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Original Article

Effects of atorvastatin on elderly patients with acute myocardial infarction

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Abstract: Objective: This study aimed to investigate the therapeutic effect of atorvastatin on elderly patients with acute myocardial infarction (AMI). Material and Methods: 150 elderly patients with AMI admitted in our hospital were randomly selected for the prospective analysis and were divided into 3 groups according to the treatment dose: 50 patients administered with 30 mg atorvastatin were categorized as the high-dose group (HG) and 50 patients administered with 10 mg atorvastatin were categorized as the low-dose group (LG). 50 patients who only received routine treatment without atorvastatin were included in the control group (CG). Results: After treatment, the hsCRP and CK-MB levels in HG were lower than those in LG and CG, and those in LG were significantly lower than those in CG ($P < 0.05$). The left ventricular end-diastolic diameter, left ventricular end-systolic diameter, and NT-proBNP level were significantly lower after treatment than before treatment in the three groups ($P < 0.05$). The carotid plaque size and thickness in HG were significantly improved than those of LG and CG ($P < 0.05$). HG showed more obvious variations in left ventricular ejection fraction than that of LG and CG ($P < 0.05$). The levels of total cholesterol, triglyceride, and low-density lipoprotein cholesterol in the three groups after treatment were significantly lower than those before treatment ($P < 0.05$), of which after treatment the levels in HG were significantly lower than those in LG, and the levels in LG were significantly lower than those in CG ($P < 0.05$). The incidence of major adverse cardiovascular events (MACE) in CG was significantly higher than that in HG and LG. Conclusion: Atorvastatin calcium is effective in the treatment of senile AMI, which can effectively reduce the serum levels of hs-CRP and CK-MB of MACE and improve carotid plaque in patients. Moreover, high doses of atorvastatin are more effective in controlling inflammation than low doses of this drug.

Keywords: Atorvastatin, elderly acute myocardial infarction, therapeutic effect, hs-CRP, CK-MB

Introduction

Acute myocardial infarction (AMI) is a cardiovascular and cerebrovascular disease caused by coronary thrombosis resulting from the erosion of coronary atherosclerosis or inflammatory unstable plaques [1]. AMI has the characteristics of acute onset, rapid progression, poor prognosis, and high mortality. The incidence of AMI is still increasing in recent years, and this disease has a serious impact on the health and quality of life of patients, especially for elderly patients [2, 3]. Studies have shown that many inflammatory cells and endothelial cells are involved in the pathogenesis of AMI [4]. Other studies have suggested that the inflammatory response can be an independent risk factor for cardiovascular disease, which is one of the major factors leading to endothelial dysfunction [5, 6]. Moreover, many studies [7] have shown that high-sensitivity C-reactive protein (hs-CRP) can be used as a predictor of AMI, and its expression level is related to the degree of coronary atherosclerosis. It has also been reported [8] that there is a significant increase in the levels of myocardial enzymes, especially creatine kinase (CK), in the serum of patients with AMI. However, the mechanism of AMI formation has not been elucidated.

At present, AMI is mainly treated by starting thrombolytic therapy as early as possible, which is beneficial in protecting the body's functions and reducing mortality [9]. Statins are a class of drugs that have anti-inflammatory, anti-thrombosis, and plaque-stabilizing effects. Studies have shown that such drugs can block the progression of AMI from multiple causes [10]. In

terms of treatment, some studies have suggested that statin drugs should be taken as early as possible within 24 h of the onset of AMI [11]. Atorvastatin is a drug that has been widely used to treat AMI. Although some studies have found that the therapeutic effect of atorvastatin on AMI is related to the dose used, there is no definitive conclusion on the dose with the best efficacy in clinical practice [12].

Therefore, in order to investigate the efficacy of atorvastatin in elderly patients with AMI, we compared and analyzed the effects and safety of high-dose and low-dose atorvastatin, with the hope to provide more theoretical bases for the clinical use of this drug.

