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Efficacy and mechanism of action of atherosclerosis in patients with statins.

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Abstract

Objective: To investigate the efficacy and mechanism of action studies of statins for patients with atherosclerosis.

Methods: 104 cases of atherosclerosis were selected from our hospital and randomly divided into control group, simvastatin group, pravastatin group, atorvastatin group according to the random number table. Determination of four groups of patients before treatment and triglyceride six months after total cholesterol, high density lipoprotein cholesterol and low-density lipoprotein cholesterol levels, while measuring their bilateral carotid artery intima-the thickness of the middle, Spectrophotometry using content in blood NO and nitric oxide synthase (NOS), porridge the maximum sample diameter and thickness of plaque and statistics patients experienced adverse reactions.

Results: Statin group before and after treatment in triglyrcerid (TG), total cholesterol (TC), and low density lipoproteincholoesterol (LDL-C) values show a downward trend, HDL-C showed a rise trend. Compared with the control group, the difference was statistically significant (P<0.05), while the interior was no significant difference (P>0.05) ; the overall efficacy in the statin group after treatment efficiency is over 95%, compared with the control group, there was statistically significant difference (P<0.05) ; the maximum diameter of the statin group with IMT and plaque before treatment difference was statistically significant (P<0.05), Elevated levels of serum NO and NOS, whereas no significant difference (P>0.05) between the groups. Follow-up results showed that statins safe and effective in the use of the process.

Conclusions: Statins is safe, effective and reliable for the treatment of atherosclerosis.

Keywords: Atherosclerosis, Statins, Simvastatin, Pravastatin, Atorvastatin.

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Introduction

Cardiovascular and cerebrovascular diseases are one of main diseases harmful to human health. With the improvement of people's living standard and the acceleration of working speed, the morbidity and mortality of cardiovascular and cerebrovascular diseases increase year by year [1]. It is reported by the research [2-5] that atherosclerosis is the main pathobiologic basis inducing cardiovascular and cerebrovascular diseases. Therefore, controlling atherosclerosis is an important method to prevent and treat cardiovascular and cerebrovascular diseases. In recent years, a series of prospective researches demonstrated [6-9] that lipid-lowering agent could affectively control the morbidity and mortality of cardiovascular and cerebrovascular diseases. Among the lipid-lowering agents, the clinical application of 3-hydroxy-3-methylpentacyl coenzyme A (HMG-CoA) reductase inhibitor-statin is the most extensive. It could reduce the synthesis of cholesterol by inhibiting the activity of HMG-CoA reductase and also decrease the secretion of liver lipoprotein at the same time to regulate blood glucose. Clinically, common statins mainly include simvastatin, lovastatin, pravastatin, atorvastatin, etc. The research discussed the curative effect of statins on atherosclerosis patients and the action mechanism study through the detection of different statins on atherosclerosis patients' blood lipid level, (IMT) and atheromatous plaque maximum diameter and thickness.

Information and Method

General information

A total of 104 atherosclerosis patients admitted and treated in our hospital from December 2014 to December 2016 were selected, including 68 men and 36 women, aged from 38-79, with the average age (56.9 ± 4.9). Refer to the inclusion criteria and exclusion criteria [10,11]: Inclusion criteria: 1) diagnosed as atherosclerosis patients through color Doppler ultrasound detection; 2) the patients did not take any lipid-lowering agents within 15 d before receiving treatment; 3) obvious immunologic rejection occurred in patients; 4) the patients did not have operation history within half a year; 5) the patients did not have blood disease. Exclusion criteria: those with severe abnormal liver function, renal insufficiency or serious

thyroid function failure. The 104 atherosclerosis patients were divided into 4 groups randomly according to the numerical method, i.e., Control Group (n=26), Simvastatin Group (n=26), Pravastatin Group (n=26) and Atorvastatin Group (n=26). All patients or their family members signed on Patients Informed Consent prepared by Institute of Medical Ethics of our hospital before treatment.

Research on drugs

Simvastatin tablets, Zocor, produced by Merck Sharp & Dohme Limited, 20 mg/tablet; pravastatin, Puhuizhi, approved number: GYZZ 20050456, produced by Shanghai Modern Pharmaceutical Co., Ltd., 20 mg/tablet; atorvastatin, Lipitor, approved number: GYZZ 20120050, produced by Pfizer Ireland Pharmaceuticals, 20 mg/tablet.

