

Original Research Article

Therapeutic effect of co-administered salvianolate and atorvastatin calcium on coronary heart disease patients with angina pectoris, and their blood lipid levels

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Abstract

Purpose: To investigate the clinical effect of combination of salvianolate and atorvastatin on blood lipids of coronary heart disease patients with angina pectoris (CHD-AP).

Method: Patients with CHD-AP ($n = 104$) from January 2016 to January 2017 were randomly assigned to two groups: control group treated with atorvastatin (10 mg/day), and study group was administered atorvastatin (10 mg/day, oral) plus salvianolate (200 mg/day in 5 % glucose, iv). Palpitation, chest distress, improvement in myocardial ischemia, myocardial function, and hemodynamics were determined and used to assess treatment effectiveness in the two groups. Differences in blood lipid profiles were also investigated.

Results: Improvement in palpitation, chest distress, myocardial ischemia and myocardial function in the study group were significantly higher than in the control group ($p < 0.05$). In the study group, total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triacylglycerols (TGs) significantly decreased, relative to the control group ($p < 0.05$).

Conclusion: Treatment of CHD-AP patients with combination of salvianolate and atorvastatin significantly ameliorates coronary heart disease and angina pectoris, and also reduces their blood lipid levels.

Keywords: Salvianolate, Atorvastatin, Coronary heart disease, Angina pectoris, Blood lipids

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INTRODUCTION

Coronary heart disease (CHD) is a clinically common cardiovascular disease with high mortality and disability. The safety of life of patients with CHD is seriously threatened. The disease results from changes in coronary function. Coronary atherosclerosis causes

transient myocardial ischemia or hypoxia, leading to chest pain which is the main clinical manifestation of the syndrome [1]. Coronary heart disease (CHD) is often associated with hyperlipidemia due to significant elevation of blood TC and TGs, and decreased blood levels of HDL-C. Total cholesterol (TC) and TG levels are significantly elevated, often accompanied by

decreases in HDL-C. Decreases in HDL-C and elevated LDL-C are important risk factors for the occurrence of CHD [2].

Salvianolate is a medicinally active component of *Salvia miltiorrhizae*, a traditional and natural medicine for enhancing blood flow and eliminating blood stasis. It is popularly employed for treating CHD and AP. *Salvia miltiorrhizae* contains lipid-soluble and water-soluble phenolic compounds, with salvianolate as the most important water-soluble active component. Salvianolate is employed as a therapeutic agent for diseases associated with the cardiovascular system [3]. Statins are clinically used as intensive lipid-lowering drugs. They act through a mechanism involving specific inhibition of HMG-CoA reductase activity, thereby inhibiting cholesterol biosynthesis, and reducing the blood levels of TC and LDL-C [4]. The present study was carried out to assess the impact of combined administration of salvianolate injection and atorvastatin calcium on patients with CHD-AP, and its effect on blood lipid profiles.

METHODS

Subjects

A total of 104 patients with CHD-AP from January 2016 to January 2017 were enrolled in our hospital. They comprised 50 men and 54 women within the age range of 45 - 75 years (mean age = 58 years), with weekly incidence of angina pectoris ≥ 2 . Patients with drug allergy, pregnant and lactating patients, patients with severe damage to the major organs (heart, liver and kidney); cancer patients, patients who underwent interventional therapy and coronary artery bypass grafting, and patients with mental disorders were excluded. The diagnostic and inclusion criteria used in this clinical study were in line with the diagnostic criteria for CHD angina in the Nomenclature and Diagnostic Criteria for Ischemic Heart Disease. The study received approval from the ethics committee of Affiliated Hospital to Changchun University of Chinese Medicine (Approval No. CUCM-2017043), and was performed in line with the Helsinki declaration of 1964 as amended in 1996 [5].

Treatments

The patients (n = 104) were randomly and double-blindly divided into study and control groups (52 patients per group). As shown in Table 1, both groups were comparable with respect to age, gender, and average number of angina punctures.