Materials and methods

General information

150 patients with AMI admitted in our hospital were randomly selected. They had been all treated with conventional AMI therapy. The patients were divided into three groups according to the treatment dose: 50 patients administered with 30 mg atorvastatin were categorized as the high-dose group (HG) and 50 patients administered with 10 mg atorvastatin were categorized as the low-dose group (LG). 50 patients who only received routine treatment without atorvastatin were included in the control group (CG). The serum hs-CRP and CK isoenzyme (CK-MB) levels, cardiac function indices and plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, carotid plaque, and major adverse cardiovascular events (MACE) were compared before and after treatment.

Patients who met the diagnostic criteria for AMI were considered eligible for this study [13]. The exclusion criteria were as follows: severe liver and kidney dysfunction or other tumors, coagulopathy, immune disease, use of lipid or antithrombotic drugs in the past 1 month, and atorvastatin intolerance or allergy. All patients and their families agreed to participate in the experiment and the informed consent form was signed by patients or their families. This study was approved by the ethics committee of People's Hospital of Yichun City.

Experimental drugs

Urokinase was purchased from Guangdong Tianpu Biochemical Pharmaceutical Co., Ltd. (drug approval No. H20113006). Isosorbide dinitrate tablets were purchased from Shandong Renhetang Pharmaceutical Co., Ltd. (drug approval No. H20084488). Aspirin was purchased from Guangzhou Jiuming Pharmaceutical Co., Ltd. (GYZZ H44020839). Low molecular weight heparin calcium was purchased from Shenzhen Saibao'r Biological Medicine Co., Ltd. (drug approval No. H20052319). Atorvastatin was purchased from Zhejiang Hongyuan Pharmaceutical Co., Ltd. (drug approval no. H20123302). The hs-CRP immunoturbidimetric kit was purchased from Beijing Kemei BiotechnolHGy Co., Ltd. (Beijing certificate No. [2010] 2400569). The CK-MB immunoprecipitation kit was purchased from Jiaxing Botai Biotechnology Development Co., Ltd. (Zhejiang certificate No. [2013] 2400021).

Experimental methods and analyzed indices

Urokinase, nitric acid ester, low molecular weight calcium, anticoagulant, aspirin, and beta-receptor blockers were used according to the specific conditions of the patients. Accordingly, patients in HG took 30 mg atorvastatin calcium every night, and those in LG took 10 mg atorvastatin calcium every night for 4 weeks. The left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular ejection fraction (LVEF) of the 2 groups were compared using ultrasound before and after treatment and the carotid plaque size and thickness were recorded and measured. The plasma NT-proBNP were measured and compared before and after treatment in both groups. The incidence of MACE within 1 month after treatment was recorded and compared. The MACE events included cardiogenic shock, myocardial infarction, and acute heart failure. Adverse reactions, such as included nausea, vomiting, abdominal pain, and diarrhea, occurred during treatment among the three groups were compared.

Statistical methods

In this study, SPSS18.0 software (Boyi Zhixun [Beijing] Information Technology Co., Ltd.) was used for statistical analysis of the data, and the measurement data were expressed as means ± standard deviations. The t-test was used for comparisons between the 2 groups, and the chi-square test was used for counting data. $P <$

