Tropical Journal of Pharmaceutical Research May 2022; 21 (5): 1095-1100
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v21i5.26

Original Research Article

Effectiveness of simvastatin/aspirin combination in the treatment of coronary heart disease in the elderly, and its effect on cardiac function and levels of inflammatory factors

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Sent for review: 20 September 2021 *Revised accepted: 27 April 2022*

Abstract

Purpose: *To investigate the efficacy of simvastatin plus aspirin in the treatment of coronary heart disease in the elderly, and its effect on cardiac function and inflammatory factor levels.*
Methods: *Eighty-seven identified elderly patients with coronary heart disease who were admitted to Nantong First People's Hospital, Nantong, China between January 2020 and June 2021 were recruited and assigned at a ratio of 1:1 to receive either conventional treatment (group A) or simvastatin plus aspirin (group B). The clinical endpoint was treatment efficacy.*
Results: *No significant differences were found between the two groups in respect of their baseline data ($p > 0.05$). Simvastatin plus aspirin was associated with a significantly higher treatment efficacy versus conventional treatment ($p < 0.05$). The patients, after joint therapy, had more cases of grade I cardiac function and fewer cases of grade III cardiac function, compared with conventional treatment group ($p < 0.05$). The application of simvastatin plus aspirin resulted in lower levels of triglycerides (TGs), total cholesterol (TC), fasting plasma glucose (FPG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) than the conventional treatment ($p < 0.05$). Simvastatin plus aspirin was also associated with lower levels of interleukin (IL)-6 and hypersensitive-c-reactive-protein (hs-CRP) when compared with conventional treatment ($p < 0.05$). Furthermore, simvastatin plus aspirin produced a similar incidence of adverse events with conventional treatment ($p > 0.05$).*
Conclusion: *Simvastatin/aspirin combination therapy is effective in the treatment of coronary heart disease in the elderly. It efficiently lowers glucose levels, lipid metabolism, and inflammatory factors, but enhances the cardiac function of patients.*

Keywords: *Coronary heart disease, Simvastatin, Aspirin, Inflammatory factors, Cardiac function*

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INTRODUCTION

Coronary heart disease is a common ischemic heart problem in which luminal narrowing or occlusion occurs after atherosclerosis of the coronary arteries, leading to myocardial ischemia, hypoxia, or necrosis, in addition to chest pain, chest tightness, and other uncomfortable symptoms [1,2]. According to the China Statistical Year book of Health and Family Planning, the mortality associated with coronary heart disease among Chinese residents has

shown a significant upward trend since 2012, with a marked increase in incidence among young people [3-5].

The clinical treatment of coronary heart disease is based on the principles of early detection, early hospitalization, and early treatment in order to rapidly restore blood perfusion to the myocardium, reduce mortality, and improve prognosis. The treatment of this disease involves lifestyle changes, pharmacological interventions, and surgical treatment, among which pharmacological treatment is primarily to control the disease condition in the patient. Aspirin, a cyclooxygenase inhibitor, is the cornerstone of antiplatelet therapy which is recommended for long-term oral administration in patients without contraindications [6-8]. Simvastatin, a lipid-lowering drug that has been previously used for weight loss and as a lipid-lowering agent, has also been found to inhibit the onset of heart disease in people who are at high risk [9].

In this study, the combination of simvastatin and aspirin was introduced in elderly patients with coronary heart disease in addition to conventional treatment. The clinical efficacy of the combined treatment was investigated.

METHODS

Patients

Inclusion criteria

Eighty-seven identified elderly patients with coronary heart disease who were admitted to Nantong First People's Hospital, Nantong, China between January 2020 and June 2021. All patients with a confirmed diagnosis as per the clinical criteria for coronary heart disease [10]; with a left ventricular ejection fraction of 40 - 60 %, and blood pressure of < 160/100 mmHg; and with no use of aspirin or statins 3 months before treatment, were included in this study. Patients and their families provided written informed consent forms after being informed of the details of the study.

Exclusion criteria

Patients in the following categories were excluded: patients who were allergic to simvastatin or aspirin; patients with other organic heart diseases; patients with other serious malignancies or liver disease or kidney disease; those with serious infectious systemic diseases; and patients with communication disorders, cognitive impairments, physical activity disorders, or low compliance with the study.

Screening of patients and grouping

Between January 2020 and June 2021, 87 elderly patients with coronary heart disease were recruited. They were assigned (1:1) to receive either conventional treatment (group A) or simvastatin plus aspirin in addition to conventional treatment (group B). This study was approved by the ethics committee of Nantong First People's Hospital (approval no. NT20190223). The study protocol was in strict accordance with the Helsinki Declaration [11].

