

Effects of rosuvastatin on pentraxin 3 level and platelet aggregation rate in elderly patients with acute myocardial infarction undergoing elective interventional therapy: a double-blind controlled study

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Abstract. – OBJECTIVE: To investigate clinical effects of rosuvastatin on blood lipid levels, hemorheological profiles, vascular endothelial function, pentraxin 3 (PTX-3) level, the number of granule membrane glycoprotein (GMP-140) molecules and platelet aggregation rate in elderly patients with acute myocardial infarction (AMI) undergoing elective percutaneous coronary intervention (PCI).

PATIENTS AND METHODS: Total of 120 elderly patients admitted with AMI undergoing elective PCI from July 2014 to January 2016 were selected. The patients were divided into the control group and the experimental group based on the rule of random number generation and double-blind controlled trial, 60 cases in each group. All of 120 patients were treated with routine medications; the experimental group was orally administered with rosuvastatin 1 week before PCI. Blood lipid levels, hemorheological profiles, vascular endothelial function, PTX-3, the number of GMP-140 molecules and platelet aggregation rate were compared between two groups before treatment with rosuvastatin and 10d after elective PCI.

RESULTS: Triglycerides, plasma total cholesterol, and low-density lipoprotein levels were significantly lower ($p<0.05$) in the experimental group when compared with the control group; plasma viscosity, fibrinogen, the viscosity of blood in the high shear rates and in the low shear rates in the experimental group were significantly lower than those of the control group ($p<0.05$); FMD and NMD in the experimental group were significantly higher than those of the control group ($p<0.05$); ET-1, TXA2 levels in the experimental group were lower, however, PGI2, NO as well as NOS in the experimental group were higher, when compared the control group, the differences were statistically sig-

nificant ($p<0.05$); PTX-3, the number of GMP-140 molecules and platelet aggregation rate in the experimental group were significantly lower than those of the control group ($p<0.05$).

CONCLUSIONS: Oral administration of rosuvastatin 1 week before PCI can significantly improve the blood lipid levels and hemorheological profiles, enhance endothelial function, reduce the PTX-3 level and the number of GMP-140 molecules, decrease the platelet aggregation rate, therefore improving prognosis in elderly patients with AMI undergoing PCI.

Key Words

Rosuvastatin, AMI, PCI, Vascular endothelial function, Pentraxin 3, Platelet aggregation.

Introduction

The primary aim of the clinical treatment for the patients with acute myocardial infarction (AMI) is recanalization of occluded vessels, but recanalization is not able to effectively restore myocardial reperfusion in the acute phase, nearly 1/3 of patients with AMI exhibit poor prognosis due to a combination of coronary microvascular dysfunction and reperfusion injury¹. Evidence has shown that statins drugs reduce blood lipids levels and inhibit inflammatory responses thus maintaining atherosclerotic plaque stability and improved endothelial function^{2,3}. In this study, for the elderly patients in our hospital with AMI undergoing elective PCI, oral administration with rosuvastatin 10d before PCI achieved good effectiveness, which is summarized as follows.

Patients and Methods

Patients

Hundred and twenty elderly patients admitted with AMI undergoing elective PCI from July 2014 to January 2016 were selected as the study subjects.

Selection criteria:

- 1) myocardial enzymes elevation is at least three times normal;
- 2) duration of chest pain for 30 min⁴;
- 3) ECG shows ST-segment elevation is not less than 2.0 mm in at least two leads⁵;
- 4) the patients are provided with the informed consent for the study.

Exclusion criteria: the patients with severe liver and kidney dysfunction, acute heart failure, the history of coronary artery bypass surgery, malignant tumors, or cardiogenic shock^{6,7}.

Out of the 120 patients, 76 were males and 44 females with an average age of 61-72 years, mean age (54.2 ± 4.6 years). The patients were divided into the control group and the experimental group based on the rule of random number generation and double-blind controlled trial, 60 cases for each group. There was no significant difference in general information of the patients between the two groups ($p > 0.05$). Thus, two groups could be compared. This study was approved by the Ethics Committee of Yantaishan Hospital. Signed written informed consents were obtained from the patients and/or guardians.

