

The index and improvement effect of using Danhong injection to patients with atherosclerosis symptoms of coronary heart disease (CHD)

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Abstract: The clinical effects of coronary heart disease unstable angina treated by Danhong injection as well as its influence on Hcy (Homocysteine), Hs-CRP (High sensitivity C-reactive protein) and NT-proBNP (N-Terminal pro-brain natriuretic peptide) were observed. 72 cases of hospitalized patients in Gaomi city people's hospital cardiology department confirmed to the standard of coronary heart disease unstable angina were selected, and were divided randomly into experimental group (red) and the control group with 36 cases in each group. Based on conventional western medicine treatment, experimental group combined with Danhong injection 20 ml; while the control group with blood producing needle 400 mg. After two weeks treatment, symptoms were observed before and after treatment. Hcy (Homocysteine), Hs-CRP (High sensitivity C-reactive protein) and NT-proBNP (N-Terminal pro-brain natriuretic peptide) of two groups were lowered before and after treatment, there was statistical difference ($P < 0.05$). The comparison of Hs-CRP (High sensitivity C-reactive protein), NT-proBNP (N-Terminal pro-brain natriuretic peptide) between two groups after treatment was statistically different, experimental group was better than that of control group, ($P < 0.05$). Danhong injection is traditional Chinese medicine preparations to treat coronary heart disease unstable angina for its curative effect affirmation and good safety, and its improvement on Hcy (Homocysteine), Hs-CRP (High sensitivity C-reactive protein), NT-proBNP (N-Terminal pro-brain natriuretic peptide) and other laboratory index and is worthy of clinical use and further study.

Keywords: Danhong injection, Unstable angina, Blood stasis block type.

INTRODUCTION

Unstable angina is an unstable myocardial ischemia syndrome caused by the imbalance between supply and demand of myocardium oxygen. It is one of the common expressive types of acute coronary syndromes. It is often difficult to predict the progression of UA (Unstable angina) disease, the occurrence rate and mortality rate of acute myocardial infarction were respectively 12%-13% and 3%-18% within a year (Chinese Medical Association Cardiology Branch, 2010). With continuous improvement of people's living standard and the change of lifestyle and dietary structure in recent years, its attack rate presents the up rise trend year by year, and it has become one of the leading causes of death and disability in the world, and become an important health problem of hospitalized patients with millions around the world.

MATERIALS AND METHODS

This research is conducted according to some random, single blind, parallel control design. All the selected cases come from hospitalized patients in cardiovascular internal medicine ward from March 2013 to March 2014, of which

72 cases were qualified. According to the proportion of 1:1 and the random numbers randomly divided these patients into experimental group (Danhong injection plus conventional treatment group) 36 cases, control group (Blood flux freeze-dried and regular treatment group) 36 cases.

Diagnostic criteria

Western medicine diagnostic criteria

With reference to the *Diagnosis and Treatment guidelines of Unstable Angina and Non-ST Segment Elevation Myocardial Infarction* (Chinese Medical Association Cardiology Branch and Editorial Board of Journal of China Angiocardiopathy, 2007) made by Chinese Society of Cardiology of Chinese Medical Association and Editorial Board of Chinese Journal of Cardiology in 2007, unstable angina were divided into the following subtypes: deteriorating labor angina: illness aggravate suddenly which is manifested as chest pain attacks more often and with long endurance, activity worshipping value reduced significantly of induce angina. To classify labor angina (CCSC increase above grade I and at least the level III) according to the Canadian college of cardiology, the effect of nitroglycerin relieve symptoms is weakened, within 2 months course of the disease; Incipient labor

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angina: newly occurred angina pectoris within 2 months (from no angina or a history of angina, but in the past half year did not attack angina); Resting angina: angina occurred in rest or quiet state, and the lasting time of attack is relatively long (usually in 20 minutes or more), containing nitroglycerin is less effective, within one month course; Variant angina pectoris: angina occurs when having a rest or general activity and ECG shows temporary raise of ST segment during the attack.

Chinese medicine syndrome diagnostic criteria

The diagnosis criteria of blood stasis resistance syndrome was referred to the Guiding Principle of Clinical Research on Coronary Heart Disease Treated by New Traditional Chinese Medicine (trial implementation) (Xiaoyu, 2002) organized and compiled by State Drug Administration (table 2).