Treatments

Patients in group A were given conventional therapeutic drugs such as β-blockers, nitrates, and Ca^{2+} channel blockers according to their conditions [12,13]. Patients in group B received simvastatin (specification: 10 mg, manufacturer: Jiangsu Kang Yuan Meilu Bio-pharmaceutical Co. Ltd, NMPA approval no. H20103628) orally every night, in addition to conventional treatment, at a starting dose of 20 mg. Dose adjustments were made more than 4 weeks apart, with a maximum dose of 40 mg per day, taken in the evening. The dose of simvastatin was reduced accordingly when the LDL-C level dropped to 75 mg/dL or the TC level decreased to less than 140 mg/dL. Aspirin enteric soluble tablets were given (specification: 100 mg x 30 s, manufacturer: Bayer Healthcare Ltd., NMPA approval no. J20130078) at a dose of 1 tablet/day after meals, or at doses of 75 - 300 mg daily for unstable angina pectoris.

Evaluation of indicators/parameters

Detailed general information such as age, gender, BMI, disease duration, disease type, Canadian Cardiovascular Society Classification (CCSC), and comorbidities such as hypertension, diabetes, and typical chest pain, were recorded.

Efficacy evaluation criteria were developed as outlined earlier [14]. Treatment outcome was *markedly effective* if the patient's angina symptoms completely disappeared or changed from severe to mild, and the resting electrocardiogram (ECG) returned to normal; or *effective* if angina was relieved, resting ECG ischemic ST-segment rebounded by 0.1 mv or more, or T-wave was lowered by 50 % or more. In contrast, treatment was *ineffective* if angina symptoms showed no reductions, and the resting ECG did not show any significant improvement or became even worsened. The cardiac function of patients was assessed according to the Killip classification: grade I: without pulmonary rales

and third heart sounds; grade II: pulmonary rales with a range of rales being less than 1/2 of the lung field; grade III: with a range of rales greater than 1/2 of the lung field (pulmonary edema); grade IV: patients in shock.

Fasting venous blood was collected from the patients in the morning and used for the determination of total cholesterol (TC), triglycerides (TGs), fasting blood glucose (FPG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Serum levels of inflammatory factors, namely interleukin-6 (IL-6) and hypersensitive C-reactive protein (hs-CRP), were determined using enzyme-linked immunosorbent assay (ELISA), and adverse reactions of the patients during treatment were recorded.

Statistical analysis

SPSS 22.0 was used for data analysis, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to plot graphs. Counting data are expressed as numbers and percentages {n (%)}, and were analyzed using χ^2 test. Measurement data are expressed as mean ± SD and were analyzed with *t*-test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

General information on patients

No significant differences were found between the two groups in baseline data ($p > 0.05$, Table 1).

Clinical efficacy

Simvastatin plus aspirin was associated with a markedly higher treatment efficacy versus conventional treatment ($p < 0.05$, Figure 1).

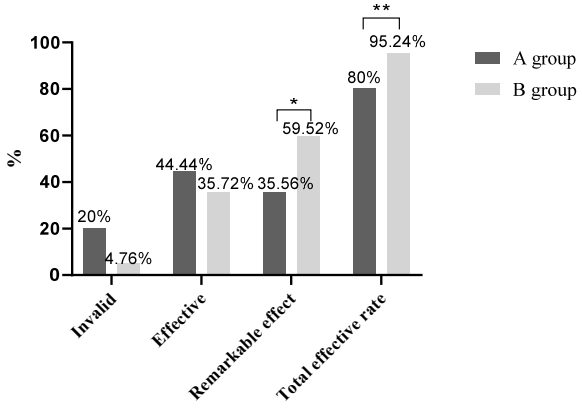

Figure 1: Comparison of clinical efficacy between two groups of patients (%). Group A had 9 cases of ineffective and 36 cases of effective in total, including 20 cases of effective and 16 cases of markedly effective; Group B had 2 cases of ineffective and 40 cases of effective in total, including 15 cases of effective and 25 cases of markedly effective. *P = 0.025, comparison of markedly effective cases between the two groups of patients; **p = 0.033, comparison of total effectiveness between the two groups of patients.

Cardiac functions

The patients after joint therapy had more cases of grade I cardiac function and fewer cases of grade III cardiac function versus conventional treatment ($p < 0.05$) (Table 2).