Study Design

Both groups of patients received routine medications before PCI surgery, including angiotensin converting enzyme (ACE) inhibitor, β -receptor blocker, Aspirin and Clopidogrel (Yangzijiang, Taizhou, China). In some patients with a sudden reduction, even complete interruption of blood flow of coronary artery, Tirofiban and Nitroglycerin (Yangzijiang, Taizhou, China) were administered accordingly. Patients in the experimental

group were orally administered with rosuvastatin 1 week prior to PCI: a single dose of 10.0 mg, once daily before bedtime.

Laboratory Assessment

Factors compared between the control group and the experimental group before treatment with rosuvastatin and 10d after PCI were

- 1) Comparison of levels of blood lipids including triglyceride (TG), serum total cholesterol (TC), low-density lipoprotein (LDL-C).
- 2) Comparison of hemorheological profiles such as plasma viscosity, fibrinogen, viscosity of blood in the high shear rates and the low shear rates.
- 3) Comparison of vascular endothelial function including endothelium-dependent vasodilation (FMD), non-endothelium-dependent vasodilation (NMD), diameter of brachial artery.
- 4) Comparison of vasoactive substances levels such as serum endothelin (ET-1), thromboxane (TXA2), prostacyclin (PGI2), nitric oxide (NO), nitric oxide synthase (NOS).
- 5) Comparison of levels of serum PTX-3.
- 6) Comparison on the number of GMP-140 molecules and platelet aggregation rate.

Statistical Analysis

All data were statistically analyzed using SPSS 20.0 (IBM, NY, USA) and was presented as means ± standard deviation ($\bar{x} \pm s$). The Student's *t*-test was used for the statistical analysis, Differences were considered statistically significant at $p < 0.05$.

Results

Comparison of Levels of Blood Lipids Before Treatment with Rosuvastatin and 10d After PCI

There were no significant differences in TG, TC, and LDL-C before treatment with rosuvasta-

Table 1. Comparison of levels of blood lipids before treatment with Rosuvastatin and 10d after PCI ($\bar{x} \pm s$, mmol/L).

Group	TG		TC		LDL-C	
	Before treatment	10d after PCI	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	2.45 ± 0.36	1.17 ± 0.09 [^]	5.68 ± 0.43	3.01 ± 0.35 [^]	4.85 ± 0.44	2.19 ± 0.32 [^]
Control group (n=60)	2.51 ± 0.42	1.45 ± 0.18	5.73 ± 0.57	4.41 ± 0.57	4.81 ± 0.53	3.31 ± 0.46

[^] $p < 0.05$ vs. the control group.

Table II. Comparison of hemorheological profiles before treatment with Rosuvastatin and 10d after PCI ($\bar{x} \pm s$, mmol/L).

Group	Plasma viscosity (mPa·s)		Fibrinogen (g/L)		Viscosity of blood in the high shear rates (mpa·s)		Viscosity of blood in the low shear rates (mpa·s)	
	Before treatment	10d after PCI	Before treatment	10d after PCI	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	2.87±0.57	1.41±0.21 [^]	4.51±0.62	2.19±0.44 [^]	5.36±0.57	3.77±0.48 [^]	16.35±1.45	9.16±1.03 [^]
Control group (n=60)	2.92±0.65	1.92±0.53	4.54±1.02	3.49±1.37	5.41±0.66	4.82±0.56	16.27±1.33	12.08±2.57

[^] $p < 0.05$ vs. the control group.

tin between the two groups ($p > 0.05$). The levels of TG, TC, and LDC-L in the experimental group were significantly lower than those of the control group 10d after PCI ($p < 0.05$) as shown in Table I.

Comparison of Hemorheological Profiles Before Treatment with Rosuvastatin and 10d After PCI

There were no significant differences in plasma viscosity, fibrinogen, the viscosity of blood at the high shear rates and the viscosity of blood at the low shear rates between the two groups before treatment with rosuvastatin ($p > 0.05$); at the 10th day after PCI. But the plasma viscosity, fibrin, the viscosity of blood in the high shear rates as well as the viscosity of blood in the low shear rates were significantly lower than those of the control group ($p < 0.05$) as shown in Table II.

