EFFECT OF DIFFERENT DOSES OF ROSUVASTATIN ON SERUM HDL SUBTYPES IN PATIENTS WITH HYPERLIPIDEMIA AND CORONARY HEART DISEASE

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ABSTRACT

Objective: *Analyze the effect of different doses of rosuvastatin on serum high-density lipoprotein cholesterol (HDL-C) subtypes in patients with hyperlipidemia and coronary heart disease.*

Methods: *A sample of 300 patients with hyperlipidemia complicated with coronary heart disease in our hospital from May 2017 to April 2019 were selected as the research objects. According to their different dosages, the patients were divided into an experimental group (rosuvastatin 20 mg/d, 150 cases) and a control group (rosuvastatin 10 mg/d, 150 cases). The blood lipid levels of the two groups were compared before and after treatment. The levels of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), liver and kidney function (alt, AST, SCR, BUN), HDL subtypes (HDL2b, HDL3) and C-reactive protein (CRP) were measured, and the incidence of adverse reactions was recorded.*

Results: *After treatment, TC, LDL-C and CRP were significantly lower than those before treatment in the two groups. AST, alt, SCR and BUN, were significantly higher than those before treatment (P<0.05). LDL-C levels in the experimental group were significantly lower than those measured in the control group (P<0.05), and there was no significant difference in TC, TG, HDL-C and CRP between the two groups after treatment (P>0.05). After treatment, the levels of HDL2b and HDL3 in the two groups were significantly higher than those measured before treatment (P<0.05), but there was no significant difference in the levels of HDL2b and HDL3 between the two groups after treatment (P>0.05). The incidence of adverse reactions was 6.67% in the experimental group and 4.00% in the control group, and there was no significant difference between the two groups (P>0.05).*

Conclusion: *20 mg and 10 mg doses of rosuvastatin have effects on serum HDL subtypes in patients with hyperlipidemia and coronary heart disease, and this changes the structure and function of high-density lipoproteins. High-dose rosuvastatin can be used in clinical treatment, which can significantly and safely reduce the level of LDL-C with a significant clinical effect.*

Keywords: *Rosuvastatin, hyperlipidemia, coronary heart disease, HDL-C subtype.*

DOI: 10.19193/0393-6384_2022_1_8

Received *March 15, 2020;* ***Accepted*** *October 20, 2020*

Introduction

Coronary heart disease, a clinical multiple cardiovascular disease, refers to the atherosclerotic lesions on the coronary artery that are caused by vascular cavity obstruction. This condition can lead to heart hypoxia, ischemia caused by heart disease, patients experiencing more pre-cardiac pain and more onset angina or compression pain. For about one-third of patients, their first coronary heart disease causes sudden death, causing serious harm to the health of the elderly[(1)]. Patients with coronary heart disease are mostly accompanied by hyperlipidemia, and its coronary atherosclerosis is the main pathological change of coronary heart disease. High-density lipoprotein cholesterol (HDL-C) contains approximately 20% to 30% of the total human cholesterol, reducing the risk of coronary heart disease. Low HDL levels can serve as a separate risk factor for coronary heart disease, especially

in clinical practice, where many LDL-C levels are below 70 mg/dl[2]. A 1 mg/dl increase of HDL-C has been demonstrated to result in 2% and 3% decreases in male and female risks of coronary heart disease, respectively[3]. HDL and their apolipoproteins, which offer direct anti-atherosclerosis and vascular protective mechanisms, may be capable of promoting cholesterol reversal transport, antioxidant functions and anti-inflammatory functions, improving vascular endothelial function and transporting proteins with endogenous biological activity. Clinical studies have found that patients with coronary heart disease have had a significantly higher HDL-C level after treating either rosuvastatin or atorvastatin[4].

Rosuvastatin is a selective HMG-CoA reductase inhibitor, and its lipid reduction effectiveness has been demonstrated in several large clinical trials in which it was used to fight atherosclerosis, reverse plaque, and assist with cell signaling, cell proliferation, anti-osteoporosis and collagen synthesis[5]. However, for rosuvastatin, there is insufficient clinical evidence (especially in patients with coronary heart disease in China) regarding the impact of drugs on the HDL → HDL2 and cholesterol reversal processes. Therefore, the purpose of this study was to analyze the effects of different doses of rosuvastatin on serum HDL subtypes in patients with hyperlipidemia and coronary heart disease.

