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Original Article

Clinical analysis of different doses of atorvastatin calcium tablets on cerebral vascular interventional therapy in patients with ischemic cerebrovascular disease

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Abstract: Objective: To analyze the clinical efficacy of different doses of Atorvastatin calcium tablets on cerebral vascular interventional therapy in patients with ischemic cerebrovascular disease. Methods: A total of 110 patients whose ischemic cerebrovascular diseases were treated with cerebral vascular interventional therapy in Daqing Oilfield General Hospital from October 2015 to October 2017 were randomized to the experimental group (n=55) and the control group (n=55). The control group was given 20 mg Atorvastatin calcium tablets three days before the administration of contrast agent and after cerebrovascular interventional therapy while the experimental group was given 80 mg Atorvastatin calcium tablets three days before the contrast media were used and 40 mg Atorvastatin calcium tablets after cerebrovascular interventional treatment. The incidence of contrast induced nephropathy (CIN), blood lipids, liver function, renal function, and hs-CRP level were compared between the two groups. Results: There were no significant differences between the two groups in the incidence of CIN, the serum levels of ALT, AST, LDL-C, HDL-C, TG, and TC at postoperative 24 and 72 hours respectively, and hs-CRP, Cys-C, β2-MG, Ccr, BUM, and Scr at preoperative 24 hours (all $P>0.05$). Compared with the control group, the experimental group showed lower hs-CRP, Cys-C, β2-MG, BUM, Scr at postoperative 72 hours. Compared with the control group, the experimental group demonstrated higher Ccr at postoperative 72 hours (all $P<0.05$). Conclusion: A higher dose of Atorvastatin calcium tablets can effectively improve the renal function after cerebral vascular interventional therapy in patients with ischemic cerebrovascular disease, and reduce the incidence of CIN, which is safer and worthy of reference.

Keywords: Atorvastatin calcium tablets, ischemic cerebrovascular disease, cerebral vascular interventional therapy, clinical efficacy

Introduction

At present, the ongoing process of population aging and the changes in people's living environment and dietary pattern have led to the increased incidence in China of cerebrovascular diseases, among which the incidence of ischemic cerebrovascular disease is relatively high [1]. As medical science and technology develop rapidly, cerebral vascular interventional therapy is widely used in the treatment of ischemic cerebrovascular disease, significantly reducing hypoxia and ischemia of brain tissues. Nevertheless, treatment is a traumatic surgery after all, which can aggravate the inflammatory reaction caused by cerebral ischemia and increase the incidence of contrast induced nephropathy (CIN) [2, 3]. The good tolerability of Atorvastatin calcium tablets means the adverse reactions are often transient or mild, including elevated transaminases, flatulence, and constipation. These side effects had little impact on liver and renal functions, and therefore, discontinuation of medication is generally unnecessary. In order to analyze the clinical effects of different doses of Atorvastatin calcium tablets on the liver and renal functions in patients whose ischemic cerebrovascular diseases were treated with cerebral vascular interventional therapy, a total of 110 patients with ischemic cerebrovascular disease were recruited who received cerebral vascular interventional thera-

Table 1. Comparisons of general data in two groups

Group	Gender (male/female)	Mean age (($\bar{x}$ ± sd) years)	BMI (($\bar{x}$ ± sd) kg/m^2)
Experimental group (n=55)	35/20	55.41 ± 8.62	22.25 ± 3.66
Control group (n=55)	33/22	55.83 ± 7.14	22.57 ± 5.18
χ^2/t	0.154	0.278	0.374
P	0.695	0.781	0.709

Note: BMI, body mass index.

py in Daqing Oilfield General Hospital from October 2015 to October 2017.

Materials and methods

General information

This study was approved by the Ethics Committee of Daqing Oilfield General Hospital [4]. A total of 110 patients whose ischemic cerebrovascular diseases were treated with cerebral vascular interventional therapy in Daqing Oilfield General Hospital from October 2015 to October 2017 were recruited for this study. The patients were randomized to the experimental group (n=55) and the control group (n=55).

Inclusion criteria: Patients met the diagnostic criteria for acute ischemic cerebrovascular disease of 2001 [5]; patients who were older than 18 years and younger than 80 years; patients whose relatives had also signed informed consent before entry into the study.

