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Original Article

Effects of rosuvastatin combined with clopidogrel bisulfate on blood lipids, cardiac function and inflammatory factor levels in elderly patients with coronary heart disease

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Abstract: Objective: To investigate the effects of rosuvastatin combined with clopidogrel bisulfate on blood lipids, cardiac function, and inflammatory factor levels in elderly patients with coronary heart disease (CHD). Methods: A total of 100 elderly patients with CHD treated in our hospital from January 2018 to January 2020 were retrospectively selected and assigned to the control group (n=50) and the observation group (n=50) according to different types of medications. The control group was treated with clopidogrel bisulfate, while the observation group was treated with clopidogrel bisulfate combined with rosuvastatin. T_1, T_2, T_3, and T_4, which indicated 5, 10, 15, and 20 days after medication respectively, were set up to observe the changes of relevant indexes in the two groups after medication. The changes in blood lipids, cardiac function, and inflammatory factors were compared between the two groups. Results: The clinical efficacy of the observation group was superior to the control group (P<0.05). No significant differences were determined in the levels of TC and LDL-C at T_1 and T_2 between the two groups (P>0.05); however, the observation group obtained lower TC and LDL-C levels than the control group at T_3 and T_4 (P<0.05). The levels of hs-CRP, TNF-α, BNP and NT-proBNP were not significantly different between the two groups at T_1 and T_2 (P>0.05), and lower levels of hs-CRP, TNF-α, BNP and NT-proBNP were observed in the observation group than in the control group at T_3 and T_4 (P<0.05). The two groups presented no significant differences in the left ventricular ejection fraction (LVEF) level and the Wall Motion Score Index (WMSI) score (P>0.05). After treatment, the observation group scored higher in the LVEF level and lower in the WMSI score than the control group (both P<0.05). The adverse reaction rate of the two groups was similar (P>0.05). Conclusion: Rosuvastatin combined with clopidogrel bisulfate is effective in the treatment of elderly patients with CHD, which can effectively improve the cardiac function of patients and reduce the levels of blood lipids and inflammatory factors.

Keywords: Rosuvastatin, clopidogrel bisulfate, elderly patients, coronary heart disease, blood lipids, cardiac function, inflammatory factors

Introduction

Coronary heart disease (CHD) is a type of cardiovascular disease with a high incidence in the elderly population, which mainly refers to heart disease caused by myocardial ischemia and hypoxia due to vascular stenosis and obstruction. The disease severely impairs the cardiac function of patients and can lead to heart failure or sudden death without timely treatment [1, 2]. Relevant studies have shown that vascular endothelial function damage, mainly derived from atherosclerosis, is the main trigger for the onset of CHD. The clinical treatment of CHD is drug therapy and surgical treatment [3, 4]. Conventional medications for CHD include antiplatelet drugs and aspirin. Clopidogrel bisulfate protects vascular endothelium, stabilizes plaques, and prevents thrombosis, but it has no significant efficacy in regulating blood lipids. Rosuvastatin is a statin drug with an outstanding effect on regulating blood lipids [5, 6]. Rosuvastatin calcium is used to treat hypercholesterolemia with an excellent effect of lowering blood lipids. It is mainly suitable for diet management and patients with hyperlipidemia and

hypercholesterolemia that cannot be effectively controlled. Oral medications for the treatment of diseases require avoidance of foods that interfere with the pharmacokinetics of the drug. Patients are advised to have a light diet, abstain from smoking, drinking, and high cholesterol foods, eat more fruits and vegetables, and do moderate exercise. Therefore, the therapeutic efficacy of rosuvastatin combined with clopidogrel bisulfate in elderly patients with CHD was investigated in this study.

Materials and methods

General data

This study is a retrospective trial. A total of 100 elderly patients with CHD treated in our hospital from January 2018 to January 2020 were assigned to the control group (n=50) given clopidogrel bisulfate therapy and the observation group (n=50) given combination therapy of clopidogrel bisulfate plus rosuvastatin. In the control group, there were 27 males and 23 females with age ranged from 51 to 76 years. In the observation group, there were 26 males and 24 females with age ranged from 52 to 78 years.