Materials and methods

Subjects

A total of 300 patients with hyperlipidemia complicated with coronary heart disease admitted to our hospital from May 2017 to April 2019 were selected as the research subjects.

This study was approved by the ethics committee of the hospital.

Inclusion criteria:

• All patients received coronary angiography and met the diagnostic criteria in the Guidelines for Diagnosis and Treatment of Coronary Heart Disease[6];

• All patients met the diagnostic criteria of hyperlipidemia in the Chinese Guidelines for the Prevention and Treatment of Adult Dyslipidemia[7];

• No use of anti-lipid medication or steroid therapy over the last 3 weeks;

• Patients aged 30 to 75 years of age with liver and kidney dysfunction clinically diagnosed as less than moderate and severe;

• Complete clinical case data could be obtained;

• All patients and their family members agreed to participate in this study.

Exclusion criteria:

• Those previously contraindicated to rosuvastatin;

• Patients with acute myocardial infarction within half a year;

• Patients with active liver and gallbladder diseases, severe renal insufficiency or renal failure;

• Patients with drug-induced hypercholesterolemia or familial hypercholesterolemia;

• Patients with a recent history of drug abuse, alcoholism or mental disorders;

• Pregnant or lactating patients.

Patients were divided into an experimental group (rosuvastatin 20mg/d, 150 cases) and control group (rosuvastatin 10mg/d, 150 cases) according to their different dosages. Comparisons of age, gender and other aspects of patients in the two groups are shown in Table 1.

Methods

After admission, all patients received conventional treatment for coronary heart disease: strict control of blood glucose and blood pressure as well as the same lifestyle and dietary interventions. Patients in the experimental group and the control group were treated with rosuvastatin calcium, 20 mg and 10 mg doses, (AstraZeneca Pharmaceuticals Co., Ltd., 5mg/tablet, batch number: 20170421) after every dinner for 12 weeks, respectively.

Observation indexes

Before and after treatment, a 5ml sample of fasting venous blood was taken from each patient in the morning and left standing at room temperature for 30 minutes. After centrifugation, the supernatant was taken, and an automatic biochemical analyzer was used to detect the total cholesterol (TC), triglycerin (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), cerealthirdtransaminase (ALT), aspertate aminotransferase (AST), serum creatinine (SCr), blood urea nitrogen, (BUN) and c-reactive protein (CRP) levels. Additionally, an HDL subtype determination was performed via microfluidic electrophoresis methods, and the incidence of ADR during treatment was recorded in both groups.

Statistical methods

The data in this study were analyzed with the SPSS 21.0 software package, and the measurement

data were expressed as means plus/minus standard deviations ($\bar{x}\pm s$). A t-test was used to compare the data of the experimental group to the data of the control group, and all of the count data were expressed as percentages.

In all statistical tests used, a P-value of less than 0.05 was considered to indicate a statistically significant result.

Results

Comparison of general data between the two groups

As shown in Table 1, there were no significant differences in gender, age, BMI, course of disease or complications between the two groups (P>0.05).

General information	Experimental group (n=150)	Control group (n=150)	χ^2/t	*P*
Gender (male/female)	81/69	77/73	0.214	0.644
Average age (years)	68.15±7.45	67.52±9.33	0.646	0.519
BMI (kg/m^2)	24.18±1.36	23.89±1.47	1.774	0.077
Course of hyperlipidemia(year)	6.45±1.02	6.13±1.89	1.255	0.211
Course of coronary heart disease (year)	5.41±1.13	5.58±1.08	1.332	0.184
Hypertension	77 (51.33)	75 (50.00)	0.053	0.817
Diabetes	32 (21.33)	30 (20.00)	0.081	0.776
Obesity	78 (52.00)	77 (51.33)	0.013	0.908

Table 1: Comparison of general data between the two groups ($\bar{x}\pm s$), (n(%)).