Comparison of Vascular Endothelial Function Before Treatment with Rosuvastatin and 10d After PCI

Before treatment, no significant differences were observed in FMD, NMD and the diameter of brachial artery between the two groups ($p > 0.05$); FMD and NMD in the patients from

the experimental group were significantly higher when compared with the control group ($p < 0.05$), but no significant differences in brachial artery diameter between the two groups 10d after PCI ($p < 0.05$) (Table III).

Comparison of Vasoactive Substances Before Treatment with Rosuvastatin and 10d After PCI

No significant differences were shown in ET-1 and TXA2 between the two groups before treatment ($p > 0.05$). The levels of ET-1 and TXA2 in the experimental group were significantly lower ($p < 0.05$), however, NO and NOS were significantly higher when compared with the control group 10d after PCI ($p < 0.05$) (Tables IV, V).

Comparison of Levels of PTX-3 Before Treatment with Rosuvastatin and 10d After PCI

No significant differences were shown in PTX-3 levels between the two groups before treatment ($p > 0.05$). The PTX-3 level in the experimental group was significantly lower than that in the control group 10d after PCI ($p < 0.05$) (Figure 1).

Table III. Comparison of vascular endothelial function before treatment with Rosuvastatin and 10d after PCI ($\bar{x} \pm s$, mmol/L).

Group	FMD (%)		NMD (%)		Diameter of brachial artery (mm)	
	Before treatment	10d after PCI	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	7.37±0.15	11.36±1.42 [^]	12.85±2.53	19.53±3.18 [^]	4.02±0.36	4.09±0.23 [^]
Control group (n=60)	7.42±0.25	9.22±1.07	12.81±2.62	15.26±2.11	4.03±0.41	4.07±0.24

Table IV. Comparison of levels of blood lipids before treatment with Rosuvastatin and 10d after PCI ($\bar{x} \pm s$, mmol/L).

Group	ET-1 (pg/L)		TXA2 (ng/L)	
	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	81.62±6.08	55.38±5.92 [^]	82.33±5.47	46.26±4.98 [^]
Control group (n=60)	80.76±7.07	78.28±9.13	82.06±4.82	77.32±8.35

[^] $p < 0.05$ vs. the control group.

Table V. Comparison of PGI2, NO, NOS before treatment with Rosuvastatin and 10d after PCI ($\bar{x} \pm s$, mmol/L).

Group	PGI2 (ng/L)		NO (μ mol/L)		NOS (U/mL)	
	Before treatment	10d after PCI	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	56.75±4.52	86.35±9.11 [^]	48.62±3.17	77.19±8.24 [^]	14.25±3.32	28.06±4.27 [^]
Control group (n=60)	56.65±5.01	64.86±7.23	49.03±3.05	57.94±7.42	14.67±3.47	17.67±2.54

[^] $p < 0.05$ vs. the control group.

Comparison of the Number of GMP-140 Molecules and Platelet Aggregation rate before treatment with Rosuvastatin and 10d after PCI

Before treatment, the number of GMP-140 molecules and the platelet aggregation rate were not significantly different between the two groups ($p > 0.05$). The number of GMP-140 molecules and platelet aggregation were significantly lower in the experimental group than in the control group 10d after PCI ($p < 0.05$) (Table VI).

Discussion

Nowadays, PCI is a major method of reperfusion therapy for the patients with AMI. However, the age of patients, the mechanical damage caused by operation, and even ischemia reperfusion injury itself will aggravate the coronal microvascular injury. Studies suggest that there is minimal correlation between reflow phenomenon caused by severe microvascular damage and deterioration in the prognosis of patients, therefore, it can be said that microvascular endothelial function is a prominent factor in the clinical assessment of the