Table 1. Baseline data

Factor	High dose group	Low dose group	Control group	F/X^2	P
Gender				0.053	0.974
male	26 (52.00)	27 (54.00)	26 (52.00)		
female	24 (48.00)	23 (46.00)	24 (48.00)		
Age				0.053	0.974
≥ 66	23 (54.00)	22 (44.00)	23 (54.00)		
< 66	27 (46.00)	28 (56.00)	27 (46.00)		
BMI				0.161	0.923
≥ 23	23 (46.00)	22 (44.00)	24 (48.00)		
< 23	27 (54.00)	28 (56.00)	26 (52.00)		
Infarct site				0.427	0.981
Lower wall	16 (32.00)	15 (30.00)	16 (32.00)		
Anterior wall	15 (30.00)	14 (28.00)	16 (32.00)		
Inferior wall and posterior wall	19 (38.00)	21 (42.00)	18 (36.00)		
Risk factors				0.142	0.921
Diabetes	21 (42.00)	20 (40.00)	22 (44.00)		
Hypertension	29 (58.00)	30 (60.00)	28 (56.00)		
Coagulation function					
APTT s	28.95 ± 2.88	29.01 ± 2.73	29.03 ± 2.71		
PT s	12.13 ± 1.07	12.15 ± 0.97	12.11 ± 0.96		
FIB g/l	3.05 ± 0.21	3.02 ± 0.20	3.06 ± 0.19		
TT s	14.71 ± 1.52	14.66 ± 1.49	14.69 ± 1.50		
History of surgery				0.068	0.967
yes	13 (26.00)	14 (28.00)	13 (26.00)		
no	37 (74.00)	36 (72.00)	37 (74.00)		
Renal function index (μmol/L)					
creatinine	63.51 ± 4.22	64.02 ± 4.18	64.04 ± 4.15	0.258	0.773
Urea	5.56 ± 0.73	5.61 ± 0.81	5.58 ± 0.79	0.052	0.949
uric acid	321.51 ± 15.72	319.37 ± 16.02	320.27 ± 16.05	0.228	0.797
Cardiac function index					
LVEDD	50.29 ± 6.15	51.04 ± 6.22	50.78 ± 6.17	0.19	0.827
LVESD	40.12 ± 4.05	39.98 ± 4.11	40.04 ± 4.07	0.145	0.985
LVEF	43.34 ± 4.91	43.27 ± 5.01	43.29 ± 5.03	0.003	0.997
Diseased vessel				0.202	0.995
Single branch lesion	13 (26.00)	13 (26.00)	14 (28.00)		
Double branch lesion	20 (40.00)	19 (38.00)	20 (40.00)		
Multibranch lesion	17 (34.00)	18 (36.00)	16 (32.00)		

0.05 indicates a statistically significant difference.

Results

General materials

There were no significant differences in gender, age, and risk factors among the three groups ($P > 0.05$) (**Table 1**).

Cardiac function indices in three groups after treatment

In HG, the LVEDD, LVESD, and LVEF (cardiac function indices) were 42.73 ± 4.61 mm, 33.85 ± 3.16 mm, and 54.04 ± 7.53%, respectively. In LG, the LVEDD, LVESD, and LVEF were 48.05 ± 5.34 mm, 37.21 ± 3.56 mm, and 47.82 ± 6.21%, respectively. In CG, the LVEDD, LVESD, and LVEF were 48.31 ± 4.59 mm, 38.26 ± 2.67

Table 2. Cardiac function indexes of two groups after treatment

Index	High-dose group	Low-dose group	Control group	F	P
LVEDD (mm)	42.73 ± 4.61	48.05 ± 5.34	48.31 ± 4.59	21.00	< 0.001
LVEDD (mm)	33.85 ± 3.16	37.21 ± 3.56	38.26 ± 2.67	26.72	< 0.001
LVEF (%)	54.04 ± 7.53	47.82 ± 6.21	43.25 ± 4.21	38.94	< 0.001

Table 3. Size and thickness of carotid plaque before treatment

Time	High dose group	Low dose group	Control group	F	P
Carotid size (cm^2)	0.16 ± 0.03	0.17 ± 0.04	0.16 ± 0.04	1.220	0.298
Carotid thickness (mm)	2.58 ± 0.46	2.57 ± 0.51	2.55 ± 0.47	0.051	0.951

Table 4. Size and thickness of carotid plaque after treatment

Time	High dose group	Low dose group	Control group	F	P
Carotid size (cm^2)	0.04 ± 0.01	0.08 ± 0.02	0.13 ± 0.03	217.9	< 0.001
Carotid thickness (mm)	1.95 ± 0.24	2.29 ± 0.33	2.42 ± 0.42	25.77	< 0.001

