Effect of Atorvastatin on lower extremity function of patients with hypertension and peripheral arterial disease

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Abstract: This paper aims to discuss the short-term effect of Atorvastatin on lower-extremity function of patients with hypertension and peripheral arterial disease (PAD). 40 patients with hypertension and ankle-brachial index (ABI) less than 0.9 were divided into the control group (20 cases) and Atorvastatin group (20 cases) and treated for 6 months. The variation between the 6-min walk and the gait speed of 4-m-walk before and after the treatment were respectively observed. With regard to the two groups, differences of the drop-out values before and after the treatment were adjusted in accordance with gender, ages, body mass index (BMI), difference values of systolic pressure, ABI, difference values of total cholesterol (TC), difference values of low density lipoprotein, triacylglycerol, smoking and drug-taking situation. After the treatment, the 6-min walk had no obvious change between the two groups ($P>0.05$), but the 4-m normal and rapid walking speed changed obviously ($P<0.01$). Short-term therapy with atorvastatin can significantly delay the decline of the walking speed in short distance and improve the lower-extremity function of patients with hypertension and PAD.

Keywords: Atorvastatin; Hypertension; Peripheral arterial disease; Lower-extremity function.

INTRODUCTION

Peripheral arterial disease is a serious complication of atherosclerosis (AS) in patients with hypertension, often occurs in the lower extremity, with the main clinical manifestations of intermittent claudication, which has great influence on the quality of life of patients (Makin *et al*., 2001). In addition, the morbidity and mortality of cardiovascular disease were significantly higher in patients with peripheral arterial disease (Criqui *et al*., 1997). Statins, belonged to the hydroxymethyl glutaryl coenzyme inhibitors, are clinically widely used lipid-lowering drugs, which is mainly used in the treatment of hyperlipidemia and AS (Murrow *et al*., 2012). The domestic and foreign research for AS and hyperlipidemia has confirmed that statins can inhibit endothelin production by a variety of mechanisms to improve endothelial function, which is beneficial to the improvement of arterial elasticity and the long-term treatment can even reverse the atherosclerotic plaque (Mi and Wang, 2011; Blazing, 2010). At present, there are few studies on the effect of statins on the treatment of patients with hypertension. This research adopted the common detection method of ABI, walking distance and walking speed, aiming to observe the effect of Atorvastatin on lower-extremity function of peripheral arterial disease in patients with hypertension.

MATERIALS AND METHODS

General information

The experiment subjects were selected from the outpatients or hospitalized patients in the People's Hospital, who were diagnosed as primary hypertension decidedly through medical history, physical examination or laboratory examination, and secondary hypertension, liver disease, kidney disease, chronic heart failure, ischemic heart disease, diabetes, and malignant tumor, etc were all excluded. Inclusion criteria: (1) Patients are taking anti-hypertensive drugs regularly; (2) TC between 416- 612mmol/L (180-240mg); (3) Blood pressure is stable and no more than 2 levels, that is, systolic blood pressure (SBP) <180 mmHg, and diastolic blood pressure (DBP) <110 mmHg; (4) The patient has not taken lipid-lowering drugs and ABI <0.9. Exclusion criteria: (1) patients had received angiopasty operation on the lower limb; (2) patients cannot walk; (3) patients with mental disorders; (4) patient can not accurately complete the lower limb function determination. A total of 40 cases were included and randomly divided into control group (20 cases) and Atorvastatin group (20 cases), with informed consent. And the gender, age, BMI, SBP, DBP, ABI, TC, low density lipoprotein (LDL), high-density lipoprotein (HDL), three acyl glycerin (TG), smoking, and medication etc between the two groups were not statistical significance ($P>0.05$). Therefore, the two groups were comparable.

Therapeutic scheme

The included patients were still taking anti-platelet agents and anti-hypertensive drugs. Based on this, the control group were given 1 tablet placebo to each patient and the Atorvastatin group were given Atorvastatin (Trade Name: Lipitor, Pfizer Pharmaceutical Co., Ltd.), with 10 mg for oral every night. Before treatment, all patients in two groups were examined and recorded the blood pressure, height, body mass, heart rate, blood fat, liver and kidney function, ABI, 6-min walk and 4-m walking speed. And

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Table 1: Comparison of the variance of the blood pressure and blood fat between the two groups before and after treatment (x ± s, n=20)