Method

Low-sugar and low-fat diet was adopted for all patients during hospitalization period for treatment. For the patients of the Control Group, regular diet control, antiplatelet drugs, anticoagulation and non-statins were provided for treatment; for the patients of the Simvastatin Group, simvastatin was offered based on regular treatment, 20 mg/time, 1 time/d; for the patients of the Pravastatin Group, pravastatin was provided based on the regular treatment and the method and dosage were similar to those of Simvastatin Group; for the patients of the Atorvastatin Group, atorvastatin was offered based on the regular treatment and the method and dosage are similar to those of Simvastatin Group.

Detection index

Venous blood samples were taken from all patients before treatment to determine their triacylglycerol (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) level and the determination on these levels again according to the same method 6 months after the treatment; color ultrasonography was conducted on carotid artery for 4 groups of patients before and after treatment, to determine the bilateral arterial intima-intima medium thickness (IMT) (taking the average value) and measure the maximum diameter and thickness of atheromatous plaque. Spectrophotometric method was adopted for detecting NO and NOS contents in the blood. NO and NOS were operated according to the corresponding kit instructions (purchased from Nanjing Institute of Biological Engineering). Finally, count the cases of patients with adverse reaction.

Evaluation on treatment effect

By referring to the literature of McKinney [10,12], it was determined in this research that excellent treatment effect was achieved if TG reduced by ≥ 40%, TC reduced by 20%-40%, HDL-C rose by ≥ 0.26 $mmol \cdot L^{-1}$ or LDL-C reduced by ≥ 20%-40%; the treatment was effective if TG reduced by ≥ 20%-40%, TC reduced by 10%-20%, HDL-C rose by ≥ 0.1-0.26 $mmol \cdot L^{-1}$ or LDL-C reduced by ≥ 10%-20%; it meant invalid if none of the above was reached.

Statistical analysis

SPSS17.0 statistical software was adopted for analyzing experimental data, the measurement data was represented by ($\bar{x} \pm s$), t was adopted for inspection of various indices and comparison of the groups before and after treatment and $P<0.05$ indicated that the difference had statistical significance.

Results

Blood-lipid changes for four groups of patients before and after treatment

For three groups of patients receiving statins treatment before and after treatment, the TG, TC and LDC-C values before and after the treatment showed a downward trend, while HDL-C value an upward trend. The comparative difference between Control Group and three statins groups had statistical significance ($P<0.05$), while the comparative difference among three statins groups had no statistical significance ($P>0.05$) (Table 1).

Table 1. *Comparison of blood-lipid changes for four groups of patients before and after treatment.*

Group		TG (mmol-1)	TC ($mmol^{-1}$)	HDL-C ($mmol^{-1}$)	LDL-C ($mmol^{-1}$)
Control Group	Pre-treatment	2.01 ± 0.49	5.34 ± 1.34	1.24 ± 0.36	4.97 ± 1.02
	Post-treatment	1.98 ± 0.76	5.22 ± 1.39	1.43 ± 0.63	4.87 ± 0.98
Simvastatin Group	Pre-treatment	1.97 ± 0.98	5.90 ± 1.98	1.07 ± 0.92	4.88 ± 1.33
	Post-treatment	1.24 ± 0.36*	3.09 ± 1.09*	1.42 ± 0.36*	1.98 ± 0.99*
Pravastatin Group	Pre-treatment	1.83 ± 0.84	5.87 ± 1.83	1.64 ± 0.35	4.35 ± 1.34
	Post-treatment	1.07 ± 0.92*	2.98 ± 1.06*	2.30 ± 0.47*	2.03 ± 0.74*
Atorvastatin Group	Pre-treatment	2.03 ± 0.86	6.01 ± 1.94	2.15 ± 0.63	4.93 ± 1.22
	Post-treatment	1.64 ± 0.35*	5.97 ± 1.87*	2.83 ± 0.48*	2.05 ± 0.68*

Note: Compared with the Control Group, *P<0.05

Comparison of lipid-lowering effects for four groups of patients before and after treatment

The curative effects after treatment of atherosclerosis with simvastatin, pravastatin and atorvastatin indicated that the overall effective rate was over 95% and such a result had statistical difference (P<0.05) while compared with Control Group, which indicated that the effect of statins in treating atherosclerosis was outstanding. See Table 2 for results.

Table 2. Evaluation on lipid-lowering effects for four groups of patients before and after treatment.

Group	Cases	Evaluation on treatment effect		
		Effective rate (n, %)	Obvious effective rate (n, %)	Inefficiency rate (n, %)
Control Group	26	13 (50%)	3(11.5%)	61.5%
Simvastatin Group	26	19 (73.08%)*	7 (26.92%)	100%
Pravastatin Group	26	18 (69.23%)*	7 (26.92%)	96.15%
Atorvastatin Group	26	19 (73.08%)*	6 (23.08%)	96.15%

Note: Compared with the Control Group, *P<0.05

Carotid artery IMT and plaque changes for four groups of patients before and after treatment

It could be seen from the results that there was no obvious change in maximum diameter and thickness of MT and plaque for the patients of Control Group before and after treatment, while those of other three groups treated with statins were shortened obviously and the plaque thickness got thinner obviously; the comparative difference before and after treatment had statistical significance (P<0.05), while the comparison among IMT, maximum diameter and thickness of each group had no statistical difference (P>0.05) (Table 3).