Standard of incorporate cases

These cases should conform to the western medicine UA diagnosis standard (Cunxiao, 2012) adopted or formulated in this research; conform to the traditional Chinese medicine disease name and syndrome criterion (Jing and Lim, 2012; Bo and Zhongxiang, 2012) adopted or formulated in this research; the attack time per week was no less than 2 times; age between 45-75; the electrocardiographic examination at least should conform to one of the follows: there is ischemic changes in the tranquillization electrocardiographic examination results In the attack of angina pectoris; there is obvious ischemic changes in tranquillization electrocardiogram or motion testing electrocardiogram positive; informed consenters. Meet all of above standards can be incorporated.

Exclusion criteria

Those who do not conform to the diagnosis or

incorporation standards: After inspection confirmed that the chest pain caused by AMI, gallbladder heart syndrome, stable angina, severe neural functional disease, acute pericarditis, menopausal syndrome, hyperthyroidism, aortic stenosis, acute myocarditis, pulmonary embolism, pneumothorax, etc; systolic pressure is larger than 180Hg and/or diastolic blood pressure is larger than 110mn1Hg; severe heart and lung dysfunction or arrhythmia; severe primary disease of liver, kidney and hemopoietic system, severe electrolyte disturbance, mental disease or progressive disease; gestation or breast feeding women, psychopath; allergic constitution; bleeding tendency patients; PCI or CABG operation history within one year. If these cases conform to one of these standards, then it can be excluded.

Patient exclusion criteria

Those who do not conform to the incorporation standards; conform to the incorporation standard but without treatment.

Withdrawal criteria

Those who can not tolerate when allergy or untoward effect occur; those who are not suitable or willing to further treatment after the appearance of certain severe complication or other diseases in the process of treatment; those who are not willing to continue treatment for poor effect; subjects are with bad compliance or using the forbidden drug regulated in this program. If they conform one of the above criteria, then they would be exited.

Treatment method and course of treatment

All cases will have a rest, light diet and avoid alcohol and cigarettes, avoid emotional stimuli according to each condition, merger respiratory infection patients will plus appropriate antibiotic therapy; in the acute phase, patients

Table 1: the angina grading by CCSC

Grading	Characteristics
Grade I	The general physical activity won't cause angina, such as walk and go upstairs, but nervous, fast and continue exerting would cause the attack of angina.
Grade II	Daily physical activities are limited, walking fast or go upstairs, climbing, walking after meal or go upstairs, cold or walking in the wind, emotional can cause angina attack, or attack in a few hours after waking up. Under normal circumstances, flat ground walk with normal speed of 200m or step on more than one layer stairs are limited.
Grade III	Daily physical activities are obviously limited. Under normal circumstances, angina would attack by flat ground walk with normal speed of 100-200m or step on more than one layer stairs.
Grade IV	The symptom of angina would appear only with slight activity or rest.

Table 2: The diagnosis criteria of Chinese medicinal syndrome blood stasis resistance syndrome

Name	Explanation of syndrome
Main syndrome	Chest paroxysm pricking or angina, fixation, sense of suppression in the chest;
Second syndrome	Palpitation and breathe hard, gloomy complexion, cyanotic lips;
Tongue picture	Tongue nature dark purple with petechiae, ecchymosis, the hypogloeis venation cyanoze
Pulse condition	Thready pulse astringent or knot generation.

Notice: with one of the primary syndrome of chest pain, chest distress, and other symptoms with 2 items and tongue picture, then it is diagnosed.

will stay in bed for 1-3 days with oxygen, ECG monitoring and so on; In experimental group, Danhong injection (manufacturer: He Ze step pharmaceutical Co., LTD., approved by; Z20026866) 20ml was plus to 5% GS100ml or 5% NS100ml on the basis of conventional treatment of western medicine, static drop, 1 times a day (Youze, 2012; Meng, 2012); blood and producing needle (manufacturer: Heilongjiang treasured island pharmaceutical Co., LTD., approved by; Z20026437) 400 mg was added in GS100ml 5% or 5% NS100m on the basis of conventional western medicine therapy, static drop, 1 times a day. Both two groups are of a course of 2 weeks. Conventional western medicine treatment (table 3).