Exclusion criteria: Patients who received nephrotoxic drugs two weeks before entry into the study; patients with severe organ dysfunctions in kidney, liver or heart; patients complicated by infectious diseases, systemic immune diseases or hypertension; patients who were allergic to iodine contrast medium; patients with poor treatment compliance.

Methods

The two groups were given 500 mL of 0.9% Sodium Chloride Physiological Solution (manufacturer: Shandong Qidu Pharmaceutical Co., Ltd.; specification: 4.5 g: 500 mL) through intravenous injection 12 hours before the administration of contrast agent. The control group was orally given 20 mg of Atorvastatin calcium tablets (manufacturer: Pfizer Pharmaceuticals Co., Ltd.; specifications: 10 mg/tablet) per day from 3 days before the administration of contrast agent to postoperative period, while the experimental group orally received 80 mg Atorv-astatin calcium tablets per day during the three days before the administration of contrast agent and 40 mg Atorvastatin calcium tablets per day in the postoperative period [6].

Indicators

Primary indicators include renal function, hs-CRP levels, and the incidence of CIN. All participants had 5 mL of fasting venous blood collected 24 hours before surgery and 72 hours after surgery respectively. These blood samples were centrifuged at a rate of 4,000 r/min. Within the next 2 hours, an automatic biochemical analyzer was used (manufacturer: Shenzhen iCubio Biomedical Technology Co., Ltd.; model: iChem-520) to detect Triglyceride (TG), total cholesterol (TC) through an enzymatic method, which refers to the hydrolysis of TG to lipase and glycerol and the phosphorylation of the glycerol with adenosine triphosphate (ATP) and glycerokinase (GK). The analyzer was also used to detect aspartate aminotransferase (AST), alanine aminotransferase (ALT), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) through a microplate-based method, which refers to the following procedures: the first well was regarded as the standard one, and the second and third wells were viewed as low-value quality control and high-value quality control respectively. The quality control serum in each well was 20 μL. Then 20 μL sample and 200 μL working solution were added per well. After shaken, the microplate was put into a microplate reader and was incubated for 10 minutes at 37°C. The first readings were carried out with the dominant wavelength of 192 nm, and the second readings were carried out after 13 minutes. The results were later analyzed by laboratory management software. Levels of cystatin C (Cys-C) and hs-CRP were measured by turbidimetric inhibition immunoassay (TINIA) while contents of creatinine clearance (Ccr), β2-microglobulin (β2-MG), blood urea nitrogen (BUN), and serum creatinine (Scr) were measured by the enzymatic endpoint assay. The incidence of CIN was calculated by the following formula: (the number of cases with CIN/

Table 2. Comparisons and analyses of blood lipids in two groups ($\bar{x}$ ± sd)

Group	LDL-C (mmol/L)		TC (mmol/L)		TG (mmol/L)		HDL-C (mmol/L)	
	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h
Experimental group (n=55)	2.19 ± 0.42	2.18 ± 0.54	4.43 ± 1.18	4.32 ± 1.03	1.68 ± 0.41	4.26 ± 0.64	1.22 ± 0.28	1.21 ± 0.31
Control group (n=55)	2.17 ± 0.39	2.17 ± 0.39	4.46 ± 1.15	4.36 ± 1.04	1.65 ± 0.38	4.25 ± 0.56	1.21 ± 0.24	1.22 ± 0.28
T	0.259	0.111	0.135	0.203	0.398	0.087	0.201	0.178
P	0.797	0.912	0.893	0.840	0.691	0.931	0.841	0.860

Note: LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triacylglycerol; HDL-C, high density lipoprotein cholesterol.

Table 3. Comparisons and analyses of liver function indicators in two groups ($\bar{x}$ ± sd)

Group	ALT (U/L)		AST (U/L)	
	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h
Experimental group (n=55)	28.62 ± 6.14	29.68 ± 4.14	25.25 ± 3.14	26.25 ± 3.09
Control group (n=55)	28.59 ± 6.22	29.57 ± 4.28	25.24 ± 3.19	26.28 ± 3.22
t	0.025	0.137	0.017	0.048
P	0.980	0.891	0.987	0.960

Note: AST, aspartate aminotransferase; ALT, alanine aminotransferase.

