ORIGINAL ARTICLE

Effect of Guhong injection combined with atorvastatin on angina pectoris of coronary heart disease and its influence on Hemorheology and oxidative stress

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ABSTRACT

Objective: To explore the effect of Guhong injection combined with atorvastatin on CHD patients with angina pectoris and its influence on hemorheology and oxidative stress.

Methods: 80 CHD patients with angina pectoris admitted to our hospital from December 2018 to December 2019 were randomly divided into the observation group (40 cases) and the control group (40 cases) by use of the random number table. The patients in the control group were treated with atorvastatin, while those in the observation group were treated with Guhong injection on the basis of the control group. The course of treatment was 2 weeks for each group. The treatment effect, the frequency of angina pectoris seizure and its duration before and after treatment, the changes of hemorheology indexes and oxidative stress and the occurrence of adverse reactions were compared between the two groups.

Results: the total effective rate of the observation group (92.50%) was higher than that of the control group (70.00%) ($p <$ .05). The frequency of angina pectoris seizure and its duration in these two groups after treatment were lower than those before treatment (Observation group: $t = 25.588, 23.009$; Control group: $t = 16.587, 16.263$; $p < .05$); After treatment, the frequency of angina pectoris seizure and its duration in the observation group were lower than those in the control group ($t = 15.191, 9.425$; $p < .05$). In the observation group, the hemorheology indexes after treatment were lower than those before treatment ($t = 6.742, 15.224, 6.983, 23.537, p < .05$); the hemorheology indexes after treatment in the observation group were lower than those in the control group ($t = 5.201, 13.913, 5.539, 13.745$; $p < .05$). In the observation group, the level of serum SOD after treatment was higher than that before treatment, while the levels of LPO and MDA after treatment were lower than those before treatment ($t = 10.839, 6.924, 8.466$; $p < .05$); the level of serum SOD after treatment in the observation group was higher than that in the control group, while the levels of LPO and MDA after treatment in the observation group were lower than those in the control group ($t = 6.171, 6.432, 5.394$; $p < .05$). The incidence of adverse reactions in the observation group was lower than that in the control group ($p < .05$).

Conclusions: Guhong injection combined with atorvastatin has an obvious clinical effect on CHD patients with angina pectoris, and it can improve hemorheology indexes and oxidative stress reaction with fewer adverse reactions.

Key Words: Guhong injection, Atorvastatin, CHD with angina pectoris, Efficacy, Hemorheology, Oxidative stress

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1. INTRODUCTION

Coronary heart disease is one of commonly seen cardiovascular diseases, and CHD with angina pectoris is a clinical syndrome manifested by myocardial ischemia and acute or transient ischemia-hypoxia in myocardial cells caused by hemadostenosis on the basis of coronary atherosclerosis.[1,2] According to the statistics, the incidence of CHD with angina pectoris is increasingly upregulated. The clinical manifestations are mainly chest pain, radiating pain and chest distress, sometimes accompanied by tachypnea, palpitation and shortness of breath etc., seriously affecting patients' physical and mental health and life quality.[3,4] Currently, the western medicine treatment for CHD patients with angina pectorisis is mainly focused on the conventional symptomatic treatment. Even though it is able to relieve clinical symptoms, it cannot fundamentally cure the disease.[5] Therefore, it is important to find a safe and effective method for the treatment of CHD with angina pectorisis.[6] This study was designed to explore the effect of Guhong injection combined with atorvastatin on CHD patients with angina pectoris and its influence on hemorheology and oxidative stress.

2. DATA AND METHODS

2.1 General information

According to the relevant diagnostic standards in Denomination and Diagnostic Criteria for Ischemic Heart Disease,[7] 80 CHD patients with angina pectoris admitted to our hospital from December 2018 to December 2019 were selected and randomly divided into the observation group (40 cases) and the control group (40 cases) by use of the random number table. The observation group was made up of 28 cases of male patients and 12 cases of female patients, aged 63-73 (69.39 ± 6.57), with a course of 2-13 (6.37 ± 1.78) years. The control group contained 27 cases of male patients and 13 cases of female patients, aged 61-74 (68.18 ± 5.98), with a course of 2-15 (7.08 ± 1.65) years. There was no statistically significant difference in general data between two groups (p > .05).