Table 1: Basic profile of patients

Group	Male	Mean age (years)	Number of angina punctures per week
Study	24	58.91 \pm 3.94	2.31 \pm 0.22
Control	26	57.05 \pm 4.18	2.55 \pm 0.34
χ^2	0.353	0.865	0.154
<i>p</i>	0.527	0.278	0.725

Patients in both groups were given routine treatment. In addition to the conventional treatment, the control group received oral atorvastatin calcium tablets (Pfizer Ireland Pharmaceuticals Production, approval no.: Chinese medicine standard 15J2200) at a dose of 10 mg/day, 30 min after dinner. The study group was given routine treatment and oral atorvastatin calcium tablets (10 mg/day), in addition to intravenous infusion of salvianolate (Shanghai Green Valley Pharmaceutical Co. Ltd., Guoyao Zhunzizhong 0050249) at a dose of 200 mg/day in 5 % glucose. Treatment in the two groups lasted for 8 weeks [6].

Evaluation of clinical effectiveness

Clinical effectiveness was evaluated as outlined earlier [7]. The categorizations used were as follows:

Effective: Implied disappearance of palpitations and chest tightness; normalization of patient's ECG or dynamic ECG ST segment or T wave; *significant effect:* Implied disappearance of palpitations and chest tightness; improvement in ECG or dynamic electrocardiogram ST-T without normalization, e.g., ST segment rebound > 0.05 mV, low T wave, or T wave recovery from low to erect, or decrease of ST segment to 0.05 mV - 0.10 mV; and *invalid:* No improvement in palpitation, chest tightness and ECG ST-T.

Determination of cardiac function and hemodynamics

SA9000 Hemodynamic Tester was used to measure cardiac function. The parameters measured were ejection fraction (EF), cardiac output (CO), as well as hemodynamics such as plasma viscosity (PV), whole blood viscosity high cut (WBVHC) and platelet adhesion rate (PAR) [8].

Evaluation of blood lipid levels

The blood lipid profiles of the study group and the control group before and after treatment were measured. Fasting venous blood (3 mL) was

taken from each patient in the morning, and the serum was separated by centrifugation within 2 h. The TC levels were determined by the endpoint method, and glycerol was determined by the oxidase method. The serum levels of TGs, HDL-C and LDL-C were determined using the procedures described in a previous study [9].

Statistical analysis

Count data are presented as percentage, while measurement data are presented as mean \pm standard deviation (SD). Groups were compared using *t*-test. All statistical analyses were done with SPSS version 19.0 software. Values of *p* < 0.05 were assumed significant.

RESULTS

Amelioration of palpitation and chest tightness

After 8 weeks of treatment, improvements in palpitations and chest tightness were observed. Table 1 shows that the total effectiveness in the control and study groups were 71.2 % and 92.3 %, respectively. Improvements in palpitations and chest tightness were significantly higher in

the study group than in the control group (*p* < 0.05).

Amelioration of myocardial ischemia

Table 3 shows that the total effectiveness in the control and study groups were 61.5 and 82.7 %, respectively, with greater amelioration of myocardial ischemia in study group patients than in control patients (*p* < 0.05).

Cardiac function

Before treatment, cardiac function parameters (EF and CO) were comparable in the two groups. However, there were significant post-treatment increases in EF and CO in both groups, with higher increase in the study group (*p* < 0.05), as shown in Table 4.

Hemodynamic parameters

Pre-treatment hemodynamic function parameters (PV, WBVHC and PAR) were comparable between the two groups (Table 5). However, after treatment, these parameters significantly decreased in the study group (*p* < 0.05).

Table 2: Effect of treatment on palpitations and chest tightness

Group	Significantly effective	Effective	Ineffective	Overall effectiveness (%)
Control	21	16	15	71.2
Study	31	17	4	92.3*

**P* < 0.05, compared with the control group

Table 3: Effect of treatment on myocardial ischemia

Group	Effective	Significantly effective	Ineffective	Overall effectiveness (%)
Control	19	13	20	61.5
Study	28	15	9	82.7*

**P* < 0.05, relative to control group

Table 4: Effect of treatment on cardiac function (mean \pm SD)

Cardiac function index	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
EF (%)	43.22 \pm 3.55	54.21 \pm 2.55*	42.98 \pm 3.12	69.22 \pm 3.66*#
CO (L/min)	42.54 \pm 3.21	50.33 \pm 3.14*	43.67 \pm 3.45	58.34 \pm 2.88*#

