

Original Article

Effect of Dan Hong injection on PON1, SOD activity and MDA levels in elderly patients with coronary heart disease

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Abstract: Objective: To research the effect of Dan Hong injection (DHI) on PON1, SOD activity and MDA levels in elderly patients with coronary heart disease (CHD). Methods: 98 elderly patients with CHD diagnosed by coronary angiography were randomly divided into conventional treatment group and DHI treatment group, measured and analysis the serum PON1 activity, SOD and MDA levels before and after treatment in the two groups. Results: PON1 and SOD activity in elderly CHD patients were significantly lower than elderly non-coronary heart disease group, there was a significant difference between the two groups ($P < 0.01$); and MDA level in elderly CHD patients was significantly higher than elderly non-coronary heart disease group, there was a significant difference between the two groups ($P < 0.01$). There was a major change in PON1 activity, SOD and MDA after 4 weeks DHI treatment ($P < 0.05$). There was different degrees of change in PON activity, SOD and MDA after 4 weeks conventional treatment when compared with pre-administer DHI, but did not reach significant difference ($P > 0.05$); PON1 activity, SOD and MDA had significant different after 4 weeks treatment in DHI group compared with the conventional treatment group ($P < 0.05$). Conclusions: There is lipid peroxidation in the elderly patients with the coronary heart disease. DHI can raise serum PON1, SOD activity and lower MDA to improve the antioxidant effect in elderly patients with coronary heart disease.

Keywords: Dan Hong injection, elderly, coronary heart disease, paraoxonase, malondialdehyde, superoxide dismutase, lipid peroxidation

Introduction

Traditional Chinese medicine (TCM) offers many advantages in clinical treatment. In TCM, combination therapy is the most commonly employed therapeutic approach, and the construction of a prescription containing multiple drugs, namely, a formula, each with distinct mechanisms, aims to amplify the therapeutic efficacy and lessen the adverse effects of each individual agent [1]. Generally, multiple active ingredients are aimed at multiple targets, exerting a systemic effect [2]. DHI is a standardized water-soluble complex containing extracts of the traditional Chinese remedies Radix Salvia miltiorrhiza (Danshen) and Flos Carthamus tinctorius L. (Honghua) [3]. Clinical studies [4-9] have shown that DHI can effectively improve the clinical symptoms in patients with coronary heart

disease, but its exact mechanism is still unclear. So, we have measured paraoxonase (PON) and superoxide dismutase (SOD) and Malondialdehyde (MDA) levels before and after application of DHI in elderly patients with coronary heart disease, to explore the possible mechanism of DHI for the treatment of coronary heart disease.

Materials and methods

Materials

158 cases in this study from May 2010 to May 2011 received in the department of Cardiology of 1st hospital of Xi'an Jiaotong University Medicine School, 98 cases of them as an object found that more than one stenosis blood vessels $\geq 50\%$ by coronary angiography, were ran-

Effect of Dan Hong injection on PON1, SOD and MDA

Table 1. The comparison of conventional and of Danhong injection group ($\bar{x} \pm s$)

Project	DHI group	Conventional group	P value
Cases	50	48	
Male/Female	45/5	43/5	
Age (years)	73.46 ± 9.34	72.56 ± 9.62	> 0.05
hypertension	36 (72%)	35 (72.92%)	> 0.05
diabetes	16 (32%)	15 (31.25%)	> 0.05
SBP (mmHg)	145.15 ± 5.22	144.20 ± 5.31	> 0.05
DBP (mmHg)	76.39 ± 5.18	77.27 ± 5.85	> 0.05
HR (times/min)	73.73 ± 4.25	74.54 ± 4.17	> 0.05

Table 2. Levels of PON1, SOD, MDA in elderly CHD and elderly non-CHD group ($\bar{x} \pm s$)

Project	N	PON1 ($\mu\text{kat/L}$)	SOD (U/ml)	MDA (nM/ml)
Elderly CHD	98	101 ± 73 [#]	42.8 ± 4.8 [#]	9.7 ± 1.4 [#]
Elderly non-CHD	25	123 ± 53	55.7 ± 5.4	5.3 ± 0.7

Note: [#]P < 0.01, compared with the levels in elderly non-CHD group.

Table 3. Levels of PON1 activity, SOD and MDA before and after treatment in two groups ($\bar{x} \pm s$)

Project	N	Before treatment	After treatment
DHI treatment group 50			
PON1 ($\mu\text{kat/L}$)		100 ± 67	116 ± 73
SOD (nU/ml)		44.5 ± 4.3	56.4 ± 5.1 ^{*#}
MDA (nmol/ml)		9.2 ± 1.4	5.5 ± 0.4 ^{*#}
Conventional therapy group 48			
PON1 ($\mu\text{kat/L}$)		103 ± 67	109 ± 52
SOD (nU/ml)		43.8 ± 3.2	45.4 ± 3.9
MDA (nmol/ml)		9.1 ± 1.3	7.8 ± 0.5

Notes: ^{*}P < 0.05, compared with before treatment; [#]P < 0.05, compared with conventional therapy.

domly divided into conventional therapy group of 48 patients (43 males and 5 females, with an average age of 72.56 ± 9.62 years) and DHI treatment group of 50 patients (male 45 cases and 5 females, with an average age of 73.46 ± 9.34 years), the control group 25 patients with coronary artery stenosis ≤ 25% (20 males and 5 females, mean age 72.25 ± 9.41 years). The medical history of each patient was asked on admission, and did physical examination, X-ray, electrocardiogram, echocardiogram, and related laboratory tests and so on. The patients with peripheral vascular disease, endocrine disease, liver and kidney diseases, inflammation and malignancy were excluded. Conventional treatment group and DHI treatment group were not statistically different in characteristics, blood pressure and heart rate (**Table 1**).

