Original Article

Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events in patients with non-ST-segment elevation acute coronary syndrome

Hanyu Liu¹, Xiongfei Shi¹, Xingzong Zhang¹, Yun Lin¹, Mingli Zhou²

¹Department of Laboratory, The First Affiliated Hospital of Yunnan University of Traditional Chinese Medicine, Kunming 650000, Yunnan, China; ²The Second Ward of Cardiovascular Department, The Second Affiliated Hospital of Kunming Medical University, Kunming 650000, Yunnan, China

Received April 14, 2020; Accepted June 2, 2020; Epub September 15, 2020; Published September 30, 2020

Abstract: Objective: To investigate the effect of self-made blood stasis-expelling decoction (BSD) on liver function and cardiovascular events in patients with non-ST-segment elevation acute coronary syndromes (NSTE ACSs) as well as statin-induced elevation of aminotransferase levels (SEALs). Methods: 103 patients with NSTE ACS and SEALs were randomly divided into the control group (CG, n = 51) that underwent ezetimibe treatment, and the observation group (OG, n = 52) that received additionally self-made BSD for 3 months. The following indicators were compared, including the efficacy, total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBiL), phosphocreatine kinase (CK), creatine kinase isoenzyme (CPK-MB), and the incidence of cardiovascular events. Results: The clinical efficacy of the OG was remarkably higher than that of the CG (P<0.05). The two groups showed significantly reduced post-treatment TC, TG, and LDL-C levels; In comparison of the CG, the above indicators in the OG improved more significantly (P<0.05); After treatment, ALT, AST, TBiL, CK, and CK-MB in both groups were significantly decreased (P<0.05); The above indicators in the OG were significantly deceased in comparison with CG (P<0.05); The total incidence of cardiovascular events in OG was 9.62% (5/52) which was significantly lower than 33.33% (17/51) of CG (P<0.05). Conclusion: Self-made BSD can significantly improve myocardial damage, effectively regulate blood lipid levels, improve liver function and reduce cardiovascular events in patients with NSTE ACS and SEALs.

Keywords: NSTE ACSs, self-made BSD, statin-induced elevation of aminotransferase levels, liver function, cardiovascular events

Introduction

Non-ST segment elevation acute coronary syndromes (NSTE ACS) involve a clinical spectrum ranging from unstable angina (UA) to non-ST-segment elevation myocardial infarction (NSTEMI), with high morbidity and mortality [1, 2]. If early and effective clinical interventions are not implemented, it may induce major adverse cardiac events (MACE) and a poor prognosis. Coronary atherosclerosis is the main pathological basis of ACS, and hyperlipidemia is the crucial risk factor for ACS. Studies have shown that [3, 4] lipid-lowering treatment can accelerate plaque regression, lower the mortality of ACS, effectively prevent the progression of atherosclerotic lesions, and reduce the incidence of MACE. Therefore, lipid-lowering therapy has become an important component of ACS treatment. Statins are commonly used to treat non-ST-segment elevation ACS [5, 6].

Although it has overt lipid-lowering effect, side effects such as liver damage and elevated transaminase levels are also common. In severe cases, liver-protective treatment should be supplemented [7, 8]. The incidence of elevated transaminases levels by statins is about 0.5%-3%. Previous studies [9] suggested discontinuing statin medications, hepatoprotective treatment, and used ezetimibe as an alternative lipid-lowering therapy. However, the overall efficacy was not satisfactory. Cho et al [10] found that Tongxinluo capsules is a drug composed of traditional Chinese herbs and insects used for cardiovascular diseases, which can
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

effectively decease lipids and hs-CRP levels, and reduce cardio-cerebrovascular events and rehospitalization rates. Traditional Chinese medicine believes that the pathogenesis of this disease lies in deficiency of qi, blood stasis, phlegm turbidity and stagnation of qi, and the treatment should focus on protecting liver and benefiting qi, regulating qi and activating blood circulation, and removing turbidity and stasis. Based on this, our study explored the efficacy of self-made BSD on NSTE ACS patients with SEALs, and its effects on liver function and cardiovascular events.

Material and methods

Baseline data

We enrolled 103 NSTE ACS patients with SEALs from January 2017 to June 2019. The patients aged below 79 years. The diagnosis of ACS is based on the diagnostic criteria established by the American College of Cardiology and the American College of Cardiology. After treatment with statins, there is a 3-fold increase in transaminases and alanine aminotransferase.

All patients did not have any history of liver disease such as chronic hepatitis B, hepatitis A, and liver tumors. For the standpoint of Traditional Chinese medicine. All patients exhibited syndrome of phlegm and blood stasis: tightening, choking or heavy pressure feeling in the cheat, shortness of breath, heavy head and legs, greasy or slippery tongue coating, and slippery pulse. The patient has clear consciousness and signed the consent form. This study was conducted under the approval of the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University. Patients with liver damage caused by malignant tumors, with acute cerebrovascular diseases, and cognitive dysfunction were excluded. 103 patients with NSTE ACS and SEALs were randomly divided into the observation group (OG, n = 52, aged 42-78 years, BMI 18.55-37.06 kg/m²) and control group (CG, n = 51, 45-79 years, BMI 18.53-36.95 kg/m²).

Methods

Inclusive and exclusive criteria

Inclusive criteria: Patients who conformed to the above diagnostic standards; who aged between 18 and 80 years; and who were conscious and signed the written consent form. Exclusion criteria: Patients who were complicated with malignant tumor, acute cerebrovascular disease, cognitive dysfunction and other causes of liver damage; who were allergic to the drugs used in our study; who were pregnant or lactating; who were taking immunosuppressive drugs; and who had poor compliance and didn’t cooperate with the study.