Inclusion criteria

(1) Patients who were diagnosed with CHD by coronary angiography; (2) Patients who were diagnosed for the first time and had no history of treatment; (3) Patients with life expectancy >3 years; (4) Patients with cognitive ability and communication skills.

Exclusion criteria

(1) Patients with severe insufficiency of the heart, kidney, liver, and other organs; (2) Patients with heart failure; (3) Patients with thyroid disease; (4) Patients with chronic infection; (5) Patients with rheumatism or malignant tumors. This study was approved by the internal ethics committee (No.2017-11-12), and the patients and their family members were informed of the objectives and procedures of this study and signed the informed consent form.

Methods

Patients in both groups received conventional treatment, including oral administration of antiplatelet drugs and dietary and lifestyle guidance. The control group was treated with clopidogrel bisulfate (Sanofi (Hangzhou) Pharmaceutical Co., Ltd., SFDA Approval No. J20180029), 75 mg/time, qd, administered orally after dinner. On this basis, the observation group was supplemented with rosuvastatin calcium tablets (Nanjing Zhengda Tianqing Pharmaceutical Co., Ltd., SFDA Approval No. H20080670) 10 mg/time, qd, administered orally at bedtime. The medication was administered for 40 consecutive days in both groups and was discontinued immediately in case of any abnormal symptoms.

Outcome measures

T_1, T_2, T_3, and T_4, which indicate 5, 10, 15, and 20 days after medication respectively, were set up to observe the changes of relevant indexes in the two groups after medication. Fasting venous blood (6 mL) at T_1, T_2, T_3, and T_4 were collected from all the enrolled patients and was centrifuged at 3000 r/min for 15 min with a centrifugal radius of 5 cm to obtain serum. Serum levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were determined using the DT-200 automated biochemical analyzer (Shengshi Dotop Jiangsu Biological Technology Co., Ltd.). Enzyme-linked immunosorbent assay kits (Shenzhen Kang Sheng Bao Bio-Technology Co., Ltd.) were used to determine serum high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor-α (TNF-α) levels. Determination of plasma BNP and NT-proBNP levels was performed using the immunoseparation method. The detection was carried out in strict accordance with the instructions provided with the kit.

When cardiac function index was concerned, a color Doppler blood flow meter was used to measure the left ventricular ejection fraction (LVEF) and the wall motion score index (WMSI) of patients before and after treatment.

Clinical efficacy was categorized into the following types. Markedly effective: clinical symptoms, such as palpitations and chest discomfort disappeared, with TC and LDL-C decreased by ≥ 1.0 mmol/L; Effective: clinical symptoms were alleviated, with TC and LDL-C decreased by 0.5-1.0 mmol/L; Ineffective: the symptoms failed to meet the above criteria or even deteri-

Table 1. Comparison of general data

Group	gender		Age ($\bar{x}$ ± sd)	BMI (kg/m^2)	Previous medical history		Smoking	Drinking
	male	female			Hypertension	Diabetes		
Observation group (n=50)	27	23	63.1±5.42	23.4±2.5	22	16	30	8
Control group (n=50)	26	24	62.53±5.36	22.7±2.1	18	12	26	4
X^2/t	2.364		1.364	1.516	0.667	0.793	0.649	1.515
P	0.536		0.635	0.133	0.414	0.373	0.420	0.218

Table 2. Comparison of clinical efficacy between the two groups [n, (%)]

		Markedly effective	Effective	Ineffective	Total effective rate
Observation group	50	32 (64.00)	16 (32.00)	2 (4.00)	48 (96.00)
Control group	50	22 (44.00)	18 (36.00)	10 (20.00)	40 (80.00)
X^2					6.601
P					0.014