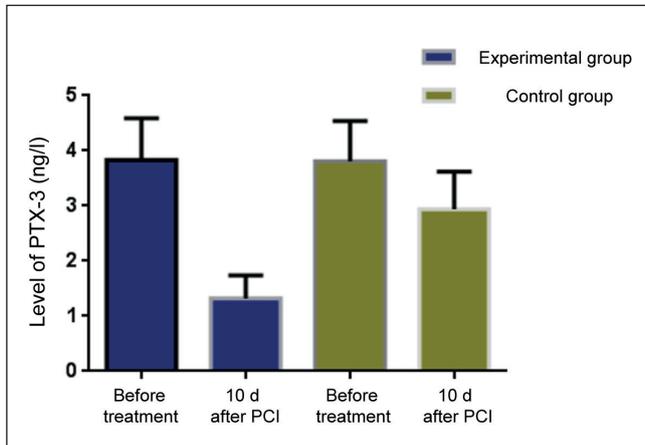


Figure 1. Comparison of levels of PTX-3 before treatment with Rosuvastatin and 10d after PCI.

Table VI. Comparison on the number of GMP-140 molecules and platelet aggregation rate before treatment with Rosuvastatin and 10d after PCI (\pm s).

Group	Number of GMP-140 molecules (M/platelet)		Platelet aggregation rate (%)	
	Before treatment	10d after PCI	Before treatment	10d after PCI
Experimental group (n=60)	1205.35 \pm 126.28	578.43 \pm 133.57 [^]	73.36 \pm 11.47	49.85 \pm 16.15 [^]
Control group (n=60)	1194.82 \pm 123.77	894.63 \pm 153.58	74.06 \pm 12.43	62.52 \pm 18.84

[^] $p < 0.05$ vs. the control group.

prognosis for patients with AMI⁸⁻¹⁰. Related studies have shown that¹¹⁻¹⁴, vascular endothelial dysfunction is the pathological basis for severe cardiovascular events and restenosis following PCI. The degree of vascular endothelial dysfunction is closely associated with the endothelial activation state. Therefore, how to improve blood lipids, hemorheological profiles, and vascular endothelial function of patients before PCI has great significance for prognosis and rehabilitation of patients¹⁵⁻¹⁷. Rosuvastatin belongs to the class of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors and acts primarily in the liver. It increases the number of receptors on the surface of liver LDL cells, accelerate the process of LDL uptake and metabolism, inhibit the hepatic VLDL synthesis, ultimately changing the LDL, VLDL levels of the body¹⁸⁻²¹. Studies^{22,23} have shown that short-term use of rosuvastatin before PCI can improve postoperative myocardial perfusion, have a marked protective effect against myocardial injury, meanwhile, it can reduce the incidence of postoperative cardiovascular events. Our experimental results showed that, the patients in the experimental group, at 10d after PCI, triglyceride, serum total cholesterol, low-density lipoprotein, plasma viscosity, fibrinogen, the viscosity of blood in the high shear rates and in the low shear rates, endothelium-dependent and non-endothelium-dependent vascular diastolic function, as well as vasoactive substances of were significantly improved than those of the control group, which is consistent with previous studies^{24,25}. PTX-3 is the first human acute phase response protein with long pentameric structure. It can be secreted by macrophages, endothelial cells, dendritic cells, smooth muscle cells and fibroblasts under the stimulation of inflammatory cytokines. Therefore, it mainly derives from the damaged heart and blood vessels tissues and reflects the local inflammatory state. This study showed that PTX-3 was significantly lower in the experimental group when compared with the control group 10d after operation ($p < 0.05$), implying that preoperative

treatment with rosuvastatin has a beneficial effect on reducing the inflammatory response in patients. GMP-140, expressed on the platelet membrane surface, is a viscous protein and a marker of platelet activation and thrombosis. The platelet aggregation rate can more directly reflect the platelet aggregation and thrombosis state. The number of GMP-140 molecules and platelet aggregation rate in the experimental group were significantly lower than those of the control group at 10d after PCI ($p < 0.05$), which implies that rosuvastatin can directly inhibit platelet aggregation and destruction, preventing further damage to coronary blood vessels.

Conclusions

In the elderly patients with AMI undergoing elective PCI, oral administration with rosuvastatin 10d before PCI can improve blood lipids, hemorheological profiles, enhance endothelial function, reduce the patient PTX-3 level, the number of GMP-140 molecules on the platelet membrane surface as well as platelet aggregation function, thus improving prognosis.

Conflict of Interests

The authors declare that they have no conflict of interest.

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