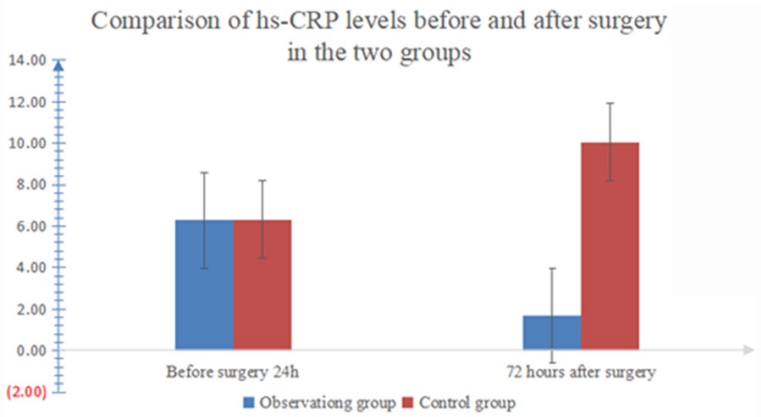

Figure 1. Comparison of hs-CRP levels between 24 hours before surgery and 72 hours after surgery in the two groups.

number of total cases) *100% = the incidence of CIN.

Secondary indicators include baseline characteristics, blood lipids and liver function. Baseline characteristics included the gender, age, and BMI of all participants. By taking 200 μL sample and 50 μL reagent, TINIA was performed to measure LDL-C, HDL-C, TG, TC, ALT, AST, after 30 seconds of reaction [7, 8].

Statistical analysis

All statistical analyses were performed with SPSS24.0 software. The measurement data are expressed as mean ± standard deviation ($\bar{x}$ ± sd). Two sets of measurement data that were normally distributed were expressed as t and were compared using the Student's t-test while the enumeration data were expressed as n, % and were compared using Chi-square test and Fisher's exact test. *P* value of <0.05 is considered significant.

Results

Comparisons of baseline characteristics between two groups

There were no significant differences between two groups in baseline characteristics such as sex, age and BMI (all P>0.05) as shown in **Table 1**.

Comparisons of blood lipids between two groups

There were no significant differences between two groups in the levels of LDL-C, TC, TG, and HDL-C at preoperative 24 and postoperative 72 hours respectively (all P>0.05) as shown in **Table 2**.

Table 4. Comparisons and analyses of renal function indicators in two groups ($\bar{x} \pm sd$)

Group	Cys-C (mg/L)		β2-MG (mg/L)		Ccr (mL/min)		BUM (mmol/L)		Scr (μmol/L)	
	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h	Preoperative 24 h	Postoperative 72 h
Experimental group (n=55)	0.86 ± 0.12	0.94 ± 0.13	2.34 ± 0.34	2.49 ± 0.34	83.26 ± 16.28	82.29 ± 18.14	6.38 ± 2.05	5.56 ± 1.14	79.25 ± 18.14	76.05 ± 14.31
Control group (n=55)	0.83 ± 0.13	1.24 ± 0.28	2.33 ± 0.31	2.78 ± 0.33	83.22 ± 16.47	65.32 ± 14.14	6.33 ± 2.04	6.69 ± 1.98	79.22 ± 18.06	93.62 ± 15.77
t	1.257	7.207	0.161	4.539	0.012	5.472	0.128	3.668	0.009	6.119
P	0.211	<0.001	0.872	<0.001	0.990	<0.001	0.898	<0.001	0.993	<0.001

Note: Cys-C, cystatin C; β2-MG, β2-microglobulin; Ccr, creatinine clearance; BUM, urea nitroge; Scr, serum creatinine.

Table 5. Comparisons of hs-CRP levels and incidences of CIN in two groups

Group	hs-CRP (($\bar{x}$ ± sd) mg/L)		Incidence of CIN (n, %)
	Preoperative 24 h	Postoperative 72 h	
Experimental group (n=55)	7.89 ± 1.68	1.68 ± 0.62	1 (1.82)
Control group (n=55)	7.86 ± 1.55	10.17 ± 2.22	2 (3.64)
t/χ^2	0.097	27.316	0.343
P	0.923	<0.001	0.558

Note: CIN, contrast induced nephropathy.

Comparisons of indicators of liver function between two groups

There were no significant differences between two groups in the levels of ALT and AST at preoperative 24 and postoperative 72 hours respectively (all P>0.05) as shown in **Table 3**.

