Effect of Liandouqingmai Recipe on life quality and vascular endothelial injury in patients with coronary heart disease

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Abstract

OBJECTIVE: To observe the effects of Liandouqingmai Recipe on life quality and vascular endothelial injury in patients with coronary heart disease.

METHODS: Capitalized 101 patients with coronary heart disease were randomly divided into a treatment group (n=45) treated with Liandouqingmai Recipe and a standard treatment group (control group, n=56). A normal group of 16 healthy persons was additionally set up. Changes in ET-1 and NO levels were measured and Seattle Angina Questionnaire (SAQ) was adopted in studying life quality before and after treatment for two weeks. The data were analyzed with SPSS 16.0 statistic software.

RESULTS: The average level of ET-1 in the normal group was lower and NO higher than that of patients with coronary heart disease. There was no significant difference in the average level of ET-1 and NO and in the scores of SAQ (physical limitation (PL), angina stability (AS), angina frequency (AF), treatment satisfaction (TS) and disease perception (DP)) between the two groups before treatment (P>0.05). But after treatment, the scores of SAQ (PL, AS, AF, TS, DP) and NO level were higher than those in the control group, and ET-1 average level in the treatment group was lower than that in the control group. The negative relations between PL and ET-1 and between AF and ET-1 were found in this study.

CONCLUSION: Liandouqingmai Recipe can raise scores of SAQ and NO level and decline ET level in patients with coronary heart disease on the basis of conventional standard treatment, thus improving vascular endothelial function and life quality. Life quality is related to vascular endothelial function.

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Key words: Coronary disease; Life quality; Questionnaires; Endothelin-1; Nitric oxide; Liandouqingmai recipe

INTRODUCTION

Coronary heart disease (CHD) has become a life-threatening disease. Atherosclerosis (AS) is pathological basis of CHD and its basic pathogenesis is deficiency in origin and excess in superficiality, phlegm and blood stasis. The authors hold that AS is caused by pathogenic heat, phlegm and blood stasis jointly transferring into turbidity due to insufficiency of kidney, and "heat, turbidity and deficiency of kidney" is the most important pathogenesis. Therefore, "clearing
heat, removing turbidity and tonifying the kidney” is
the basic principle for treatment of AS. On these
grounds, Lian douqingmai Recipe the authors
developed has good clinical effects in prevention and
treatment of AS and CHD. A study has confirmed that
this recipe can decrease low density lipoprotein-chole-
terol level and atherosclerosis-inducing index in plasma
of atherosclerosis patients. It is verified that the recipe
can further decrease brachial-ankle pulse wave velocity
and increase ankle-brachial index in atherosclerosis pa-
tonists on the basis of standard treatment. So it has a
good effect of improving arterial rigidity degree and de-
creasing ultra-sensitive C-response protein (CRP), pe-
ripheral white blood cells (PBL), interleukin-6 (IL-6)
and IL-10 with a good anti-inflammatory action. At
the same time, it can decline endothelin-1(ET-1)level
and raise nitric oxide (NO) level in patients with CHD
on the basis of standard treatment so as to improve
vascular endothelial function.

This trial was designed to observe the effects of Lian-
douqingmai Recipe on life quality of CHD patients and
investigate the effects of the recipe on life quality
scores of Seattle angina questionnaire (SAQ), ET-1
and NO in patients with CHD and the correlations
between scores on one hand and ET-1 and on the
other hand. This study approved by the appropriate
ethics committees was performed in accordance with
the ethical standards laid down in the Declaration of
Helsinki.

METHODS

Diagnostic criteria of coronary heart disease
Diagnosis of coronary heart disease refers to the nam-
ing and diagnostic criteria of ischemic heart disease is-
issued by International Heart Association / Internation-
al College of Cardiology and the Named Standardiza-
tion Joint Task Team of WHO.

General data
One hundred and one CHD patients and 16 healthy
volunteers took part in this study. The 101 inpatients
in the heart department of internal medicine, Wuxi
Hospital affiliated to Nanjing University of Traditional
Chinese Medicine, from June 2007 to December 2009
were randomly divided into a Liandouqingmai Recipe
group (treatment group) and a standard treatment
group (control group) according to random number ta-
ble. Among 45 cases in the treatment group were 20
males and 25 females aged 51-87 years, 71±8 years on
average. Among 56 cases in the control group were 24
males and 32 females aged 54-86 years, 70±9 years on
average, with illness course from 2 h to 28 years, 9±11
years on average. Among 56 cases in the control group
were 24 males and 32 females aged 54-86 years, 70±9
years on average, with illness course from 1 h to 40
years, 9±13 years on average. There were no statistical
differences in age, sex and illness course between the 2
groups. 16 healthy volunteers in the normal control
group (normal group) were staff members and workers
at their posts or retirees in this hospital after their age
and sex had been matched. All the persons voluntarily
taking part in this research signed their fact-knowing
agreement prior to their inclusion in the study and
were approved by the hospital and the Moral and Ethi-
cal Committee.

