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Original Article

Dose study of rosuvastatin calcium in the treatment of coronary heart disease and hyperlipidemia

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Abstract: Objective: To study the clinical efficacy of different doses of rosuvastatin to treat elderly patients with senile coronary heart disease and hyperlipidemia. Methods: By means of retrospective analysis, 150 elderly patients with coronary heart disease and hyperlipidemia who were treated in Zhangjiakou First Hospital from January 2020 to December 2020 were selected as the study subjects. They were divided into three groups (50 patients in each group) according to the different treatment methods. All patients were given routine treatment for coronary heart disease and hyperlipidemia. At the same time, group A got 5 mg of rosuvastatin calcium per day, group B got 10 mg and group C got C, 20 mg. After 4 months of continuous treatment, changes of blood lipid level, inflammatory factors, and cardiac function in the three groups were compared before and after treatment. Finally, the incidence of adverse reactions in the three groups was statistically compared. Results: After 4 months of treatment, the levels of TC, LDL, and TG in group B were significantly lower than those of group A, and the levels of HDL were significantly higher than those in group A ($P<0.05$). There was no significant difference of the above indicators between groups B and C after 4 months of treatment ($P>0.05$). Using 2 months, 3 months, and 4 months of therapy as time points, the blood lipid levels of the B and C groups was lower than in group A ($P<0.05$); Serum hs-CRP and TNF of patients in group B and group C after 4 months of treatment were significantly lower than those of group A ($P<0.05$); The LVEF comparison between groups showed that C was higher than A ($P<0.05$); The occurrence rate between adverse reactions during the 4 months of medication did not have statistical significance ($P>0.05$). Conclusion: Rosuvastatin calcium canimprove the clinical symptoms of elderly patients with coronary heart disease complicated by hyperlipidemia, and can improve the blood lipid level, cardiac function and the level of inflammatory factors in the body, but the clinical effect is not significantly improved by increasing the application dose. This suggests that the daily application dose should be 10 mg.

Keywords: Rosuvastatin calcium, advanced age, coronary heart disease, hyperlipidemia, clinical efficacy

Introduction

Coronary heart disease (CHD) is a comprehensive disease caused by coronary atherosclerosis, that is based on lumen stenosis or blockage, resulting in a series of pathologic changes such as ischemia and hypoxia of individual myocardium and then injury and necrosis. It is also called ischemic heart disease clinically [1, 2]. Coronary heart disease is a common and frequently-occurring disease among cardiovascular diseases. Epidemiological studies show that the number of cases of CHD deaths worldwide is as high as 17 million every year. With the gradual emergence of the trend of transformation, the mortality rate has ranked at the forefront of many diseases [3, 4].

The pathologic basis of coronary heart disease is coronary atherosclerosis, and dyslipidemia is considered as one of the most important risk factors for atherosclerosis [5, 6]. Hyperlipidemia mainly refers to a disruption of triglycerides (Tg), low density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (Tc), and other factors, wherein LDL is elevated. It is con-

Table 1. Comparison of general clinical data differences ($\bar{x} \pm s$)/[n (%)]

General clinical information		Group A (n=50)	Group B (n=50)	Group C (n=50)	t/X^2	P
Gender	male	30	31	28	0.824	0.824
	female	20	19	22		
Average age (years)		65.19±3.41	65.21±3.51	65.18±3.76	0.001	0.999
Average weight (kg)		62.10±5.98	62.08±6.01	62.21±5.49	0.007	0.993
Average BMI (kg/m^2)		23.10±3.43	23.08±3.41	23.29±2.98	0.062	0.94
Coronary heart disease classification	hide	15	13	15	0.875	0.876
	angina pectoris	30	31	27		
	myocardial infarction	5	6	8		
Hypertension	Yes	13	18	15	0.551	0.552
	no	37	32	35		
Diabetes	Yes	5	8	7	0.668	0.660
	no	45	42	43		