Comparison of clinical indexes between the two groups before and after treatment

Before treatment, there was no significant difference in clinical indicators between the two groups (P>0.05).

After treatment, TC, LDL-C and CRP were significantly lower than before treatment, while AST, ALT, Scr and BUN were significantly higher than before treatment (P<0.05).

The level of LDL-C in the experimental group was significantly lower than the LDL-C level measured in the control group (P<0.05). There were no significant differences in TC, TG, HDL-C or CRP between the two groups after treatment (P>0.05). These results are shown in Tables 2 and 3.

Group	Time	TC (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)
Experimental	Before	6.48±1.16	2.21±0.65	3.92±1.10	0.83±0.19
	After	4.68±0.77*	1.76±0.25*	2.44±0.48$^{*\#}$	1.58±0.24*
Control	Before	6.47±1.12	2.11±0.45	3.89±1.20	0.80±0.27
	After	4.70±1.20*	1.80±0.26*	3.15±0.74*	1.52±0.23*

Table 2: Comparison of blood lipid levels between the two groups before and after treatment ($\bar{x}\pm s$).
Note: Compared with the same group before treatment, $^*P<0.05$; compared with the control group after treatment, $^\#P<0.05$.

Group	Time	AST (U/L)	ALT (U/L)	Scr (μmol/L)	BUN (mmol/L)	CRP (mg/L)
Experimental	Before	35.11± 9.05	37.69± 9.25	56.67± 5.25	5.70± 1.15	127.45± 26.32
	After	48.51± 9.78$^{*\#}$	45.30± 3.23$^{*\#}$	62.23± 6.67$^{*\#}$	6.90± 2.14$^{*\#}$	75.30± 12.16*
Control	Before	35.12± 10.09	37.65± 9.30	56.72± 5.30	5.68± 1.14	126.60± 25.46
	After	44.23± 10.11*	41.76± 3.82*	59.12± 6.64*	6.02± 2.11*	77.23± 15.64*

Table 3: Comparison of clinical indexes between the two groups before and after treatment ($\bar{x}\pm s$).
Note: Compared with the same group before treatment, $^*P<0.05$; compared with the control group after treatment, $^\#P<0.05$.

Comparison of HDL subtypes between the two groups before and after treatment

Before treatment, there was no significant difference in HDL2B and HDL3 levels between the two groups (P>0.05). The HDL2B level was significantly higher, and the HDL3 level was significantly lower in both groups after treatment (P<0.05). There was no significant difference in HDL2B and HDL3 levels between the two groups after treatment (P>0.05). These results are shown in Table 4.

Group	Time	HDL2b (mmol/L)	HDL3 (mmol/L)
Experimental group	Before treatment	0.32±0.28	0.57±0.23
	After treatment	0.52±0.11*	0.24±0.10*
Control group	Before treatment	0.35±0.24	0.56±0.25
	After treatment	0.51±0.16*	0.26±0.15*

Table 4: Comparison of HDL subtypes between the two groups before and after treatment ($\bar{x}\pm s$).
Note: Compared with the same group before treatment, $^*P<0.05$.

Comparison of adverse reactions between the two groups

As shown in Table 5, the incidence of ADR was 6.67% in the experimental group and 4.00% in the control group, and there was no significant difference between the two groups (P>0.05).

Group	Pharyngitis	Muscle pain	Rash	ALT Increased	Total incidence
Experimental group	3 (2.00)	4 (2.67)	2 (1.33)	1 (0.67)	10 (6.67)
Control group	2 (1.33)	2 (1.33)	1 (0.67)	1 (0.67)	6 (4.00)
χ^2					1.056
P					0.304

Table 5: Comparison of adverse reactions between the two groups (n (%)).