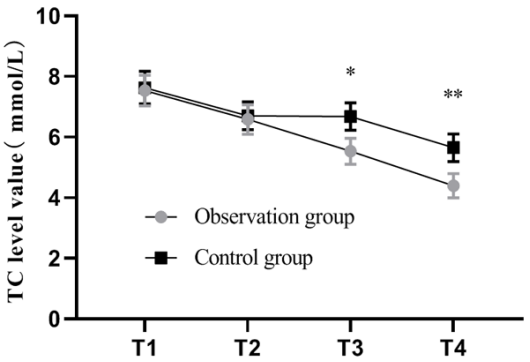

Figure 1. Comparison of TC levels at different time points between the two groups ($\bar{x}$ ± sd). Note: The abscissa represents the time points of T_1, T_2, T_3 and T_4, and the ordinate represents the TC level, mmol/L; The TC levels of patients in the observation group at T_1, T_2, T_3 and T_4 were 7.18±0.72 mmol/L, 6.24±0.69 mmol/L, 5.23±0.61 mmol/L, and 4.11±0.57 mmol/L, respectively; The TC levels of patients in the control group at T_1, T_2, T_3 and T_4 were 7.25±0.76 mmol/L, 6.38±0.65 mmol/L, 6.36±0.64 mmol/L, and 5.33±0.64 mmol/L, respectively; *indicated that there was a significant difference in the TC level at T_3 between the two groups (t=9.0374, *P<0.05); **indicated that there was a significant difference in the TC level at T_4 between the two groups (t=10.0658, **P<0.01).

orated. The total effective rate = (markedly effective + effective)/total cases ×100%.

Adverse reactions including nausea and vomiting, diarrhea, and flush were recorded and the adverse reaction rate was calculated.

Statistical methods

Data processing was performed by SPSS20.0 in this study, and data visualization was conducted by GraphPad Prism 7 (GraphPad Software, San Diego, USA). Count data were subjected to the *Chi-square* test and expressed as [n (%)]. The measurement data were expressed as ($\bar{x}$ ± sd). Independent sample t-test was used for comparison between groups and paired t-test was used for comparison within groups. The corrected *P*-value was used for comparison at different time points, P<0.05/4, that is, P<0.0125; P<0.05 indicated a statistically significant difference.

Results

General data comparison

The general data of the two groups of patients were compared and no statistically significant differences were found (all P>0.05; **Table 1**).

Comparison of clinical efficacy between the two groups

The observation group had a higher total effective rate than the control group (96.00% vs. 80.00, P<0.05; **Table 2**).

Comparison of TC levels at different time points between the two groups

No significant difference was determined in the levels of TC between the two groups at T_1 and T_2 (all P>0.05). At T_3 and T_4, TC levels decreased in both groups, with lower results in the observation group than in the control group (all P<0.05; **Figure 1**).

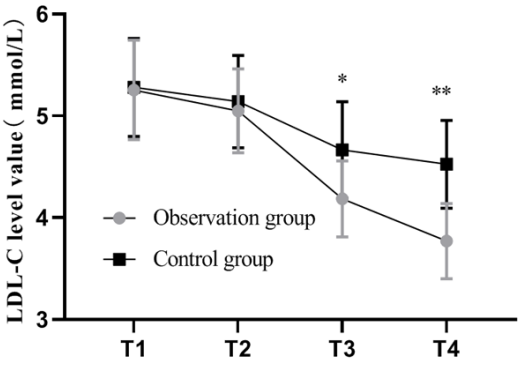

Figure 2. Comparison of LDL-C levels at different time points between the two groups ($\bar{x}$ ± sd). Note: The abscissa represents the time points of T_1, T_2, T_3 and T_4, and the ordinate represents the LDL-C level, mmol/L; The LD L-C levels of patients in the observation group at T_1, T_2, T_3 and T_4 were 4.91±0.69 mmol/L, 4.76±0.58 mmol/L, 3.92±0.53 mmol/L, and 3.51±0.52 mmol/L, respectively; The LDL-C levels of patients in the control group at T_1, T_2, T_3 and T_4 were 4.94±0.68 mmol/L, 4.82±0.64 mmol/L, 4.33±0.67 mmol/L, and 4.22±0.61 mmol/L, respectively; *indicated that there was a significant difference in the LDL-C level at T_3 between the two groups (t=3.3936, *P<0.05); **indicated that there was a significant difference in the LDL-C level at T_4 between the two groups (t=6.2634, **P<0.01).