sidered to be the most significant risk-factor of the intregrated process [7]. The number of patients with coronary heart disease combined with hyperlipidemia has been increasing year by year in recent years, and is a serious threat to life and health in China. Currently, the treatment measures for elderly patients with coronary heart disease combined with hyperlipidemia mostly rely on conservative treatment (such as diet regulation, rehabilitative exercise, etc.) and drug treatment (such as drugs for improving heart function and blood lipids), and there are many options for lipid-regulating drugs, However, different kinds of drugs have different adverse reactions, so they must be selected according to the actual situation of patients [8]. The pharmacologic action of statins is mainly to reduce LDL, and its mechanism of action can be briefly summarized as inhibiting liver uptake of LDL. In addition to their clear lipid-lowering effect, such drugs are also recommended for patients with acute coronary syndrome within 48 hours of onset, and are believed to help improve the acute inflammatory response of patients [9]. At present, there are many clinical studies on statins, but there are few studies on the dosage of statins [10]. This study intends to demonstrate the best dose of rosuvastatin calcium in the treatment of elderly patients with coronary heart disease complicated by hyperlipidemia by setting up different application dose ladders. The innovation is that the rationale for rosuvastatin is verified through the comparison of the efficacy of different drug doses, providing a clinical reference for improving outcome.

Patients and methods

General information

By means of retrospective analysis, 150 elderly patients with coronary heart disease and hyperlipidemia who were treated in Zhangjiakou First Hospital from January 2020 to December 2020 were selected as the study subjects, and they were divided into three groups (50 patients in each group) according to different treatment methods. This study was approved by the ethics committee of Zhangjiakou First Hospital. Using baseline clinical data included in three groups, such as gender, age, weight, coronary heart disease, concurrent basic disease, etc., and combinations, the results showed that the differences in the above data were not significant (P>0.05), suggesting three groups of good comparability (**Table 1**).

Inclusion criteria: (1) Patients who met the diagnostic criteria (Standards formulated by the International Heart Association and the World Health Organization) [11] and had hyperlipidemia; (2) The clinical case data are complete; (3) Those aged ≥50 years and <80 years old.

Exclusion criteria: (1) Patients with obvious primary liver disease; (2) Pulmonary heart disease, hypertensive heart disease, rheumatic heart disease; (3) Complications of cerebrovascular accident, severe trauma or major disease within half a year of surgery; (4) Drug-induced hyperlipidemia; (5) Concurrent familial hypercholesterolemia; (6) Taking drugs that affect

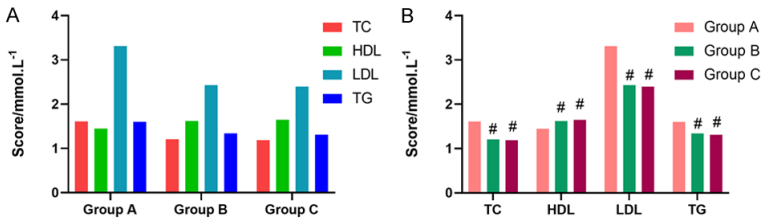

Figure 1. Comparison of blood lipid levels. After 4 months, levels of TC, LDL, and TG in group B were lower than in (A), and HDL level was higher than in (B). # represents a significant difference between the same index and group A.

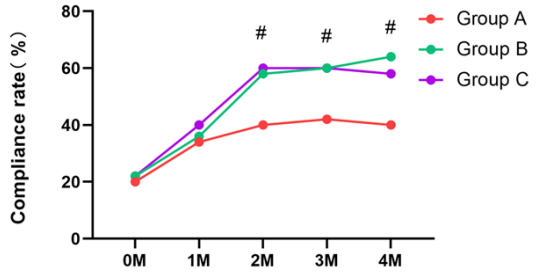

Figure 2. Comparison of the blood lipid level compliance rate in the three groups. At the three time points of 2, 3, and 4 months of treatment, the rate of reaching the standard of blood lipids in group B and group C was significantly higher than that in group A ($P<0.05$). # represents a significant difference between the same index and group A.

blood lipid metabolism; (7) Concurrent mental illness; (8) Cardiac function Grade IV; (9) Allergic to investigational drugs; (10) Inclusion in other unfinished clinical investigations.