2.2 Inclusion and exclusion criteria

Inclusion criteria: 1) patients who conformed to the diagnostic standards of CHD with angina pectoris; 2) patients who were no less than 40 years old and no more than 75 years old; 3) patients who signed informed consent forms.

Exclusion criteria: 1) chest pain resulted from other types of heart diseases and causes; 2) patients who took drugs affecting the efficacy within 2 weeks before the study; 3) patients with severe pulmonary, renal or hepatic insufficiency; 4) patients with mental diseases; 5) patients with allergic constitution.

3. METHODS

Both groups of patients were given the conventional treatment of the western medicine, including oxygen uptake, bed rest, NO donors drugs, β-receptor blockers, LMWH, statins and aspirin enteric-coated tablets etc.. On that basis, the control group of patients were required to orally take atorvastatin (Manufacturer: Guangdong Baike Pharmaceutical Co., Ltd.; Specification: 10 mg; SFDA Approval No.: H20120021; Batch No.: 1607282), the dose was 20 mg per time a day. On the basis of the control group, each patient in the observation group was additionally given 20 ml of Guhong injection dissolved in 250 ml of normal saline by ivgtt, one time per day. The course of treatment was 2 weeks for each group.

3.1 Criteria of the therapeutic effect

1) Cured: the cardiac function was improved to Grade 2, with the main manifestations almost disappeared without the use of nitroglycerin; 2) effective: the cardiac function was improved to Grade 1, with the main manifestations improved, with the dose of nitroglycerin reduced by no less than 50%; 3) ineffective: the cardiac function was not improved, and the main manifestations showed no improvements, with the dose of nitroglycerin reduced by no more than 50%, or even increased.

3.2 Indicator observation

It was required to 1) observe the frequency of angina pectoris seizure and its duration in these two groups before and after treatment; 2) observe the changes of hemorheology indexes in these two groups before and after treatment, including high blood viscosity (HBV), low blood viscosity (LBV) and plasma viscosity (PV) and fibrinogen (FIB): 4 ml of elbow venous blood was taken from each patient to isolate plasma and whole blood samples for the measurement use with the help of blood rheometer; 3) observe the changes of oxidative stress, such as superoxide dismutase (SOD), lipid peroxide (LPO) and malondialdehyde (MDA): 3 ml of elbow venous blood was taken from each patient before and after treatment respectively to centrifuge and isolate the serum (Centrifugal radius: 10 cm, centrifugation time: 10 min), and then store the sample at -20°C for the measurement use; 4) observe the adverse reactions in the two groups.

3.3 Statistical treatment

The data acquired from this study were imported into SPSS22.0 software for the statistical use. The measurement data were represented by mean ± standard deviation. All the data in this study fitted to normal distribution, with the use of t-test. The categorical data were compared by use of chi-square test. The difference (p < .05) was of statistical significance.

4. RESULTS

4.1 The comparison in the therapeutic effect between two groups

The total effective rate of the observation group (92.50%) was higher than that of the control group (70.00%) ($p < .05$), see Table 1 for details.

4.2 The comparison in the frequency of angina pectoris seizure and its duration between two groups

There were no statistically significant differences in the frequency of angina pectoris seizure and its duration before treatment between two groups ($t = 0.421, 0.431, p > .05$); the frequency of angina pectoris seizure and its duration in these two groups before treatment were lower than those after treatment (Observation group: $t = 25.588, 23.009$; Control group: $t = 16.587, 16.263$; $p < .05$); the frequency of angina pectoris seizure and its duration after treatment in the observation group were lower than those in the control group ($t = 15.191, 9.425$; $p < .05$), see Table 2 for details.