Comparison of LDL-C levels at different time points between the two groups

No significant differences were detected in the levels of LDL-C between the two groups at T_1 and T_2 (P>0.05). At T_3 and T_4, LDL-C levels reduced in both groups, with a lower level in the observation group than in the control group (all P<0.05; **Figure 2**).

Comparison of hs-CRP levels at different time points between the two groups

There were no significant differences in the levels of hs-CRP between the two groups at T_1 and T_2 (P>0.05). At T_3 and T_4, hs-CRP levels decreased in both groups, with lower levels in the observation group than in the control group (P<0.05; **Table 3**).

Comparison of TNF-α levels at different time points between the two groups

There were no significant differences in the levels of TNF-α between the two groups at T_1 and T_2 (P>0.05). At T_3 and T_4, TNF-α levels were reduced in both groups, with lower outcomes observed in the observation group than in the control group (P<0.05; **Table 4**).

Comparison of BNP levels before and after treatment in the two groups

There was no significant difference in serum BNP levels between the two groups of patients at T_1 and T_2 (all P>0.0 5). At T_3 and T_4, the BNP levels of the two groups decreased, and the results of the observation group were lower than those of the control group (all P<0.05; **Table 5**).

Comparison of NT-proBNP levels before and after treatment in the two groups

There was no significant difference in serum NT-proBNP levels between the two groups of patients at T_1 and T_2 (all P>0.0 5). At T_3 and T_4, the levels of NT-proBNP in the two groups decreased, and the results of the observation group were lower than those of the control group (all P<0.0 5; **Table 6**).

Comparison of LVEF levels before and after treatment between the two groups

The two groups were not significantly different in LVEF levels before treatment (P>0.05). After treatment, LVEF levels increased in both groups, and the observation group had high levels than the control group (P<0.05; **Figure 3**).

Comparison of WMSI scores before and after treatment between the two groups

The two groups were not significantly different in WMSI scores before treatment (P>0.05). After treatment, WMSI scores decreased in both groups, with lower results in the observation group than in the control group (P<0.05; **Figure 4**).

Comparison of adverse reactions between the two groups

The two groups presented no significant difference in the rate of adverse reactions (4.00% vs. 8.00%, P=0.842; **Table 7**).

Discussion

CHD is clinically referred to as coronary atherosclerotic heart disease. The coronary blood flow cannot meet the needs of myocardial me-

Table 3. Comparison of hs-CRP levels at different time points between the two groups ($\bar{x}$ ± sd, mg/L)

		T1	T2	T3	T4
Observation group	50	8.31±0.71	7.32±0.56	5.33±0.51	4.20±0.52
Control group	50	8.30±0.68	7.51±0.58	6.06±0.55	4.58±0.59
t		0.0719	1.6664	6.8819	3.4166
P		0.9428	0.0988	<0.001	0.0009

Table 4. Comparison of TNF-α levels at different time points between the two groups ($\bar{x}$ ± sd, μg/L)

		T1	T2	T3	T4
Observation group	50	16.70±2.80	15.3±2.21	13.82±1.81	12.82±1.42
Control group	50	16.60±2.70	15.9±2.53	14.93±2.00	14.00±1.84
t		0.1818	1.2630	2.9100	3.590
P		0.8561	0.2096	0.0045	0.0005

tabolism in case of the non-equilibrium state between the coronary blood supply and myocardial demand, which may cause myocardial ischemia and hypoxia, resulting in angina pectoris and even myocardial infarction [7-9]. Decreased physical function in the elderly leads to susceptibility to chronic diseases and therefore they are also at high risk for CHD [10, 11]. There are many triggers leading to CHD, among which the most important factor is the vascular endothelial function damage which will aggregate inflammatory factors and eventually lead to thrombosis. Clinically, the treatment of CHD is mainly through lipid regulation and vascular protection [12-14].