Intervention methods

All patients in the three groups received routine clinical treatment for coronary heart disease, including reasonable diet, health education, proper exercise. On this basis, all patients in the three groups were treated with rosuvastatin calcium tablets (manufacturer: Aliscon Pharmaceutical Co., Ltd., approval number: GYZZ J20170008), of which the dose in group A was 5 mg/d, group B was 10 mg/d, and group C was 20 mg/d. Pills were taken after dinner, continuously for 4 months (16 weeks).

Observation indicators and evaluation standards

Main observation indicators: (1) The blood lipids of the three groups of patients were monitored during the intervention. The blood samples of the three groups of patients were collected before and after treatment for 4 months to analyze the levels of TC, HDL, LDL, TG and other blood lipid factors (detected by enzyme-linked immunosorbent assay), and the differences between the groups were compared; (2) Blood samples of patients in the three groups were collected before treatment 4 months respectively, and blood lipid levels were detected to evaluate the blood lipid level compliance rate in terms of TC, TG, HDL, and LDL at normal levels; (3) The cardiac function of the three groups of patients was measured by echocardiography before treatment and after 4 months of treatment.

Secondary outcome measures: (1) Changes in serum inflammatory factor levels (detected by enzyme-linked immunosorbent assay) of three groups of patients before and after treatment. After collecting blood samples of three groups of patients before treatment and after 4 months of treatment, we used an automatic biochemical analyzer to analyze hs-CRP and TNF-α in blood samples of three groups of patients (2). The total incidence of various adverse events such as myalgia, rash, headache, and constipation, during the month was assessed.

Statistical methods

SPSS22.0 statistical software was selected to analyze the data collected in the study, in which the measured data were expressed in the form of (mean ± standard deviation). The normal distribution and variance homogeneity test were carried out. The t-test was used for the differences between the groups that met the normal distribution or variance homogeneity. The Mann-Whitney U test in as a non-parametric test was used for statistical inference of the uneven variance data. The chi-square test was used for the differences of the counted data between the groups, Chi-square and t-test were used for intra-group and inter-group comparison, one-way ANOVA was used for comparison between the three groups, and Bonferroni was used for comparison between the three groups. $P<0.05$ was taken to indicate significant difference.

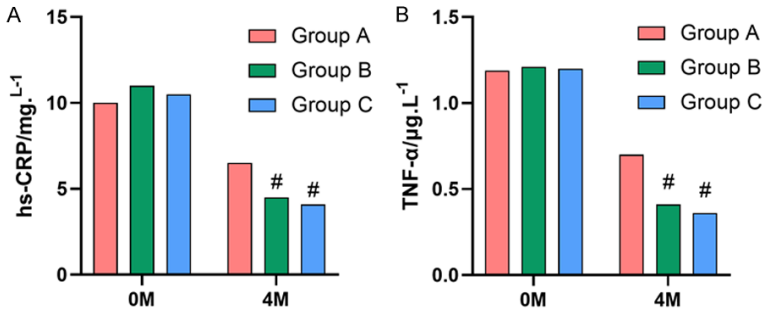

Figure 3. Serum inflammatory factors HS-CRP, and TNF-α levels. After 4 months of treatment, serum hs-CRP and TNF-α of patients in group B and group C were significantly lower than that of Group A (P<0.05). # represents the same index compared to group A, with a significant difference.