Items	Control group		Atorvastatin group	
	Before treatment	After treatment	Before treatment	After treatment
SBP/(mmHg)	153.01±10.35	149.01±9.65	148.10±9.23	141.21 ±8.83#
DBP/(mmHg)	85.35 ±8.34	82.35±7.84	82.39 ± 8.13	79.59 ±7.42
TC/(mmol/L)	5.78 ±0.77	5. 82±0.79	5.69 ± 0.73	5.03 ±0.70 #
LDL/(mmol/L)	3.53 ±0.54	3. 54±0.55	3.49 ± 0.50	2.95 ±0.45#
HDL/(mmol/L)	1.41 ±0.39	1.43±0.40	1.39 ± 0.31	1.41 ±0.31
TG/(mmol/L)	1.87 ±0.46	1.89±0.47	1.79 ± 0.43	1.58 ±0.42

Table 2 Comparison of the variance of lower limbs function between the two groups before and after treatment (x±s, n=20)

Items	Control group	Atorvastatin group
	Mean value after adjustment	Mean value after adjustment
6-min walk/m	-8.310 (-13.23 ± -3.38)	-5.170 (-8.2400 ± -2.1000)
Normal speed of 4 m-walk/(m/s)	-0.003 (-0.004 ± -0.002)	0.004 (0.0025 ± 0.0055)##
Rapid speed of 4 m-walk/(m/s)	-0.020 (-0.035 ± -0.005)	-0.004 (-0.0210 ± 0.0130)#

Note: compared with the control group, #P<0.05, ##P<0.01.

these examination were repeated again after 6-month treatment.

Observation indexes

ABI detection

The CVProfileDO2020 determinator made in American HDI Company was used to synchronously record the blood pressure. The patients were required to take off their shoes and socks, lying on their backs to rest for 5 min at the room temperature of 21°C before the ABI determination. 12cm*40 cm cuff was put on the bilateral upper arm to measure the bilateral upper arm systolic pressure, taking the higher value; then the cuff was put on the bilateral ankles, and the Doppler probes or stethoscope were placed in the posterior tibial artery or dorsalispedis artery to measure the bilateral ankle systolic pressure taking the higher value. ABI was the ratio of the ankle pressure to upper arm pressure.

6-min walk

According to the international common standards, the patients walked back and forth along a straight corridor about 30m, recording the maximum distance within 6 minutes (Guyatt *et al*., 1985).

Gait speed of 4 m-walk

With the above method, the gait speed of 4 m-walk was the ratio of the measured time (s) at the normal speed and rapid speed of 4 m-walk. And the rapid speed referred to the maximum speed patients could walk (Guralnik *et al*., 2000).

STATISTICAL ANALYSIS

SPSS/PC10.0 software package was used for statistical analysis. Measurement data was expressed by standardized mean difference (SMD) (x±s), checked by the matching t. The comparison of the counting data tested by chi-square. And the variance of lower limb functions were analyzed by multiple linear regression.

RESULTS

The variance of the blood pressure and blood fat between the two groups before and after treatment were compared, as shown in table 1.

The variance of lower limbs function between the two groups before and after treatment were compared, as shown in table 2.

DISCUSSION

The effect of statins on the function of lower extremity in patients with peripheral arterial disease has been studied abroad, but there is no consensus. This research showed that compared with the control group, the decline in the walking speed at normal or rapid speed in the short distance (4m) of the patients with PAD after Atorrastatin treatment was significantly slowed down, with statistical significance, indicating that statins had a favorable effect on PDA. It is suggested that statins can improve the blood pressure and blood lipid and meanwhile stabilize the atherosclerotic plaque of the arterial wall, thus preventing or delaying the progression of the disease (Ross *et al*., 1999). The anti infective effect of statins is another important factor. Long term inflammation in the body is the main cause of the decline of muscle function, and it is also associated with age (Ferrucci *et al*., 2002); Statins also play a certain role in improving artery endothelial function (Zhang *et al*., 2012). At the same time, the anti-

infection effects of statins mainly work on the rapid type II muscle fiber and with comparatively less effects on the low speed type I muscle fiber. The function of statins on arterial endothelial function is mainly reflected in short distance walking speed, not walking endurance (Yang *et al*., 2012), which can just explains that statin treatment has no significant change in walking distance of 6 min, but has a significant effect on delaying the decline in the short distance (4 m) in normal and fast walking speed.

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