***P* < 0.05, relative to pre-treatment value; #*p* < 0.05, control group relative to study group

Table 5: Impact of treatments on hemodynamic parameters (mean \pm SD)

Hemodynamic index	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
PV (mPa·s)	3.66 \pm 0.55	3.02 \pm 0.32*	3.71 \pm 0.76	2.32 \pm 0.23*#
WBVHC (mPa·s)	2.43 \pm 0.34	1.98 \pm 0.33*	2.49 \pm 0.35	1.66 \pm 0.23*#
PAR (%)	6.55 \pm 1.21	5.12 \pm 1.14*	6.33 \pm 1.01	4.22 \pm 0.88*#

**p* < 0.05, relative to pre-treatment value; #*p* < 0.05, control group relative to study group

Table 6: Effect of treatment on blood lipid levels (mean \pm SD)

Blood lipid	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
TC (mM)	6.56 \pm 1.44	5.27 \pm 0.81*	6.67 \pm 1.56	4.26 \pm 0.77*#
TG (mM)	2.45 \pm 0.41	2.03 \pm 0.39*	2.43 \pm 0.44	1.66 \pm 0.51*#
HDL-C (mM)	1.31 \pm 0.40	1.41 \pm 0.31	1.32 \pm 0.51	1.61 \pm 0.45
LDL-C (mM)	3.70 \pm 0.81	2.98 \pm 0.77*	3.75 \pm 0.85	2.25 \pm 0.66*#

* $P < 0.05$, relative to pre-treatment; # $p < 0.05$, study group vs. control group

Effect of combination therapy on blood lipid profiles

As depicted in Table 6, before treatment, in blood lipid levels did not differ significantly between the two groups ($p > 0.05$). However, 8 weeks post-treatment, the blood lipid levels of both groups were significantly improved, with better improvements in the study group patients than in control patients ($p < 0.05$).

DISCUSSION

Coronary heart disease is an often-encountered cardiovascular condition in clinics. It is one of the common causes of death in patients. The pathological mechanism involved in the disease is vascular atherosclerosis. At present, CHD-AP occurs at younger ages, unlike before. In severe cases, CHD-AP degenerates into myocardial infarction leading to sudden death [9,10]. The main strategy for treating CHD-AP involves increasing the tolerance to myocardial ischemia/hypoxia, thereby enhancing myocardial microcirculation and improving myocardial blood supply.

Elevated blood lipid levels are also important factors in angina pectoris. High blood lipids are associated with marked elevations in blood TC and triglycerides, often accompanied with lowered HDL-C and elevated LDL-C. Raised blood levels of TC, TGs LDL-C are important risk elements for coronary heart disease. Atorvastatin calcium effectively inhibits endogenous synthesis of cholesterol and effectively regulates blood lipid levels by reducing blood levels of TC and LDL-C. It does these through a mechanism involving specific inhibition of HMG-CoA reductase, thereby reducing the incidence of atherosclerosis-induced angina pectoris [11].

Salvia miltiorrhizae is used as a drug to improve blood circulation, remove blood stasis and nourish blood, and it produces remarkable curative effects without adverse reactions [12]. *Salvia polyphenolate*, a water-soluble active compound isolated from *Salvia miltiorrhizae*, is widely used in the treatment of cardiovascular diseases. Its mechanism of action includes protection of myocardial membrane from

damage, and inhibition of atherosclerosis [13, 14].

These results demonstrate that combination of *Danshen* polyphenolate and atorvastatin calcium tablets in the treatment of CHD-AP produces significantly better effectiveness than the use of atorvastatin calcium tablets alone.

Study limitations

Due to limitations arising from short treatment duration and small sample size, the results obtained in this study may have certain errors. Thus, it is necessary to expand the number of subjects, and increase patients' disease tracking time in further studies.

CONCLUSION

The results obtained this study indicate that combined treatment of salvianolate and atorvastatin calcium tablets results in significantly improved therapeutic outcomes in CHD-AP patients, as well as significant reductions in their blood lipid profiles.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors read and approved the manuscript for publication. Aidong Liu conceived and designed the study; Guangyu Cheng, Qingjie Li, Lin Li, Qi Wang, Aidong Liu collected and analysed the data, while Guangyu Cheng wrote the manuscript.

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