Hs-CRP and TNF-α are related to various types of CHD. Atherosclerosis (AS) lesions in CHD patients are an inflammatory reaction. Hs-CRP can reflect the activity of AS plaques in CHD patients and provide guidance for the diagnosis of CHD classification and risk stratification. Cardiomyocyte necrosis can increase the levels of serum Hs-CRP and TNF-α. Serum Hs-CRP is positively correlated with TNF-α and plasma TG, and is negatively correlated with HDL-C and albumin. The level of Hs-CRP may be considered as a routine test in the cardiology department. This study compared Hs-CRP and TNF-α at T_3 and T_4, and the results showed that hs-CRP and TNF-α levels decreased in both groups, with significantly lower levels in the observation group than in the control group.

Conventional nitrate ester drugs can dissolve thrombus, increase myocardial blood supply, and improve cardiac function. However, they cannot effectively stabilize plaques, and their targets are single, resulting in poor overall therapeutic efficacy. Clopidogrel bisulfate protects vascular endothelium, resists platelet aggregation, and stabilizes vulnerable plaques [15, 16]. Rosuvastatin drugs enable certain cells (monocytes or macrophages) to enter the blood vessel wall, inhibiting the production of inflammatory factors. Moreover, they can increase the activity of superoxide dismutase, enhance the body's scavenging of free radicals, and inhibit the production of free radicals to exert anti-inflammatory and antioxidant effects, thereby alleviating and blocking the progression of atherosclerosis and stabilizing atherosclerotic plaques [17, 18]. In this study, the levels of TC and LDL-C were not statistically different between the two groups at T_1 and T_2 but were decreased at T_3 and T_4 with significantly lower levels in the observation group than in the control group. Similarly, serum hs-CRP, TNF-α, BNP and NT-proBNP levels were not statistically different between the two groups at T_1 and T_2 but were reduced at T_3 and T_4, with significantly lower levels in the observation group than in the control group. Similar results were also obtained by Norio Aoyama et al. [19], who demonstrated that clopidogrel bisulfate combined with rosuvastatin reduces blood lipids. The study of Song et al. [20] proved that clopidogrel bisulfate combined with rosuvastatin was effective in the treatment of elderly patients with CHD, with a significant increase in the cardiac function parameter LVEF and a significant decrease in the WMSI. In this study, no statistically significant difference was observed in the LVEF level between the two groups before treatment; however, the LVEF levels increased in both groups after treatment, with higher levels in the observation group than in the control group. WMSI scores were reduced in both groups after treatment and were significantly lower in the observation group than in the control group. It suggests that clopidogrel bisulfate combined with rosuvas-

Table 5. Comparison of BNP levels at different time points between the two groups ($\bar{x}$ ± sd, ng/L)

		T1	T2	T3	T4
Observation group	50	102.42±54.35	86.45±37.25	73.74±19.30	62.24±14.82
Control group	50	100.58±49.58	89.33±35.18	82.35±20.84	73.42±19.45
t		0.1769	0.3975	2.1430	3.2330
P		0.8600	0.6919	0.0346	0.0017

Table 6. Comparison of NT-proBNP levels at different time points between the two groups ($\bar{x}$ ± sd, ng/L)

		T1	T2	T3	T4
Observation group	50	54.13±18.42	50.42±12.54	38.41±10.45	33.45±9.44
Control group	50	53.2±20.41	49.33±13.82	45.44±11.72	41.42±10.92
t		0.2392	0.4130	3.1660	3.9040
P		0.8115	0.6805	0.0021	0.0002