Observational index

Curative effect and decision criteria

With reference to Chinese Medicine New Medicine Clinical Research Guiding Principles, and Therapeutic Effect Evaluation Standard of Coronary Heart Disease Angina Pectoris and Electrocardiogram (ECG) (Forum of Combination of TCM and WM on the Treatment of Aged Stable Angina and Arrhythmia, 1987) made by combine traditional Chinese and western medicine treatment of coronary heart disease angina pectoris in 1979. Curative effects are: (1) improvement situation of angina; (2) improvement of resting electrocardiogram; (3) improvement of syndromes; (4) laboratory index changes.

Safety observation

Related vital signs: Heart rate, heart rhythm, heart murmur, blood pressure, tongue and pulse condition, etc.

kidney function, etc.

To observe and record in detail the adverse effects or adverse events during meditation, and to judge whether exist the causal relationship with the experimental drugs.

Statistical methods

Use SPSS16.0 statistical software for data statistics. Use standard deviation ($\pm s$) to mean measurement data, according to the comparison of before and after treatment with paired t test, comparison with analysis of variance between groups, and use χ^2 test to count data, $P < 0.05$ means significant differences.

RESULTS

The Improvement Situation of Angina Before and After Treatment in both Groups (as shown in table 4).

The Improvement Situation of ECG Before and After Treatment in both Groups (as shown table 5).

Curative Effect Comparison of Patients with Syndrome of TCM between the Two Groups (table 6).

Comparison of hs CRP, Hcy, NT-proBNP Before and After Treatment Between Two Groups (table 7).

Security testing

During the test, one case in experimental group once appeared one-time vertigo; the symptoms disappeared after drug withdrawal and do not appear after continuous using it. One case in the control group once appeared mild

Table 3: Conventional Western Medicine Treatment

Treatment	Drug classification	Drug name	Usage	Note
Anti-ischemic treatment	Nitric acid lipid	Single nitrate yamanashi fatzyban	60mg po qd	Attack to nitroglycerin tablets, 0.5 mg sublingual including clothing, and repeat after 5 ~ 10 min.
	Beta blockers	Fumaric acid metoprolol	25,mg/12.5mg po bid	Intolerance and no relative contraindication can change land, sulfur zhuo or l benzene sulfonic acid amlodipine, 2.5 mg Po qd
	Calcium channel blockers	Benzene sulfonic acid amlodipine	5mg po qd	
	ACEI	Maleic acid enalaprilat slices	10mg po qd	
	ARB	Irbesartan tablets	150mg po qd	
Antiplatelet therapy		Aspirin enteric-coated metformin hydrochloride	Initial dose of 300 mg and then 100 mg Po qd	Intolerate aspirin and clopidogrel initial dose of 300 mg and then 75 mg Po qd
Anticoagulation		Low molecular heparin calcium	5000iu ih qd	Ed) discontinuation in 5 to 7 days
Lipid-lowering therapy		Atorvastatin calcium tablets	10mg po qn	

The three routine blood, laboratory examination of liver, gastrointestinal reaction which is characterized by mild

nausea, vomiting and the symptoms disappeared after drug withdrawal and do not appear again after continuous using it. Routine blood and liver and kidney function index changes of patients before and after treatment in two groups (as shown in table 8).

DISCUSSION

Anti-inflammatory effects of danhong injection in the Treatment of coronary heart disease unstable angina

Modern studies have shown that the UA initiator is inflammatory response, and also runs through the whole pathological process of the disease, thus anti-inflammatory treatment has become another key for the disease treatment. Many inflammatory factors have involved in the process of formation and the onset of UA, especially the CRP has proved to be the independent risk factors for the happening of UA. At present a series of studies have confirmed that Danhong injection can effectively reduce the inflammatory factors especially the CRP levels. By observation, Xiaoling Qiang (Xiaoling, 2009) found that use Danhong injection on the basis of giving crown expansion, anticoagulation, lipid regulation, thrombolysis therapy can significantly decrease the serum hsCRP level. And studies have confirmed (Chun *et al.*, 2013) that use Danhong injection based on conventional treatment can obviously decrease the serum CRP, IL - 6, TNF -a, MMP - 9 levels. Guan Yunyuan *et al.* (2010) have analyzed the parameter changes of hsCRP, IL-6, MCP-1 and TXB2 between Danhong group and normal group before and after treatment, the result was Danhong group decreased more obvious than normal group, which indicated that Danhong injection can significantly reduce the inflammatory factor hsCRP, IL - 6, MCP-1 and TXB2 levels and stabilize coronary atherosclerotic plaque, so as to prevent the occurrence of plaque rupture and thrombosis.