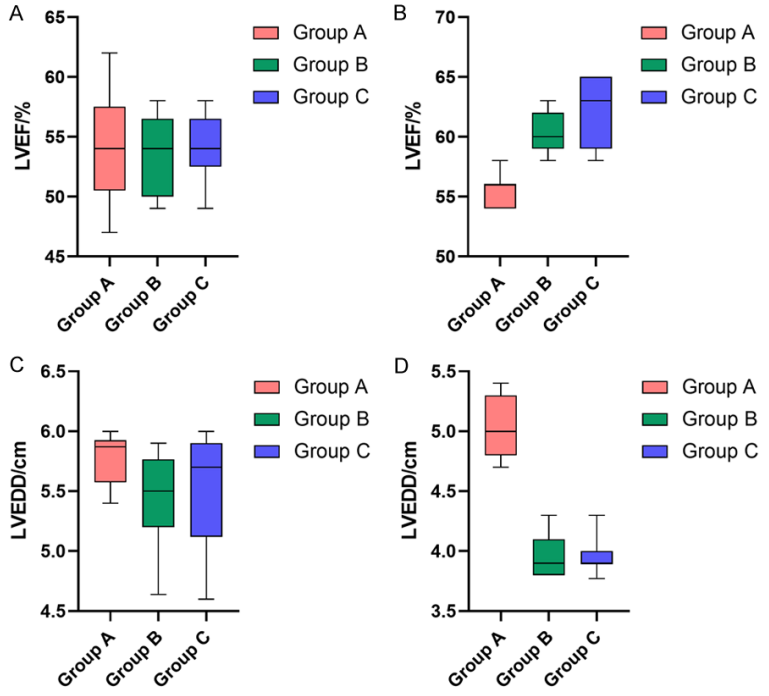

Figure 4. Analysis of cardiac function changes. After 4 months of treatment, LVEF of patients in groups B and C was significantly higher than that of group A (P<0.05) # represents that the same index is significantly different from group A.

Results

Comparison of blood lipid levels before and after treatment

There were no statistically significant differences in the levels of TC, HDL, LDL or TG (P>0.05). After 4 months of therapy, their levels in group B were obviously lower than group A, and the HDL level was obviously higher than group A. Some differences were significant (P<0.05), while other differences were not (P>0.05) (**Figure 1**).

Comparison of the compliance rate of blood lipid levels in the three groups of patients

Respectively, from 1-4 months we collected three groups of patients' blood lipid levels and evaluated differences between groups. The results showed that at 1 month of therapy, the blood lipid success rate had no significant difference (P>0.05). At the points of 2, 3, and 4 months of treatment, the standard rate of blood lipids in group B and group C was significantly higher than in A (P<0.05), while there was no significant difference in the standard rate of blood lipids between group B and group C (P>0.05) (**Figure 2**).

Analysis of changes in inflammatory factors in the three groups

The blood samples of the 3 groups were centrifuged when collected before treatment and after treatment, leaving clear blood for detection of inflammatory factors HS-CRP and TNF-α. We compared between groups. Serum HS-CRP and TNF-α levels in three groups did not differ (P>0.05). In all three groups, serum HS-CRP and TNF-α levels were lower than before treatment, and the differences were significant (P<0.05) (**Figure 3**).

Analysis of changes in cardiac cause functions before and after treatment

Echocardiography was performed on the three groups of patients before and after 4 months of treatment. Differences in LVEF of the three groups were not significant (P>0.05). LVEDD

Table 2. Comparison of adverse reactions in therapy

Group	n	Myalgia	Rash	Headache	Constipation	Total incidence
Group A	50	0 (0.00)	1 (2.00)	2 (4.00)	2 (4.00)	5 (10.00)
Group B	50	1 (2.00)	2 (4.00)	1 (2.00)	2 (4.00)	6 (12.00)
Group C	50	2 (4.00)	4 (8.00)	1 (2.00)	1 (2.00)	8 (16.00)
χ^2	-	-	-	-	-	0.656
P	-	-	-	-	-	0.843

had no significant differences (P>0.05) (**Figure 4**).

Comparison of adverse reactions in therapy

Patients were followed up for a period of 4 months, and the total incidence of events such as myalgia, rash, headache, and constipation in the three groups/during the 4-month periodwere counted. The differences between adverse reactions during the follow-up period were not significant (P>0.05), but the incidences in group B and group C were slightly higher than in Group A, which was slightly higher than Group B (**Table 2**).