Discussion

Coronary heart disease (CHD) is a clinical multiple cardiovascular disease that can lead to a variety of clinical symptoms if it is not treated in time. The interaction and mutual influence of various causes can seriously affect the normal life, physical health and mental health of patients. Abnormality of heredity, blood lipids, blood pressure and blood glucose can all lead to the occurrence and development of coronary heart disease. Meanwhile, various adverse factors can easily cause blood lipid abnormalities which can lead to cardiovascular and cerebrovascular diseases. Plasma lipids are the necessary basic cell metabolism, and dyslipidemia can easily cause acute coronary syndrome and the hardening of the arteries. Hyperlipidemia caused by a blood lipid metabolic abnormality, can lead to endothelial cell membrane damage, and cause a buildup of plaque depositions on vascular intima, thereby inducing the occurrence of coronary heart disease, a direct threat to people's physical and mental health[8]. Coronary heart disease and hyperlipidemia are among the most common cardiovascular diseases. Hyperlipidemia complicating coronary heart disease can aggravate myocardial ischemia, hypoxia and increase the risks of myocardial infarction and sudden cardiac death. In elderly patients with coronary heart disease complicated by hyperlipidemia, these risk factors are higher, although conventional drugs can have treatment effects. However, some of the drugs cause adverse reactions. Therefore, it is particularly important to select lipid-lowering drugs with reliable efficacies and high safety factors.

Blood transport and metabolism require the combination of TC, TG and apo to form lipoproteins dissolved in plasma. The lipoproteins can be divided into chylomicron and four kinds of lipoproteins (very low-, low-, medium- and high-density) via centrifugal electrophoresis[9]. HDL is an inhomogeneous lipoprotein in function, composition and density. The change of its subtype distribution may be involved in the pathogenesis of atherosclerosis. The mechanism of HDL and its apolipoprotein's direct anti-atherosclerosis and vascular protection may promote cholesterol reverse transport, antioxidant function, anti-inflammatory function, improvement of vascular endothelial function and the transport of proteins with endogenous biological activity[10]. Among these, cholesterol reverse transport refers to the reverse transport process of cholesterol from peripheral tissues, including blood vessel walls, to the liver, and HDL plays a key role in this process. The most prominent role of HDL in the body is the reversal of cholesterol. Although it has been proven that an HDL level can be used as a predictor of coronary heart disease risk, no studies have shown the effects of increasing HDL-C level as a separate clinical treatment strategy[11-12]. However, the International Atherosclerosis Society and the American Association of Lipoids have concluded through a large number of basic and clinical studies that the role of HDL-C in anti-atherosclerosis is mainly affected by the structure and function of HDL and HDL subtypes.

Rosuvastatin, as a third-generation statin, has a structure that contains a polar armour sulfonamide, which is easy for liver cells to consume, is highly hydrophilic, and has a high blood drug concentration at its three to five hour peak. Several medicines in the body have no obvious accumulation, raising the possibility of metabolic interaction with significantly smaller statins[13]. In addition to certain lipid-lowering effects, rosuvastatin also has a variety of physiological effects. For example, it is capable of reducing platelet adhesion, reducing oxidative stress, inhibiting inflammatory response and increasing atherosclerotic plaque stability, effectively enhancing therapeutic efficacy with high safety[14-15]. The results of this study showed that TC, LDL-C and CRP in the two groups were significantly lower than before treatment, while AST, ALT, Scr and BUN were significantly higher than before treatment ($P<0.05$). The levels of LDL-C measured in the experimental group were significantly lower than those measured in the control group ($P<0.05$), indicating that the two dosages of rosuvastatin significantly reduced the level of blood lipids, improved liver and kidney functions and reduced inflammatory responses. Further comparison of HDL subtype levels in the two groups showed that HDL2b levels were significantly higher and HDL3 levels were significantly lower in both groups after treatment than before treatment

(P<0.05), but there were no significant differences in HDL2b and HDL3 levels between the two groups (P<0.05). This finding suggests that the mechanism of two doses of rosuvastatin in the treatment of hyperlipidemia complicated with coronary heart disease may be realized by changing the structure and function of HDL subtypes.

In conclusion, 20 mg and 10 mg doses of rosuvastatin can affect the serum HDL subtypes of patients with hyperlipidemia complicated with coronary heart disease and change the structure and function of high-density lipoproteins. In clinical treatments, large doses of rosuvastatin can be used to significantly and safely reduce LDL-C levels with a significant clinical effect.

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Acknowledgements:
Drug Substance Rosuvastatin (ESR-14-10333)

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