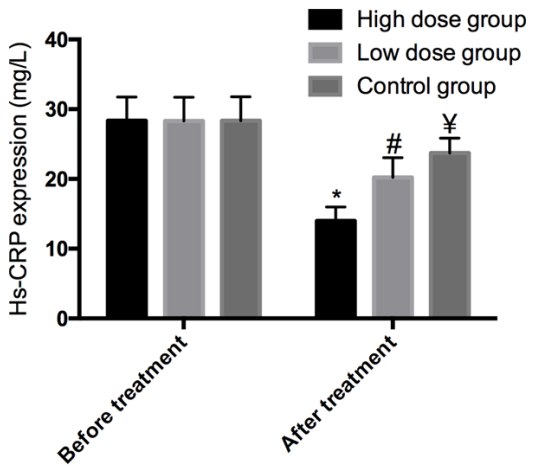

Figure 1. Comparison of high-sensitivity C-reactive protein (hs-CRP) expression before and after treatment in the three groups. The expression of hs-CRP in the three groups was significantly lower after treatment than before treatment. However, the expression of hs-CRP in HG was significantly lower than in LG and CG ($P < 0.05$). Note: compared with those before treatment, *, #, and ¥$P < 0.05$; compared with # and ¥, *$P < 0.05$; compared with ¥, #$P < 0.05$.

mm and 43.25 ± 4.21%, respectively. The LVEDD and LVESD in HG were significantly lower than those in LG and CG, whereas the LVEF in HG was higher than that in LG and CG ($P < 0.05$) (**Table 2**).

Size and thickness of carotid plaque in the three groups before and after treatment

There was no significant difference before treatment ($P > 0.05$), while the three groups achieved a reduction in the size and thickness of carotid plaque after treatment, which was more significant in HG as compared with LG and CG, and in LG as compared with the CG ($P < 0.05$, **Tables 3** and **4**).

The expression levels of hs-CRP in three groups before and after treatment

The expression levels of hs-CRP had no significant difference among the three groups before treatment ($P > 0.05$). After treatment, the hs-CRP level in HG was 13.97 ± 2.02 mg/L, whereas that in LG and CG was 20.21 ± 2.84 mg/L and 23.71 ± 2.13 mg/L, respectively. The expression levels of hs-CRP among the three groups after treatment were significantly lower than those before treatment; however, the expression of hs-CRP in HG was significantly lower than that in LG and CG, while the expression of hs-CRP in LG was significantly lower than that in CG ($P < 0.05$) (**Figure 1**).

The expression levels of CK-MB in three groups before and after treatment

The expression of CK-MB had no significant difference among the three groups before treatment ($P > 0.05$). After treatment, the CK-MB level in HG was 14.41 ± 2.05 U/L, whereas that in LG and CG was 20.23 ± 3.22 U/L and 24.63 ± 3.16 U/L, respectively. The expressions of CK-MB among the three groups after treatment were significantly lower than those before treatment; however, the expression of CK-MB in HG

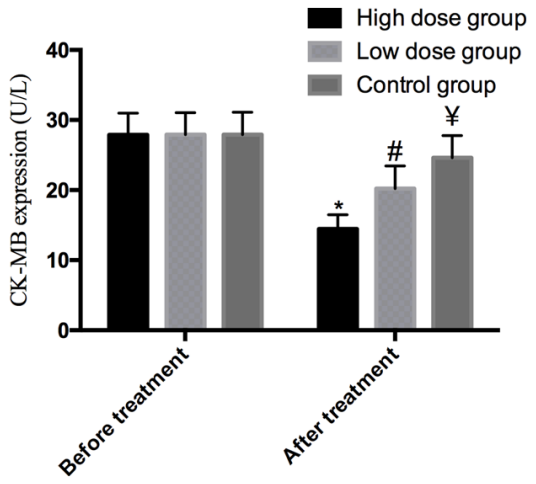

Figure 2. Comparison of CK-MB expression levels before and after treatment in three groups. The expression of CK-MB in the three groups was significantly lower after treatment than before treatment. However, the expression of CK-MB in HG was significantly lower than in LG and CG ($P < 0.05$). Note: compared with those before treatment, *, #, and ¥$P < 0.05$; compared with # and ¥, *$P < 0.05$; compared with ¥, #$P < 0.05$.