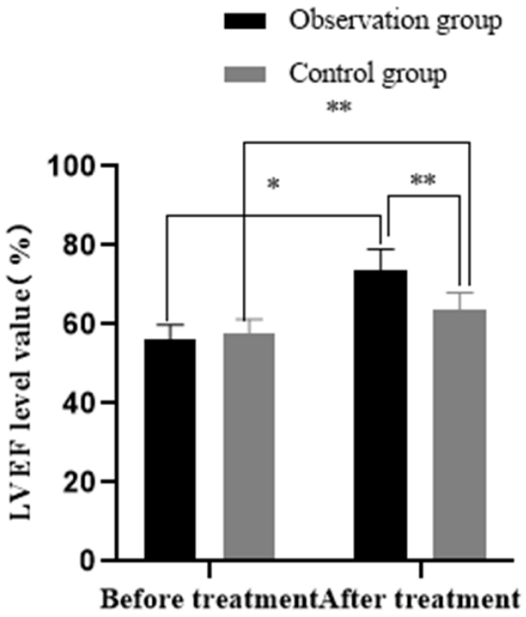

Figure 3. Comparison of LVEF levels before and after treatment between the two groups ($\bar{x}$ ± sd). Note: The abscissa indicates before and after treatment, and the ordinate indicates the LVEF level, %; The LVEF levels of patients in the observation group before and after treatment were 53.37±5.42% and 69.58±7.85%, respectively; The LVEF levels of patients in the control group before and after treatment were 54.88±5.29% and 60.41±6.30%, respectively; *indicated that there was a significant difference in the LVEF level before and after treatment in the observation group (t=3.4230, *P<0.05); **indicated that there was a significant difference in the LVEF level before and after treatment in the control group (t=16.3416, **P<0.01); **indicated that there was a significant difference in the LVEF level after treatment between the observation group and the control group (t=12.0348, **P<0.01).

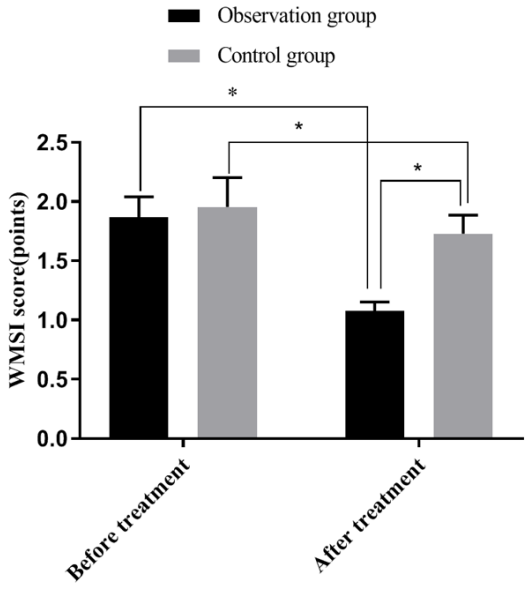

Figure 4. Comparison of WMSI scores before and after treatment between the two groups ($\bar{x}$ ± sd). Note: The abscissa indicates before and after treatment, and the ordinate indicates the WMSI score, point; The WMSI scores of patients in the observation group before and after treatment were 1.75±0.24 points and 1.02±0.11 points, respectively; The WMSI scores of patients in the control group before and after treatment were 1.78±0.35 points and 1.62±0.22 points, respectively; *indicated that there was a significant difference in the WMSI score before and after treatment in the observation group (t=19.5520, *P<0.05); *indicated that there was a significant difference in the WMSI score before and after treatment in the control group (t=2.7367, *P<0.05); *indicated that there was a significant difference in the WMSI score after treatment between the observation group and the control group (t=17.2488, *P<0.05).

Table 7. Comparison of adverse effects between the two groups [n, (%)]

		Nausea and vomiting	Diarrhea	Flush	Total adverse effects rate
Observation group	50	1 (2.00)	1 (2.00)	0	2 (4.00)
Control group	50	2 (4.00)	1 (2.00)	1 (2.00)	4 (8.00)
χ^2					0.709
P					0.842

tatin can effectively improve the cardiac function of elderly patients with CHD. Furthermore, it was found that the better clinical efficacy was found in the observation group, with a lower adverse reaction rate, which further confirmed the safety and effectiveness of rosuvastatin plus clopidogrel bisulfate in the treatment of elderly patients with CHD. The limitation of this study is that it is not a large-sample randomized controlled trial. Due to potential interference of multiple factors, the results may be biased, and the clinical evidence was of moderate credibility. Further study will be conducted in the future to obtain more reliable clinical data.

In summary, rosuvastatin combined with clopidogrel bisulfate for elderly patients with CHD can effectively improve the cardiac function of patients, protect their cardiovascular function, and effectively reduce their blood lipids and inflammatory factors levels, with high safety profile and good therapeutic efficacy, which is worthy of clinical promotion and application.

Disclosure of conflict of interest

None.

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