRP levels at 6 months after PCI (P < 0.05) (Table 3).

MACE comparison

It was found that one case appeared angina and one case presented heart failure in high-dose group, and the MACE rate was 6.7%. MACE rate in high-dose group was lower than that of normal dose group as 10% and control group as 33.3%, the difference was statistically significant (P < 0.05) (Figure 1).

Adverse reaction comparison

Adverse reaction comparison revealed that high-dose group appeared one case of dizzi-

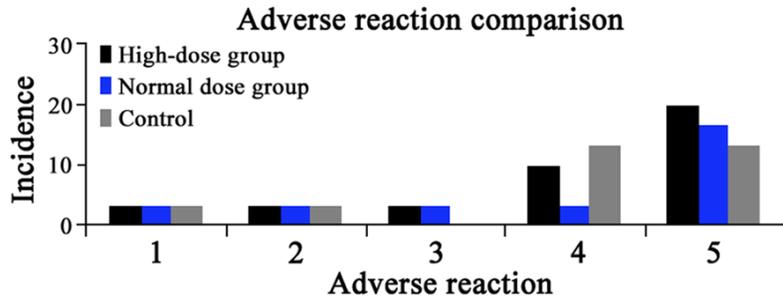


Figure 2. A. Dizziness headache; B. Gastrointestinal reaction; C. Myasthenia; D. ALT elevation; E. Adverse reaction rate.

ness headache, one case of gastrointestinal reaction, one case of myasthenia, and one case of ALT elevation. The adverse reaction rate in high-dose group was 20%, which was similar with the results in normal dose group as 16.7% and control group as 13.3% ($P > 0.05$) (Figure 2).

Discussion

The pathological basis of ACS is coronary atherosclerosis plaque rupture or erosion, leading to complete or incomplete vascular occlusion and thrombosis. It mainly includes acute ST segment elevation myocardial infarction, acute non ST segment elevation myocardial infarction, and unstable angina characterized as acute onset, high fatality rate, and high morbidity [6]. The treatment of ACS, based on anti-platelet aggregation, reducing myocardial oxygen consumption, and controlling the risk factors of coronary heart disease, is establishing blood supply promptly, including thrombolysis and PCI [7].

In this study, high-dose atorvastatin application in patients with PCI increased TIMI and TMPG grading significantly compared with low-dose atorvastatin and unused patients. TIMI level 3 is the normal level of blood flow rate in epicardial great vessel and its branch. However, small coronary artery perfusion may still have no reflow under this degree [8]. TMBG grading can reflect the perfusion status of small coronary vessel compared with TIMI [9]. This study detected TIMI and TMPG together, and indicated that high-dose atorvastatin is in favor of recover blood flow perfusion of small coronary artery.

PCI involves balloon expansion and stent implantation that may cause mechanical extru-

sion and stimulation to local tissue, leading to vascular intima injury and local inflammation reaction. CRP is an important marker that can reflect the severity of vascular inflammatory reaction [10, 11]. CRP can stimulate mononuclear cells to release a variety of inflammatory cytokines, resulting in leukocytes activation and aggravating inflammatory reaction. It further

expands the inflammatory cascade effect and promotes disease development. CRP can reflect the degree of inflammatory response in the atheromatous plaque, and closely related to the instability of coronary artery plaque [12, 13]. cTnT and cTnI are also the preferred cardiac markers [14]. In this study, it was found that high-dose atorvastatin therapy causes lower cTnI, CK-MB, and CRP levels after PCI compared with low-dose atorvastatin and unused patients. It suggested that 40 mg/d atorvastatin can effectively inhibit vascular inflammation, relieve myocardial injury, improve blood rheology, and perfect myocardial blood supply in ACS patients after PCI.

Clinical trials confirmed that statins can obviously reduce MACE in ACS patients [15]. Our experiment compared different doses of atorvastatin treatment in patients with PCI and found that high-dose atorvastatin at 40 mg/d results in only 6.7% of MACE rate, which is significantly lower than the low-dose atorvastatin and unused patients. It revealed that atorvastatin can effectively reduce the MACE in ACS patients receiving PCI treatment, which may be that statins can improve endothelial function, stable plaques, anti-inflammation, inhibit vascular smooth muscle cell proliferation and suppress platelet aggregation and thrombosis, etc. Studies have demonstrated that statins application in early stage can reduce the incidence of nonfatal myocardial infarction and angina pectoris in ACS [16]. Some studies also pointed out that high-dose atorvastatin have good security before PCI and can reduce the myocardial injury and MACE after PCI [17]. The incidence of MACE such as cardiac death, myocardial infarction, target vessel revascularization reduced by 48% at 30 days after PCI in patients

receiving long-term statins therapy [18]. It was consistent with our experimental results.

Clinical trials found that patients presented well toleration to atorvastatin and the treatment process was safe [19]. This study compared adverse reactions in different doses of atorvastatin. No subjects exit the test because of the adverse reaction. 40 mg/d atorvastatin group showed similar adverse reaction rate after PCI treatment compared with 10 mg/d atorvastatin group and unused group, suggesting that 40 mg/d atorvastatin does not increase the adverse reaction rate that is in line with other reports [20].

To sum up, high-dose atorvastatin intervention on ACS patients before PCI can promote small coronary artery blood flow perfusion recovery, improve blood rheology, inhibit vascular inflammation, relieve myocardial injury, and perfect myocardial blood supply. It also can effectively reduce the incidence of MACE with less adverse reaction. This study provided theoretical basis for conventional using atorvastatin in ACS patients before PCI.

Disclosure of conflict of interest

None.

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