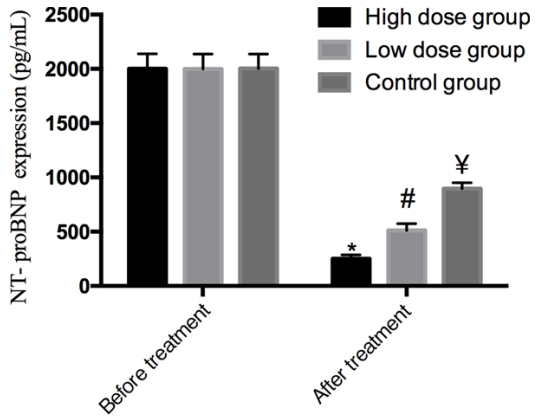

Figure 3. Plasma NT-proBNP expression levels before and after treatment in three groups. There was no significant difference in plasma NT-proBNP expression among three groups before treatment ($P < 0.05$). After treatment, the expression of NT-proBNP in HG was significantly lower than that in LG and CG. The expression of NT-proBNP in LG was significantly lower than that in CG ($P < 0.05$). Note: compared with those before treatment, *, #, and ¥$P < 0.05$; compared with # and ¥, *$P < 0.05$; compared with ¥, #$P < 0.05$.

after treatment was significantly lower than that in LG and CG ($P < 0.05$) (**Figure 2**).

Plasma NT-proBNP levels in three groups before and after treatment

There was no significant difference in expression of NT-proBNP in plasma among the three groups before treatment ($P > 0.05$). After treatment, the NT-proBNP level in HG was 251.84 ± 35.19 pg/mL, whereas that in LG and CG was 512.38 ± 61.83 pg/mL and 896.41 ± 55.31 pg/mL, respectively. The expressions of NT-proBNP in plasma among the three groups after treatment were significantly lower than those before treatment; however, the expression of NT-proBNP in HG was significantly lower than that in LG and CG ($P < 0.05$) (**Figure 3**).

Occurrence of MACE in both groups within 1 month after treatment

Within 1 month after treatment, the number of patients in HG who developed cardiogenic shock, myocardial infarction, and acute heart failure was 1, 0, and 1, respectively, and the overall incidence of MACE was 4.00%. The number of patients who developed cardiogenic shock, myocardial infarction, and acute heart failure in LG was 3, 3, and 4, respectively, and the overall incidence of MACE was 20.00%. The overall incidence in CG was 34.00%. The incidence of MACE in HG was significantly lower than that in LG, and that in LG was lower than that in CG ($P < 0.05$) (**Table 5**).

Incidence of adverse reactions during treatment in three groups

The incidence of adverse reactions was 14.00% in HG, 12.00% in LG, and 10.00% in CG. There was no significant difference among the three groups ($P > 0.05$) (**Table 6**).

Discussion

AMI is a severe coronary heart disease caused by acute myocardial necrosis resulting from long-standing severe myocardial ischemia. The pathological mechanism of AMI is mainly related to the change of plaque properties due to coronary atherosclerosis. The rupture of some unstable plaques causes the activation of the coagulation mechanism, resulting in local thrombosis and occlusion of the lumen [14, 15]. Many studies have found that inflammatory reactions play an important role in the formation of arteriosclerosis. It is also an important

Table 5. Occurrence of MACE in three groups

Index	High dose group	Low dose group	Control group	X^2	P
Cardiogenic shock	1 (2.00)	3 (6.00)	5 (8.00)	-	-
Myocardial infarction	0	3 (6.00)	6 (6.00)	-	-
Acute heart failure	1 (2.00)	4 (8.00)	6 (6.00)	-	-
Total incidence	2 (4.00)	10 (20.00)	17 (34.00)	14.45	< 0.001