Comparisons of indicators of renal function between two groups

There were no significant differences between two groups in Cys-C, β2-MG, Ccr, BUM, and Scr at preoperative 24 hours (all P>0.05). The levels of Cys-C, β2-MG, BUM, and Scr of the experimental group were markedly lower than those of the control group at 72 hours after the operation, and the content of Ccr was prominently higher than that of the control group with statistically significant differences (all P<0.001). **Figure 1** shows the hs-CRP changes in renal function in two groups 24 hours before surgery and 72 hours after surgery as shown in **Table 4** and **Figure 1**.

Comparisons of hs-CRP levels and incidences of CIN in two groups

The level of hs-CRP and incidence of CIN in two groups were compared at preoperative 24 hours with no statistical difference (both P>0.05). The hs-CRP level in the experimental group was obviously lower than that in the control group at 72 hours after surgery with a statistically significant difference (P<0.05) as shown in **Table 5**.

Discussion

With high morbidity and mortality, ischemic cerebrovascular diseases are a great threat to the human body. The extensive use of contrast agent and cerebrovascular interventional therapy contribute to the diagnosis and treatment of ischemic cerebrovascular diseases [9, 10]. With the help of contrast agent and radiographic instruments, blood vessels of cerebral hemispheres, intracranial vessels, basilar arteries and internal carotid arteries can be clearly seen. Additionally, establishment of collateral circulation, arterial occlusion and stenosis can also be effectively displayed, which provides scientific references for the use of cerebral vascular interventional therapy. However, the duration of treatment is prolonged and the prognosis is generally poor for CIN is commonly seen in patients who received cerebrovascular interventional therapy [11, 12].

Atorvastatin calcium tablets are useful in several ways. First, they can decrease serum cholesterol. Atorvastatin calcium tablets can effectively reduce the isoprenylation of Rho protein, making Rho protein unable to adhere to the stem cell membrane. Thus the inhibited activity of Rho protein effectively reduces the levels of cholesterol [13, 14]. Second, they can reduce thrombus formation. Atorvastatin calcium tablets can effectively improve the fibrinolysis, significantly inhibiting thrombosis and reducing nuclear transcription factors and inflammatory factors in the nucleus [15, 16]. Third, they can improve the function of endothelial cell. Atorvastatin calcium tablets increase the expression of eNos, thereby improving the patient's endothelial function. This results in the significantly reduced incidence of CIN [17, 18]. Fourth, they can reduce patients' immune responses and vascular inflammation. By inhibiting the activity of transcription factors and the functions of macrophages and monocytes, Atorvastatin calcium tablets play a pivotal role in immune regulation and the alleviation of inflammation. After oral administration of Atorvastatin calcium tablets, drug absorption is rapid as the plasma concentration can reach the peak within 30 minutes with relatively low absolute bioavailability. Therefore, Atorvastatin calcium tablets of different doses have a good lipid-lowering effect, leading to a significantly lowered incidence of CIN [19]. In this study,

blood lipids, liver function and the incidence of CIN in two groups were compared at postoperative 72 hours. Renal function and hs-CRP level in the experimental group were obviously better than those in the control group. In the study of Zhang et al., group A (given 20 mg Atorvastatin calcium tablets) had higher level of hs-CRP than that of group B (given 40 mg) and group C (given 80 mg), which was consistent with the results of this study. This proved that the effectiveness of a high dose of Atorvastatin calcium tablets and its efficacy in the cerebral vascular interventional therapy for patients with ischemic cerebrovascular disease [20]. Therefore, The results of our study provide references for clinical practices. But the study still has some limitations. The data of this study are too small, and the relatively short time span of the studied group might affect the results to a certain degree. It is of great necessity to expand the sample data and to extend the time span of the study to explore the long-term effect of a high dose of Atorvastatin calcium tablets in patients whose ischemic cerebrovascular diseases were treated with cerebral vascular interventional therapy. In this way, more scientific and rigorous references can be provided for clinical treatments of ischemic cerebrovascular diseases and cardiovascular diseases.

In conclusion, administration of a high dose of Atorvastatin calcium tablets in cerebrovascular interventional therapy in patients with ischemic cerebrovascular disease can effectively reduce the incidence of CIN and improve the renal function of patients and is relatively safe.

Disclosure of conflict of interest

None.

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