Analysis of the curative effect of Danhong injection on the treatment of coronary heart disease unstable angina

This research showed that the application of Danhong injection on UA patients could effectively improve the syndrome of angina (show efficiency was 38.88%, total efficiency was 94.44%); and improve Chinese medical syndrome (show efficiency was 50%, total efficiency was 91.67%), compare with the control group, the total efficiency was fairly equal between the two group, and there was no statistical difference ($P>0.05$). However, experimental group was better than the control group in show efficiency. Compared with the control group, experimental group improved electrocardiogram with the show efficiency of 33.33% and total efficiency of 77.77%, there was no statistical difference; on the improvement of blood lipid, Hcy, hs-CRP and NT-proBNP, there were improvement in both groups and the difference was of statistical significance ($P<0.05$). Its mechanism may inhibit inflammatory reaction, improve endothelial

function and red blood cell gathering. And there was no untoward effects found in the treatment, such as bleeding, allergy or hepatorenal function damage. The research results showed that Danhong injection is an effective drug for the treatment of unstable angina.

Analysis of the security of Danhong injection on the Treatment of coronary heart disease unstable angina

All the selected cases were conducted the detection of convention and hepatorenal function before and after operation in this intervention research. Comparison between pre-operation and post operation, there was no obvious abnormality in both groups. There was one case of patient appeared transient dizziness during treatment in experimental group, and it disappeared after pharmacy. There was one case of patient appeared slight digestive tract discomfort in the control group, and the syndrome disappeared after the suit case treatment. All patients have finished the treatment. It showed that there was no obvious untoward reaction on the treatment of coronary heart disease unstable angina (blood stasis type) by Danhong injection, which was safe and reliable.

To sum up, in combination with the research results indicate that Dan injection has curative effect for the treatment of coronary heart disease unstable angina pectoris, it may intervene UA through multiple channels, in multiple level, place, and targets, so as to achieve the effect on the disease treatment. Hint that Danhong injection has a special advantage in the disease treatment.

CONCLUSION

This clinical trial results show that: in total efficacy, heart function improvement and TCM symptoms improvement, the results of using Danhong injection for coronary heart disease unstable angina pectoris are as follows:

The improvement situation of the show effective rate and the total effective rate between the two groups: in experimental group, the show efficiency was 38.88%, the total effective rate was 94.44%; in control group, the show efficiency and the total effective rate were 16.67% and 86.11% respectively, the comparison between the two groups, there was no statistical difference in the total effective rate ($P>0.05$). But in terms of show efficiency, the experimental group is significantly higher than control group ($P<0.05$).

In terms of ECG improvement between the two groups: in the experimental group, the show effective group was 33.3%, the total effective rate was 77.77% and the control group was 30.22% and 72.22% respectively. And there was no statistically significant difference both in the total effective rate and the show effective rate between the two groups.

Table 4: Improvement Comparison of Patients with Angina between Two Groups

Group	Case numbers	Effective	Valid	Invalid	Aggravate	Total effective rate
Experimental group	36	14 (38.88%)	20 (55.56%)	1(2.78%)	1 (2.78%)	94.44%
The control group	36	6 (16.67%)	25 (69.44%)	4(11.11%)	1 (2.78%)	86.11%

Note: test between experimental group and the control group, total effective rate of experimental group was 94.44%, while the control group was 86.11%, after the chi-square analysis, there was no statistical differences in total effective rate between the two groups ($P = 0.691 > 0.05$), but in show efficiency, there was statistically significant difference between the two groups ($P = 0.041 < 0.05$).