4.3 The comparison in the changes of hemorheology indexes between two groups

There was no statistically significant difference in the changes of hemorheology indexes before treatment between two groups ($t = 0.132, 0.615, 0.302, 0.409$; $p > .05$); there were no obvious changes in hemorheology indexes before and after treatment in the control group ($t = 0.763, 1.512, 0.748, 0.964$; $p > .05$); the hemorheology indexes in the observation group after treatment were lower than those before treatment ($t = 6.742, 15.224, 6.983$ and 23.537; $p < .05$); the hemorheology indexes after treatment in the observation group were lower than those in the control group ($t = 5.201, 13.913, 5.539, 13.745$; $p < .05$), see Table 3 for details.

Table 1. The comparison in the therapeutic effect between two groups

Group	n	Cured (%)	Effective (%)	Ineffective (%)	Total Effective Rate (%)
Observation Group	40	28 (70.00)	9 (22.50)	3 (7.50)	37 (92.50)
Control Group	40	20 (50.00)	8 (20.00)	12 (30.00)	28 (70.00)
χ^2 Value	-	-	-	-	6.646
p Value	-	-	-	-	$< .05$

Table 2. The comparison in the frequency of angina pectoris seizure and its duration between two groups ($\bar{X} \pm$ s)

Group	Observation Time	n	Frequency of Angina Pectoris Seizure (time(s)/week)	Duration of Seizure (min/time)
Observation Group	Before Treatment	40	7.34±0.93	8.12±1.28
	After Treatment	40	3.16±0.45*#	3.08±0.53*#
Control Group	Before Treatment	40	7.26±0.76	8.24±1.21
	After Treatment	40	4.83±0.53*	4.51±0.80*

Note. * In comparison with the indicators before treatment, $p < .05$; # in comparison with the control group, $p < .05$.

Table 3. The comparison in the changes of hemorheology indexes between two groups ($\bar{X} \pm$ s)

Group	Observation Time	n	HBV (mPa·s)	LBV (mPa·s)	PV (mPa·s)	FIB (g/L)
Observation Group	Before Treatment	40	5.73±1.20	18.32±2.19	2.01±0.53	3.82±0.56
	After Treatment	40	4.1±0.87*#	11.45±1.83*#	1.29±0.38*#	1.49±0.28*#
Control Group	Before Treatment	40	5.69±1.49	18.65±2.59	1.97±0.65	3.76±0.74
	After Treatment	40	5.45±1.32	17.83±2.25	1.89±0.57	3.58±0.92

Note. * In comparison with the indicators before treatment, $p < .05$; # in comparison with the control group, $p < .05$.

4.4 The comparison in the changes of oxidative stress between two groups

There were no statistically significant differences in the changes of SOD, LPO and MDA levels before treatment between two groups ($t = 0.777, 0.297, 0.278$; $p > .05$). There were no obvious differences in the changes of SOD, LPO and MDA levels before and after treatment in the control group ($t = 0.742, 0.786$ and 0.920; $p > .05$). In the observation group, the level of serum SOD after treatment was higher than that before treatment, while the levels of LPO and MDA after treatment were lower than those before treatment ($t = 10.839, 6.924, 8.466$; $p < .05$); the level of serum SOD after

treatment in the observation group was higher than that in the control group, while the levels of LPO and MDA after treatment in the observation group were lower than those in the control group ($t = 6.171, 6.432, 5.394$; $p < .05$), see Table 4 for details.

4.5 The comparison in the incidence of adverse reactions between two groups

The incidence of adverse reactions in the observation group was lower than that in the control group ($p < .05$), see Table 5 for details.

Table 4. The comparison in the changes of oxidative stress between two groups ($\bar{X} \pm$ s)

Group	Observation Time	n	SOD（U/L）	LPO（μmol/L）	MDA（μmol/L）
Observation Group	Before Treatment	40	63.42±7.81	5.47±1.39	5.93±1.25
	After Treatment	40	79.93±5.64[*#]	3.79±0.65[*#]	3.71±1.09[*#]
Control Group	Before Treatment	40	61.87±9.90	5.38±1.32	5.84±1.62
	After Treatment	40	64.01±15.31	5.16±1.18[*]	5.49±1.78[*]

Note. [*] In comparison with the indicators before treatment, $p < .05$; [#] in comparison with the control group, $p < .05$.