Table 6. Incidence of adverse reactions during treatment in three groups of patients

Factor	High dose group	Low dose group	Control group	X^2	P
Feel sick and vomit	2 (4.00)	2 (4.00)	1 (2.00)	-	-
stomachache	2 (4.00)	1 (2.00)	2 (4.00)	-	-
diarrhea	3 (6.00)	3 (6.00)	2 (4.00)	-	-
Total incidence	7 (14.00)	6 (12.00)	5 (10.00)	0.379	0.828

factor for the rupture and thrombosis of unstable plaque [16, 17]. At present, the clinical treatment of AMI mainly involves thrombolysis and anticoagulation [18]. Atorvastatin is a kind of statin with multiple effects, including anti-inflammatory, plaque-stabilizing, and vascular endothelial function-enhancing activities [19, 20].

As a non-specific marker protein of systemic inflammation, hs-CRP is an acute-phase reactive protein synthesized by hepatocytes and induced by cytokines such as tumor necrosis factor [21]. Studies have shown that as a non-specific marker for inflammatory response or tissue damage, hs-CRP has clinical significance in the treatment and prognosis of atherosclerosis [22].

In this study, the serum hs-CRP level of HG was significantly lower than that of LG and CG, indicating that atorvastatin can effectively control the inflammatory response. Moreover, high doses of atorvastatin have better effect in controlling inflammation than low doses of atorvastatin. Myocardial enzymes are normally present in the myocardium, bones, and brain tissues. When these tissues or organs are damaged, the expression levels of myocardial enzymes will change accordingly. As an isoenzyme of CK, CK-MB is important as it reflects the degree of damage in cardiac myocytes [23]. The expression level of CK-MB in HG after treatment was significantly lower than that in LG and CG, indicating that atorvastatin can effectively improve myocardial damage. Moreover, the cardiac function indices and plasma NT-proBNP levels before and after treatment were compared among the three groups. It was found that the LVEF, LVESD, and NT-proBNP levels of the patients among the three groups were significantly improved after treatment compared with those before treatment, and those in the HG group were more significantly improved than those in the LG and CG groups. Besides, HG showed more obvious variation in the indices than that of LG and CG. These results indicate that atorvastatin can effectively improve cardiac function in elderly patients with AMI, and the effect of high-dose atorvastatin is superior to that of low-dose atorvastatin. Zhao S *et al.* [24] postulated that this may be due to the inhibition of the Na^+-Ca^{2+} exchange by atorvastatin, reducing the intracellular Ca^{2+} concentration and thereby enhancing the endothelial dysfunction and protecting the cardiac function. We have not conducted further investigations on this mechanism, which will need to be included in future experiments. Furthermore, it is discovered that atorvastatin has more prominent improvements to carotid plaque when given at high dose, indicating that high doses of atorvastatin can effectively reduce the incidence of MACE in patients. Another study [25] showed that atorvastatin can significantly reduce the incidence of MACE and mortality in patients with AMI. In the present study, we postulated that the incidence of MACE in HG was lower than that in LG, which was possibly because the improvements of cardiac function, inflammatory level, and blood lipid level were better with high-dose atorvastatin than with low-dose atorvastatin. There was no significant difference in the incidence of adverse reactions among the three groups, suggesting that atorvastatin not only has a good effect on AMI patients, but also has high safety.

Conclusions

In summary, atorvastatin can effectively improve the serum hs-CRP and CK-MB levels in elderly patients with AMI, improve the blood

lipid levels and reduce the incidence of MACE as well as adverse reactions in these patients. In addition, high-dose atorvastatin is more effective than low-dose atorvastatin. However, detailed comparisons of the dosage of atorvastatin in this study are not enough and further investigation of the mechanism of action of atorvastatin is needed. More studies are warranted to elucidate these issues in the future.

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Disclosure of conflict of interest

None.

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