Discussion

There are various risk factors for coronary heart disease, such as obesity, abnormal blood lipid metabolism, elevated blood pressure, unreasonable diet, and alcohol abuse, [12]. Excessive lipid content in the blood may affect the permeability of the vascular intima, resulting in changes to the endothelial structure, lipid infiltration of the vascular endothelium, and ultimately atherosclerosis and coronary heart disease [13]. In addition, abnormal blood lipid metabolism will increase the risk that atherosclerotic plaque ruptures and falls off, lead to changes in hemorheological indicators, inducing thrombosis, and increasing the incidence of events such as ischemic stroke and myocardial infarction. Treatment is important [14, 15]. At present, western medicine mainly relies on drug therapy to control blood lipid levels. Among the drugs, statins can effectively reduce the synthesis of cholesterol in the blood by inhibiting HMG-CoA reductase, so as to reduce blood lipid levels, improve blood rheology, and protect cardiac function [16].

This study demonstrated and analyzed the optimal dose of rosuvastatin calcium. The blood lipid levels also improved significantly after 4 months of intervention, but the improvement was smaller than for patients in Group B who received 10 mg and patients in Group C who received 20 mg, suggesting that high-dose rosuvastatin calcium gives a better improvement in patients' lipid profile. Follow-up analysis of the blood lipid level compliance rate of the three groups of patients also confirmed this perspective. The blood lipid level compliance rate of patients in group A was lower than in group B and group C, during the period from 2 months to 4 months after treatment. A study on 90 elderly patients with coronary heart disease complicated by hyperlipidemia pointed out that the LDL and TC compliance rates of the study group patients treated with 20 mg/d rosuvastatin calcium after 4 months were 86.67% and 83.33%, respectively. This was significantly higher than 53.33% and 56.67% in the control group patients treated with 5 mg/d, which is similar to the results of this study [17].

To investigate the effect of rosuvastatin on physical function, the paper further demonstrated differences in serum inflammatory factor levels and cardiac function among patients after therapy. The hs-CRP and TNF-α levels of patients in group C were significantly lower than in A after 4 months of intervention, and the cardiac function indexes in groups B and C were better than in group A. This was similar to the results of other studies. The authors of this paper believe that the reasons for the above results may be as follows: (1) Atherosclerosis is closely related to the inflammatory response in the body, and the inflammatory response will promote the process of atherosclerosis. Statins have a protective effect on vascular endothelial cells and by secreting carbon monoxide and endothelin, can inhibit the body's peroxidation reaction, thereby exerting vascular protection [18, 19]; (2) statins can protect vascular endothelial cells by reducing the secretion of endothelin, which can correct endothelial function. This can prevent or even reverse atherosclerotic plaques, thereby improving cardiac func-

tion, which has positive significance for improving quality of life [20, 21].

Finally, our study made a comparison of adverse reactions of patients at different doses. Under different doses it was shown that the incidence of adverse reactions in patients increased, but the difference between groups was not significant. The authors of this article found that the levels of blood lipids, heart function, and inflammatory factor levels were not significantly different between group B and group C, (14% vs 12%). Based on safety considerations, 10 mg/d is the best daily dose for patients [22].

The limitation of this study is that the sample size is small, the study time is too short, and the mechanism of action of rosuvastatin calcium is not analyzed through basic research due to the limitation of conditions. These factors need to be analyzed in a follow-up study to verify the value of rosuvastatin in the treatment of coronary heart disease with hyperlipidemia.

To sum up, rosuvastatin calcium has positive significance in improving the clinical symptoms, and can improve the blood lipid level, cardiac function, and the level of inflammatory factors in patients. Increasing the dose increases the occurrence of adverse reactions without improving clinical efficacy. The recommended daily dose is 10 mg.

Disclosure of conflict of interest

None.

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