Table 5. The comparison in the incidence of adverse reactions between two groups

Group	n	Gastrointestinal Reaction	Debility	Dizziness	Incidence (%)
Observation Group	40	1	1	1	7.50
Control Group	40	4	3	4	27.50
χ^2 Value	-	-	-	-	5.541
p Value	-	-	-	-	< .05

5. DISCUSSION

According to the traditional Chinese medicine, CHD with angina pectoris is considered as true heart pain, heart pain and chest discomfort, which is thought to be associated with spleen, renal and hepatic function.[8, 9] TCM theory holds that CHD with angina pectoris is probably a type of asthenia in origin and asthenia in superficiality, accompanied by cold congelation, qi stagnation, blood stasis and phlegm turbidity, which can result in heart vessel blockage stasis. Blood stasis is an important pathogenesis.[10] As a type of traditional Chinese and western medicine compound, Guhong injection is made up of aceglutamide and the extracts of safflower, which has an effect of promoting blood circulation for removing blood stasis. Modern pharmacological research indicates that[11, 12] aceglutamide is one of acetyl compounds of glutamine. It can take effect on the cardiac conducting system by enhancing the pacing function of P cells in sinoatrial nodes; the extracts of safflower can effectively eliminate free radicals, suppress the lipid oxidation of cell membranes, enhance the activity of SOD and inhibit platelet aggregation. This type of extracts can also relieve microcirculation disturbance, dilate blood vessels and improve the hemorheology indexes. Atorvastatin, which is one of lipid-lowering drugs, can block the transformation from 3-hydroxyl-3-methylglutaryl-coenzyme A to methyldihydroxyvaleric acid, enhance the effect of liver on eliminating low density lipoproteins and then decrease the level of blood

lipid. This study shows that the total effective rate of the observation group is higher than that of the control group. It is indicated that Guhong injection combined with atorvastatin can acquire a good efficacy. The frequency of f angina pectoris seizure and its duration after treatment in the observation group are lower than those in the control group, which suggests that Guhong injection combined with atorvastatin can reduce the frequency of angina pectoris seizure and its duration.

Modern medicine holds that oxidative stress and its mediated lipid metabolism and peroxidation reaction play an important role in the occurrence and development of CHD with angina pectoris.[13] SOD, one of anti-oxidative substances, can eliminate free radicals and prevent the tissues from being damaged by peroxidation and free radicals. The changes in SOD content can reflect the anti-oxidative ability.[14] Myocardial ischemia in the course of CHD can generate a large number of free radicals, which can bind to the side chains of unsaturated fatty acids and then obviously increase the LPO level in myocardial ischemia.[15] As a terminal product of lipid peroxidation, MDA can reflect the degree of lipid peroxidation and represent the rate and the intensity of lipid peroxidation.[16] This study shows that SOD level after treatment in the observation group is higher than that in the control group, and the levels of LPO and MDA after treatment in the observation group are lower than those in the control group. It is indicated that Guhong injection combined

with atorvastatin can improve the oxidative stress.

In CHD patients with angina pectoris, the blood keeps in a hypercoagulable state, with an abnormal blood coagulation and fibrinolysin system.[17] In addition, the occurrence of thrombosis and the up-regulated lipid level in CHD patients can lead to the increase of blood viscosity and the decrease of erythrocyte deformability and result in the changes of hemorheology indexes.[18, 19] The changes of hemorheology indexes are considered to be the important indicators for evaluating hypercoagulable state, which contribute to the evaluation of patients' condition.[20] This study shows that the levels of hemorheology indexes after treatment in the observation group are lower than those in the control group. It is indicated that Guhong injection combined with atorvastatin can improve the abnormal hemorheology indexes.

In conclusion, Guhong injection combined with atorvastatin has an obvious clinical effect on CHD patients with angina pectoris, and it can improve hemorheology indexes and oxidative stress reaction with fewer adverse reactions.

CONFLICTS OF INTEREST DISCLOSURE
The authors declare they have no conflicts of interest.

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