Table 3. Comparison of changes in IMT and plaque diameter and thickness of four groups of patients before and after treatment.

Group		IMT (mm)	Maximum diameter of plaque (mm)	Plaque thickness (mm)
Control Group	Pre-treatment	1.08 ± 0.67	8.35 ± 1.43	2.24 ± 0.63
	Post-treatment	1.07 ± 0.94	8.22 ± 1.46	2.13 ± 0.36
Simvastatin Group	Pre-treatment	1.07 ± 0.89	8.09 ± 1.08	2.07 ± 0.29
	Post-treatment	0.97 ± 0.63*	7.90 ± 1.29*	2.02 ± 0.46*
Pravastatin Group	Pre-treatment	1.03 ± 0.48	8.78 ± 1.38	2.04 ± 0.53
	Post-treatment	0.99 ± 0.29*	6.98 ± 1.16*	2.00 ± 0.17*
Atorvastatin Group	Pre-treatment	1.03 ± 0.86	8.10 ± 1.34	2.05 ± 0.23
	Post-treatment	0.93 ± 0.53*	6.97 ± 1.87*	2.03 ± 0.18*

Note: Compared with the Control Group, *P<0.05

NO and NOS contents comparison for 4 groups before and after treatment

Compared with pre-treatment and Control Group, NO and NOS levels of treatment groups rose obviously and the difference had statistical significance (P<0.01) (Table 4).

Table 4. NO and NOS contents for 4 groups before and after treatment.

Group		NO (μmol/L)	NOS (μmol/L)
Control Group	Pre-treatment	33.5 ± 7.4	11.8 ± 7.3
	Post-treatment	33.3 ± 8.18	12.2 ± 8.08
Simvastatin Group	Pre-treatment	34.6 ± 6.8	12.5 ± 7.6
	Post-treatment	44.5 ± 7.3*	20.6 ± 8.2*
Pravastatin Group	Pre-treatment	35.2 ± 8.0	12.9 ± 6.9
	Post-treatment	47.0 ± 8.2*	23.0 ± 7.58
Atorvastatin Group	Pre-treatment	36.5 ± 7.8	11.9 ± 6.9
	Post-treatment	48.9 ± 9.4*	22.9 ± 8.68

Note: compared with pre-treatment, *P<0.05

Safety reaction

Follow-up survey was conducted for all patients receiving treatment in this test, recording the adverse reaction of patients within 6 months after treatment. The results indicated that all patients had no obvious adverse reaction, showing that the statins was safe and valid during the usage.

Discussion

In the study, we mainly investigated the treatment effect of simvastatin, pravastatin and atorvastatin on atherosclerosis patients, analyzed the blood lipid level, carotid artery IMT and plaque maximum diameter, thickness and other factors of patients before and after treatment, and researched the safety of statins at the same time. The study results showed that the blood TC, TG, LDC-C, HDL-C, carotid plaque and IMT were significantly improved in patients with atherosclerosis after statin therapy, but the therapeutic effect on the atherosclerosis between the three kinds of statins showed no significant difference. Therefore, it suggested that statins had a good effect on atherosclerotic plaques. The research results also indicated that blood NO and NOS contents rose obviously 6 months after taking statins, carotid artery intima-intima medium thickness got thinner and plaque scores reduced obviously. Vascular endothelial injury and its dysfunction were initial factors of atherosclerosis, NO was an important active material of vascular endothelial cell and its imbalance between

endogenesis and release was closely related to the injury of endothelial function. Under the basic status, NO had the functions of regulating vascular tension, anti-platelet aggregation and leukocyte adhesion, preventing thrombosis and inhibiting early vascular atherosclerosis, while under the pathologic condition, endothelial cell dysfunction and NO level reduction caused obvious proliferation reaction of the blood vessel, promoting the occurrence and development of atherosclerosis. However, in the research, there were certain errors about the accuracy of the results due to less samples and short research time. At the same time, follow-up and statistics were conducted on indices of 4 groups of patients through half year treatment, but considering the action time of statins and the stability in patients, it still required for more action time for investigation. Therefore, the results of the experiment had a certain guiding significance and still required for further large samples for investigating and analyzing the accuracy of the research results.

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