Table 1: Comparison of general information between the two groups of patients

Parameter	Group A（n=45）	Group B（n=42）	χ^2/t	*P*-value
Age (years)	62.76±5.68	63.19±5.70	0.352	0.726
Gender			0.022	0.881
Female	20（44.44）	18（42.86）		
Male	25（55.56）	24（57.14）		
Course of disease (years)	3.84±1.04	4.02±1.13	0.774	0.441
BMI (kg/m^2）	24.16±2.31	23.95±2.54	0.404	0.687
Hypertension	26（57.78）	23（54.76）	0.080	0.777
Diabetes	24（53.33）	20（47.62）	0.284	0.594
Typical chest pain	30（66.67）	27（64.29）	0.055	0.815
Disease type			0.066	0.797
Chronic myocardial ischemia syndrome	28（62.22）	25（59.52）		
Acute coronary syndrome	17（37.78）	17（40.48）		
CCSC			**0.014**	**0.906**
Grade Ⅱ	23（51.11）	22（52.38）		
Grade Ⅲ	22（48.89）	20（47.62）		

Table 2: Comparison of Killip classification between the two groups of patients {n (%)}

Killip classification		Group A (n=45)	Group B (n=42)	χ^2/*P*-value
Grade Ⅰ	Before treatment	0（0）	0（0）	
	After treatment	3（6.67）	10（23.81）	5.023/0.025
Grade Ⅱ	Before treatment	6（13.33）	5（11.90）	
	After treatment	26（57.78）	28（66.67）	0.729/0.393
Grade Ⅲ	Before treatment	21（46.67）	21（50）	
	After treatment	12（26.67）	3（7.14）	5.804/0.016
Grade Ⅳ	Before treatment	18（40）	16（38.10）	
	After treatment	4（8.89）	1（2.38）	1.699/0.192

Table 3: Comparison of the levels of glucose and lipid metabolism between the two groups (mmol/L, $\bar{}$mean ± SD)

Parameter		Group A (n=45)	Group B (n=42)	*t* /*P*-value
TGs	Before treatment	1.80±0.27	1.79±0.30	
	After treatment	1.58±0.17	1.43±0.16	4.231/<0.001
TC	Before treatment	5.81±0.82	5.85±0.83	
	After treatment	5.20±0.66	4.59±0.62	4.435/<0.001
FPG	Before treatment	8.35±3.89	8.33±4.01	
	After treatment	7.02±1.96	6.15±1.78	2.162/0.033
LDL-C	Before treatment	3.50±0.39	3.49±0.42	
	After treatment	3.24±0.37	3.01±0.40	2.786/0.007
HDL-C	Before treatment	1.45±0.27	1.47±0.25	
	After treatment	1.31±0.22	1.04±0.18	6.239/<0.001

Glucose and lipid metabolism

The application of simvastatin plus aspirin resulted in lower levels of TGs, TC, FPG, LDL-C, and HDL-C versus conventional treatment ($p < 0.05$, Table 3).

Levels of inflammatory factors

Simvastatin plus aspirin was associated with lower levels of IL-6 and hs-CRP versus conventional treatment ($p < 0.05$) (Figure 2 and Figure 3).

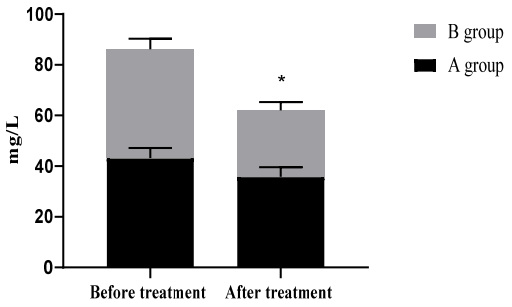

Figure 2: Comparison of IL-6 levels between the two groups of patients (mean ± SD)

The IL-6 levels of patients in group A before and after treatment were 43.22 ± 4.01 and 35.75 ± 3.8, respectively; the IL-6 levels of patients in group B before and after treatment were 42.93 ± 4.11 and 26.28 ± 3.30, respectively. **P* < 0.001, comparison of IL-6 levels between the two groups of patients after treatment.