Criteria of inclusion
Patients should meet the diagnostic criteria of coronary
heart disease and any one item of the following condi-
tions: remote myocardial infarction, hemodynamically
stable acute myocardial infarction or angina pectoris,
positive sports plate test with clinical symptom and
sign, at least one blood vessel or at least one part of a
vessel narrowing over 60% found with coronary arteri-
ography. Patients should voluntarily sign a fact-know-
ing agreement.

Criteria of exclusion
Excluded from the trial were patients with insufficien-
cy of the spleen-yang in Traditional Chinese Medicine,
hemodynamically unstable angina pectoris and acute
myocardial infarction, severe arrhythmia, other inflam-
matory diseases, severe heart diseases, severe dysfunc-
tion of liver and kidney, severe primary diseases of lung
and brain, psychosis, or refusing to sign a fact-know-
ing agreement.

Treatment methods
The patients in the treatment group and the control
group were treated with a standard treatment, including
nitrates type drugs [such as isosorbide mononitrate
tablets (Southern Betty Pharmaceutical Co., Ltd, Chi-
a)20 mg, twice each day, isosorbide dinitrate(Nanjing
Baijingyu Pharmaceutical Co., Ltd, China) 5-10 mg,
thrice daily, and nitroglycerin(Guangzhou Baiyun
Mountain Ming Xing Pharmaceutical Co., Ltd, China)
10-20 mg, twice each day, isosorbide dinitrate (Southern
Betty Pharmaceutical Co., Ltd, Sweden-Britain) 6.25-100
mg, twice each day, and bisoprolol tablets(Merck Co.,
Ltd, Germany) 2.5-5.0 mg, once each day] were used
each day, statins type drugs for regulating lipids [such
as atorvastatin calcium tablets(Pfizer, New York, The
United States)10-20 mg, once each day, and fluova-
natid sodium capsules (Beijing Novartis Pharma Com-
pany Limited, Switzerland) 40 mg, once each night],
angiotensin-converting enzyme inhibitor [Benazepril
tablets (Beijing Novartis Pharma Company Limited,
Switzerland) 10 mg, once each day, pedsupril tablets
(Le Laboratoires Servier Industrie, France) 4 mg, once
daily. For the patient with no contraindication, 
β-re-
ceptor blockers, etc. [Metoprolol tablets(AstraZeneca
Pharmaceutical Co., Ltd, Sweden-Britain) 6.25-100
mg, twice each day, and bisoprolol tablets(Merck Co.,
Ltd, Germany) 2.5-5.0 mg, once each day] were used
for a long time in a whole course. There were no statis-
tical differences between the two groups in drug kind,
dose and therapeutic course for the standard treatment. For the patients in the treatment group, Liandouqingmai Recipe composed of Lianqiao (Fructus Forsythiae) 15 g, Huanglian (Rhizoma Coptidis) 3 g, Yeliadou (Glycine soja Sieb) 15 g, Chishao (Radix Paeoniae) 10 g, Laifu (Semen Raphani) 10 g, and so on was added to the standard treatment. The recipe was prepared by Pharmaceutics Department in the hospital and the herbs were purchased from Tianjiang Pharmaceutical Factory. 250 mL of the decoction was orally taken twice a day for two weeks as one therapeutic course.

Collection and preservation of samples
Two of 4 mL venous blood taken from the patient on empty stomach in the morning within 24 h after hospitalization was slowly poured into a tube with 30 μL 10% EDTA. The mixture stood for 1 h at room temperature and centrifuged at 3000 r/min for 10 min. The supernatant was taken and poured into a tube, which was sealed and kept at -70°C for ET-1 determination. The other 2 mL venous blood poured into a dry tube stood for 1 h at room temperature and centrifuged for 10 min at 3000 r/min. A part of the supernatant put in a tube was sealed and kept at -70°C for NO determination.

Observation indexes and determination methods
ET-1 radioimmunoassay kit made by Beijing North Biotechnology Institute was used for automatic determination of ET-1 with GC911 radioimmunoanalysers (Hkust Innovation Co., Ltd, China). NO kit purchased from Nanjing Jiancheng Bioengineering Institute was used for determination of NO with 751G spectrophotometer (Shanghai Analysis Instrument plant, China). Scores of SAQ, including physical limitation (PL), angina stability (AS), angina frequency (AF), treatment satisfaction (TS) and disease perception (DP), were graded by the same deputy chief physician through paper SAQ scales. After treatment for two weeks, collection and preservation of the above-mentioned samples and scores grading were repeated. ET-1 and NO were determined together once every 6 months.

Statistical analysis
The data were analyzed with SPSS 16.0 software packet (SPSS Company, Chicago, The United States). The measurement data were expressed as mean±SD. Two-side student-t test of two independent samples was used for comparison of therapeutic effects between groups, and two-side student-t test of paired samples was used for comparison of therapeutic effects before and after treatment in groups. Correlation was analyzed with Pearson correlation. Significant level is P<0.05.