Table 5: Comparison of ECG after Treatment between Two Groups (cases)

Group	Case numbers	Effective	Valid	Invalid	Aggravate	Total effective rate
Experimental group	36	12 (33.33%)	16 (44.44%)	6 (16.67%)	2 (5.56%)	77.77%
The control group	36	11 (30.55%)	15 (41.67%)	7 (19.45%)	3 (8.33%)	72.22%

Note: before and after comparison within two group, both ECG were improved; Experimental group compared with the control group, the total effective rate of experimental group was 77.77%, while the control group was 72.22%, after the chi-square test, there was no statistically significant difference ($P=0.586>0.05$) and in show efficiency, there was also no statistically significant difference between the two groups ($P=0.795>0.05$).

Table 6: Curative Effect Comparison of TCM Symptoms after Treatment between Two Groups (cases)

Group	Case numbers	Effective	Valid	Invalid	Aggravate	Total effective rate
Experimental group	36	18 (50%)	15(41.67%)	3 (8.33%)	0 (0.00)	91.67%
The control group	36	8 (22.22%)	23(63.89%)	4(11.11%)	1(2.78%)	86.11%

Note: both the two groups have shown to have good effect to improve the symptoms of angina pectoris, the total effective rate of two group drugs are up to 91.67% and 86.11% respectively, after the chi-square analysis, there was no statistical difference between the two groups ($P = 0.453 > 0.05$), but there was statistical difference on show efficiency ($P=0.023 < 0.05$).

Table 7: Comparison of hs CRP, Hcy, NT-proBNP before and After Treatment between Two Groups

Index	Experimental group		The control group	
	Before treatment	After treatment	Before treatment	After treatment
hs-CRP(mg/L)	6.29±2.11	3.57±1.24	5.98±1.77	4.93±1.18
Hcy (umol/L)	20.23±4.73	15.39±3.39	21.24±5.28	16.53±3.68
NT-proBNP (pg/ml)	291.45±114.38	269.22±93.58	289.94±100.22	248.37±94.63

Note: comparison of Hcy, hs-CRP, NT-proBNP (Bohua, 2012) before each treatment between two groups, both had no statistical difference ($p > 0.05$); while comparison of Hcy, hs-CRP, NT-proBNP (Yilin *et al.*, 2007; Yeqing and Dongsheng, 2009) before and after treatment, the difference was statistically significant, comparison of Hcy between two groups, there was no statistically significant difference ($p > 0.05$), comparison of hs - CRP, NT - proBNP between two groups was statistically significant, the experimental group is better than that of control group ($p < 0.01$).

Table 8: Routine blood and liver and kidney function index changes of patients before and after treatment in two groups

Items	Experimental group		The control group	
	Before treatment	After treatment	Before treatment	After treatment
WBC ($\times 10^9/L$)	5.76±1.15	5.68±1.09	5.89±1.61	5.48±1.05
RBC ($\times 10^{12}/L$)	4.37±0.35	4.47±0.23	4.45±0.62	4.53±0.36
RLT ($\times 10^9/L$)	177.23±51.48	176.52±45.33	171.69±61.87	172.73±50.75
ALT (u/L)	15.49±7.38	15.34±7.07	18.95±10.39	18.59±9.48
SCr (umol/L)	89.85±25.33	92.34±16.18	99.38±24.18	98.68±15.93
BUN (mmol/L)	4.75±1.36	4.65±1.29	4.77±1.36	4.72±1.23

Note: comparison before and after treatment in one group, after the t test, $P > 0.05$, no significant changes, which shows Danhong injection has no obvious side effects and is safe and effective.

In the TCM symptoms curative effect between two groups of patients: in the experimental group, the show effective group was 50%, the total effective rate was 91.67%; and the control group was 22.22% and 86.11% respectively. There was no statistical difference between the two groups in the total effective rate, but the difference was statistically significant in two aspects of show efficiency.

Comparison of Hcy and hs-CRP, NT-proBNP between the two groups, both were significantly reduced after treatment, $p < 0.01$; comparison of Hcy after treatment between the two groups, there was no statistically significant difference; comparison of hs-CRP, NT-ProBNP after treatment between the two groups, the difference was statistically significant ($P < 0.05$).

5. In security, comparison before and after each between the two groups, there was no statistically significant difference, which proved that both the two methods are safe and effective.

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