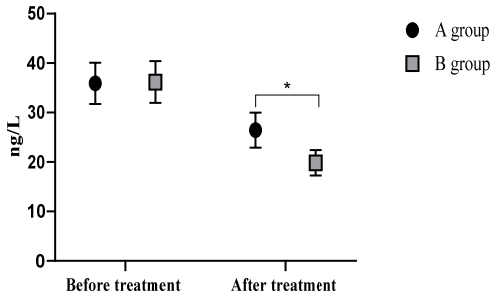

Figure 3: Comparison of hs-CRP levels between the two groups of patients (mean ± SD). The hs-CRP levels of patients in group A before and after treatment were 35.88 ± 4.17 ng/L and 26.43 ± 3.54 ng/L, respectively; the hs-CRP levels of patients in group B before and after treatment were 36.16 ± 4.22 and 19.83 ± 2.57 ng/L, respectively. **P* < 0.001, comparison of hs-CRP levels between the two groups of patients after treatment

Incidence of adverse reactions

Simvastatin plus aspirin maintained a similar incidence of adverse events versus conventional treatment ($p > 0.05$, Table 4).

Table 4: Comparison of adverse reactions between the two groups of patients

Group	Elevated alanine transaminase	Elevated aspartate transaminase	Gastrointestinal discomfort	Nausea and vomiting
A (n=4)	2 (4.44)	3 (6.67)	2 (4.44)	2 (4.44)
B (n=42)	1 (2.38)	1 (2.38)	1 (2.38)	3 (7.14)
χ^2	0.278	0.910	0.278	0.292
P-value	0.598	0.340	0.598	0.589

DISCUSSION

Due to coronary atherosclerosis, platelets are activated following plaque rupture and bleeding, leading to the release of ADP which causes further platelet adhesion and aggregation, thereby resulting in thrombosis. In addition, damage to the endothelium of the patient's blood vessels triggers vasospasm, resulting in narrowing of the coronary lumen and insufficient blood supply, followed by temporal ischemia and hypoxia in the local myocardium, all of which manifest as typical chest pain known as angina pectoris [15]. In the clinics, beta receptor antagonists are used to abate cardiac load and prevent arrhythmias, while sublingual nitrates are employed to relieve angina pectoris. Moreover, calcium channel blockers are applied if the condition remains uncontrollable. Persistent hyperlipidemia, hypertension, and hyperglycemia are high-risk factors for vascular endothelial damage, and they are highly likely to trigger chronic inflammation of the vessel wall and exacerbate atherosclerosis and plaque shedding. Therefore, the control of these risk factors through effective measures is crucial for treating coronary heart disease [16]. Aspirin is frequently used in the treatment of cardiovascular diseases, and it exerts a significant inhibitory effect on thromboxane A2, which facilitates the control of platelet aggregation and prevents thrombosis. Therefore, small doses of aspirin were used to induce antithrombotic effects in this study. Simvastatin is a statin lipid-regulating drug that effectively regulates the levels of cholesterol, triglycerides, and lipoproteins. In addition, simvastatin blocks the uptake of oxidatively-modified low-density lipoprotein by vascular endothelial cells and increases the production of nitric oxide in endothelial cells, thereby improving vascular endothelial function.

Simvastatin also inhibits the expression of adhesion factors and the secretion of related cytokines and blocks the inflammatory response caused by C-reactive protein. Currently, the efficacy of simvastatin plus aspirin for coronary heart disease in the elderly was marginally explored. Here, a retrospective investigation was conducted on patients with coronary heart disease who received simvastatin combined with aspirin in our hospital. Group B had a markedly higher total treatment effectiveness of 95.24 % than group A, which is consistent with the results of Branch *et al* [17].

Furthermore, the patients after joint therapy had more cases of grade I cardiac function and fewer cases of grade III cardiac function versus conventional treatment. The application of simvastatin plus aspirin resulted in lower levels of TGs, TC, FPG, LDL-C, and HDL-C versus conventional treatment. Simvastatin plus aspirin was associated with lower levels of IL-6 and hs-CRP versus conventional treatment. Simvastatin plus aspirin maintained a similar incidence of adverse events versus conventional treatment. These results indicate that combined treatment with simvastatin and aspirin substantially reduced levels of cholesterol, triglycerides, and lipoproteins; effectively inhibited platelet aggregation and inflammatory response, and enhanced the perfusion of coronary arteries and the endothelial function of blood vessels. Moreover, it produced a promising efficacy, and it was safe, with a low incidence of adverse effects.

CONCLUSION

The combination of simvastatin and aspirin is effective in the treatment of coronary heart disease in the elderly. It efficiently lowers glucose levels, reduces lipid metabolism and inflammatory factors, and enhances the cardiac function of patients. Aspirin and simvastatin are both primary care medications, and they are part of an effective pathway in comprehensive treatment protocols for coronary heart disease which require the combined use of anti-myocardial ischemic drugs. In addition, ibuprofen may be considered as an alternative for those who do not tolerate aspirin.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities

pertaining to claims relating to the content of this article will be borne by them.

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