RESULTS

Effects of Liandouqingmai Recipe on scores of SAQ
Before treatment, there were no significant differences in the scores of PL, AS, AF, TS and DP between the treatment group and the control group (P>0.05, Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>ET-1 (pg/mL)</th>
<th>NO (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal group (n=16)</td>
<td>-</td>
<td>42±14</td>
</tr>
<tr>
<td>Control group (n=56)</td>
<td>Before</td>
<td>90±13</td>
</tr>
<tr>
<td>Treatment group (n=45)</td>
<td>After</td>
<td>64±10</td>
</tr>
</tbody>
</table>

Notes: ET-1: endothelin-1; NO: nitric oxide; *P<0.05 as compared with the datum before treatment; †P<0.05 as compared with the datum in the control group.

Correlativity between scores of SAQ and endothelial function
There was negative correlation between ET-1 and PL,
Quality of life is defined as an individual’s perceptions of life condition under different culture background and value system in relation to its goals, expectations, standards and concerns. 29% of the patients with primary stable angina experience angina once or more a week, which is associated with greater physical limitations and worse quality of life than those with minimal angina (less than once a week over the preceding 4 weeks). Therefore, the aim of treatment of CHD is not only to ease the clinical symptoms but also to improve the patients’ quality of life. This is to evaluate the effect of drugs. Drug treatment is one of the important indexes. At present, SAQ is widely used to clinically evaluate the life quality of CHD patients. This scale is divided into 5 categories and 11 entries: limited degree of body activities (question 1), stable state of angina pectoris (question 2), heart attacks (question 3–4), treatment satisfaction (question 5–8), disease understanding (question 9–11). The total score is 100 points. The higher the score, the better the life quality and the body function of patients. Research shows that the scale’s reliability, validity and reaction degree are good, it can be used to evaluate life quality of CHD patients.

Vascular endothelial damage is the key factor to coronary heart disease. Severe endothelial dysfunction in the absence of obstructive coronary artery disease is associated with increased cardiac events. It supports the concept that coronary endothelial dysfunction may play a role in the progression of coronary atherosclerosis. Endothelial dysfunction is a systemic disorder and a key variable in the pathogenesis of atherosclerosis and its complications. Current evidence suggests that endothelial status is not determined solely by the individual risk factor burden but may be regarded as an integrated index of all atherogenic and atheroprotective factors present in an individual. ET is the most important blood-vessel-shrinking material secreted by endothelial cells. When ET content increases, local blood vessels strongly contract, making calcium enter cells to cause excessive calcium in cells. Among three ET isomers, ET-1 has the strongest effect of shrinking blood vessels. In vitro studies show that ET-1 has 10 times stronger effect of shrinking blood vessels than angiotensin II. NO is unstable and small gas molecules with a variety of biological activities and extremely short half-life. It has been confirmed as an endothelial-derived diastolic factor. NO with a strong vascular diastolic effect can inhibit platelet to be gathered and activated and protect blood vessels through the collaborative prostaglandins. In addition, NO can restrain neutrophils and mononuclear cells from infiltration into and adhesion to blood vessel walls, inhibit vascular smooth muscle cells to proliferate and resist thrombosis. NO and ET, mutually antagonistic vascular active materials released by endothelial cells, play an important role in adjusting and maintaining endothelial function. A study demonstrates that high level of ET-1 in combination with specific PKC and eNOS can inhibit endothelial cells to release NO, thus causing spasm of coronary arteries and ischemia and hypoxia of cardiac muscles.

Our previous researches have confirmed that the ET-1 level of CHD patients is significantly higher and NO concentration is significantly lower than those in the normal group, and NO is negatively related to IL-10 (r = 0.152). In this study, ET-1 was negatively related to PL and AF (r = -0.144, -0.179, P < 0.05) and NO positively related to PL (r = 0.134, P = 0.056), indicating that damage to endothelial function is closely related to CHD patients’ life quality, especially PL and AF.

We have found that Liandouqingmai Recipe can decline ET-1 level and raise NO level in patients with coronary heart disease on the basis of standard treatment. This study suggests better endothelial function can improve the life quality of CHD patients. After treatment, ET-1 level significantly decreased (P < 0.05) and NO did not significantly change in the control group, ET-1 level decreased and NO increased significantly in the treatment group (both P < 0.05), indicating that damage to endothelial function is closely related to CHD patients’ life quality, especially PL and AF.

Notes: ET-1: endothelin-1; NO: nitric oxide; PL: physical limitation; AS: angina stability; AF: angina frequency; TS: treatment satisfaction; DP: disease perception; There was significant correlation at 0.05 level (bilateral).
REFERENCES


7 International Heart Association/International College of Cardiology and the Named Standardization Joint Task Team of WHO. The naming and diagnostic criteria of ischemic heart disease. Zhonghua Xin Xue Guan Bing Za Zhi 1981; 9(1): 75-76


10 Behrendt D, Ganz P. Endothelial function. From vascular biology to clinical applications. Am J Cardiol, 2002; 90 (10C): 40L-48L