Research methods

Coronary angiography: According to the guidelines for coronary angiography of ACC/AHA, the coronary angiography was performed for each patient and coronary artery narrow degree was judged. The conventional treatment group has been given nitroglycerin, calcium antagonists and β -blockers, etc; DHI treatment group has been given the basis of conventional treatment and DHI 30 ml daily (JiNan Buchang Pharmaceutical Co., Ltd., National medicine accurate Z20026-866). Recorded every patient's heart rate, blood pressure, ECG, echocardiogram and related laboratory test results, such as liver and kidney function after treatment for each patient. Blood were collected before and after 4 weeks treatment (control group blood samples only once). Blood samples were stored at -45°C until PON1, SOD and MDA being measured.

Outcome measures

(1) PON1 activity: reference using acetic acid benzyl ester method [10].

(2) SOD and MDA. Were measured according to the kit instructions (purchased from Nanjing Institute of Biomedical Engineering cohesion).

Statistical analysis

All Statistical analyses were performed with SPSS11.0/PC Package, and all values were expressed as mean ± standard deviation ($\bar{x} \pm s$). The comparisons of the level of PON1, SOD and MDA were made by using Student's T-test, and the criteria for significance difference was P < 0.05.

Results

Levels of PON1, SOD and MDA of elderly patients with coronary heart disease

PON1 and SOD activity of elderly CHD patients were significantly lower than elderly non-coronary heart disease group, there was a significant difference between the two groups (P < 0.01); and MDA level of elderly CHD patients was significantly higher than elderly non-coro-

Effect of Dan Hong injection on PON1, SOD and MDA

nary heart disease group, there was a significant difference between the two groups ($P < 0.01$) (Table 2).

Levels of PON1, SOD and MDA of two groups before and after treatment

There was a major change in PON1 activity, SOD and MDA after 4 weeks DHI treatment ($P < 0.05$). There was different degrees of change in PON activity, SOD and MDA after 4 weeks conventional treatment when compared with pre-application, but no significant difference was observed ($P > 0.05$); PON1 activity, SOD and MDA had significant different after 4 weeks treatment in DHI group compared with the conventional treatment group ($P < 0.05$) (Table 3).

Discussion

We know that the body produces oxygen free radicals through the enzyme system and non-enzymatic system. The amount of MDA who can damage biofilm often be reflected in the extent of lipid peroxidation. SOD can remove lipid peroxides, play a vital role for reducing lipid peroxidation by regulating the balance of body's oxidation and antioxidant, prevent the formation of atherosclerosis. PON, which synthesized by the liver and combined with the HDL arylesterase, is a calcium-dependent glycoprotein, studies have shown that PON1 could prevent oxidative modification of LDL and partially protect hydrolyzed lipid peroxides, and reduce the accumulation of oxidized lipid [11, 12].

Clinical study found that elderly patients with CHD decline in anti-oxidation, PON1 and SOD levels lowered and MDA increased [10, 13]. This study showed: PON1, SOD activity of elderly CHD patients was significantly lower than that of elderly non-CHD patients ($P < 0.01$), while MDA was significantly higher than elderly non-CHD patients ($P < 0.01$), consistent with previous findings. Therefore, it is a very important that antioxidant therapy to improve blood PON1, SOD activity, reduced MDA and other lipid peroxides in the treatment of coronary heart disease for old age.

As China's growing elderly population, the morbidity and mortality of CHD are rising. Need to find an effective method for the treatment of CHD. In recent years, results of combining Chinese and Western medicine treatment for elderly CHD are obvious, it has opened up new avenues for clinical treatment.

DHI involves injecting a popular Chinese herb preparation derived from the aqueous extracts of Danshen and Honghua at a raw material dose ratio of 3:1. Previous studies have demonstrated that Danshen extract, the main constituent of DHI, can dilate cerebral arteries, lower vascular resistance and blood viscosity, enhance erythrocyte deformability, clear oxygen free radicals, improve adenosine triphosphatase activity, and protect brain tissues against hypoxia [14-16]. Furthermore, Honghua extract has been found to possess multiple pharmacological activities, including vasodilation, antioxidation, oxygen-free-radical scavenging [17]. The components of DHI extracted from Danshen and Honghua included danshensu, salvianolic acids, hydroxy safflower yellow A, protocatechuic acid, protocatechuic aldehyde, flavonoids, and phenylethanoid glycosides, and thus DHI has also shown several therapeutic effects in animal experiments, such as antioxidation, anti-inflammatory, vasodilation, neuroprotection, anticoagulation, antithrombosis, and antifibrinolytic activities [18-22].

After 4 weeks treatment, the study found that serum PON1, SOD activity increased and MDA decreased significantly in DHI group. This result revealed that DHI can inhibit free radical production, improve PON1, SOD activity, removing MDA and other lipid peroxides for elderly coronary heart disease. Prompted an increase in serum PON1 and SOD activity, and reduced MDA levels may be one of the important mechanisms for DHI to treatment elderly CHD effectively.

Disclosure of conflict of interest

None.

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Effect of Dan Hong injection on PON1, SOD and MDA

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