Outcome measurement

Clinical efficacy

Remarkable effective: ECG showed ST segment elevation ≥0.1 mV and improvement in their angina ≥2; Effective: ECG showed ST segment elevation ranged from 0.05 to 0.1 mV, improvement in their angina = 1; ineffective: ST segment elevation was less than 0.05 mV and angina did not improve or worsen. Total efficiency = 100%-inefficiency.

Blood lipid levels

After fasting for 10 hours, 5 ml of venous blood was collected from patients before and after treatment, and the patients’ cholesterol (TC) and triglyceride (TG) were detected by oxidase method. The serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were measured by endpoint assay.
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

### Table 1. Baseline data (mean ± SD, n)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Gender</th>
<th>Age (year)</th>
<th>BMI (kg/m²)</th>
<th>Smoking</th>
<th>Dring</th>
<th>Stains</th>
<th>Hepatoprotective drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td>Atorvastatin</td>
<td>Rosuvastatin</td>
</tr>
<tr>
<td>Observation group</td>
<td>52</td>
<td>32</td>
<td>20</td>
<td>59.05±6.23</td>
<td>25</td>
<td>36</td>
<td>35</td>
<td>9</td>
</tr>
<tr>
<td>Control group</td>
<td>51</td>
<td>30</td>
<td>21</td>
<td>58.29±6.67</td>
<td>28</td>
<td>32</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td>χ²/t</td>
<td></td>
<td>0.079</td>
<td>0.598</td>
<td>0.387</td>
<td>0.480</td>
<td>0.483</td>
<td>0.952</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.778</td>
<td>0.551</td>
<td>0.699</td>
<td>0.488</td>
<td>0.487</td>
<td>0.813</td>
<td></td>
</tr>
</tbody>
</table>
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

Liver function

5 ml of venous blood was collected from patients before and after treatment, centrifuged at 3000 r/min for 10 min to separate the serum. Later, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured by rate method with HITACHI-7080 automatic biochemical analyzer (Hitachi, Japan); Total bilirubin (TBil) was determined by vanadate oxidation method.

Levels of myocardial injury indicators

Venous blood was drawn from the patients before and after treatment. DuPont RXL automatic biochemical analyzer and supporting reagents were used to determine phosphocreatine kinase (CK) and creatine kinase isoenzyme (CPK-MB) levels.

Cardiovascular events including myocardial infarction, angina, heart failure, malignant arrhythmia, and all-cause deaths were recorded.

Comparison of liver function indices in both groups

After treatment, the ALT, AST and TBil of both groups were significantly decreased (P<0.05); The efficacy of the OG was remarkably higher than that of the CG (P<0.05, Table 2).

Statistical analysis

SPSS19.0 statistical software was adopted for data processing. The measurement data conforming to the normal distribution were expressed by mean ± standard deviation (mean ± SD), and compared by t test. Count data were expressed by ratio and examined by χ² between groups. Rank sum test (Z test) was used for comparison of two groups of nonparametric (interval or not normally distributed) data, and P<0.05 was considered statistically significant.

Results

Baseline data comparison

No significant difference was found between the two groups in gender, age, body mass index, smoking, drinking, consumption of statins and hepatoprotective drugs (all P>0.05), which were comparable (Table 1).

Comparison of clinical efficacy in both groups

The efficacy of the OG was remarkably higher than that of the CG (P<0.05, Table 2).

Comparison of blood lipid levels in both groups

After treatment, the TC, TG, LDL-C of the both groups were remarkably reduced (P<0.05); In comparison with the CG, the above indicators in the OG improved more significantly after treatment (P<0.05); There was no significant change in HDL-C levels in both groups before and after treatment (P>0.05), suggesting that BSD can significantly improve the level of blood lipid in patients with NSTE ACSs and SEALs (Figure 1).

Comparison of liver function indices in both groups

After treatment, the ALT, AST and TBil of both groups were significantly decreased (P<0.05);
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

**Figure 2.** Comparison of liver function indexes between the two groups. Note: Compared with before treatment, *P*<0.05; compared with control group, #*P*<0.05.

**Figure 3.** Comparison of myocardial injury indexes between the two groups. Note: Compared with before treatment, *P*<0.05; compared with control group, #*P*<0.05.

these indicators were more remarkably reduced in the OG after treatment (P<0.05), suggesting that BSD can improve the liver function of patients (Figure 2).

**Comparison of myocardial injury indexes**

After treatment, CK and CK-MB in both groups were significantly reduced (P<0.05), which were more significantly decreased in the OG than in the CG (P<0.05), suggesting that BSD can improve the degree of myocardial damage in patients (Figure 3).

**Comparison of cardiovascular events**

The total incidence of cardiovascular events in the OG and CG were 9.62% (5/52) and 33.33% (17/51), respectively, and the OG was remarkably lower than the CG (P<0.05), suggesting that BAD can prevent the cardiovascular events (Table 3).

**Discussion**

Non-ST-segment elevation ACS is one common type of ACS, mainly caused by incomplete occlusion of coronary arteries by atherosclerotic plaques. Clinically, intensive statin therapy aimed to regulate blood lipids, reduce inflammatory factors, and stabilize atherosclerotic plaques to prevent complications. The non-ST-segment elevation ACS needs stricter lipid-lowering requirements, and the LDL-C needs to be controlled below 1.8 mmol/L, or 30%-50% lower than the baseline. Therefore, in clinical practice, large doses of statins are used for the lipid-lowering therapy. As the dose of statins increases, the toxic and side effects towards liver and muscle gradually emerge. The liver damage caused by statins is dose-dependent [11, 12].

Studies found that the incidence of liver damage caused by statins is about 1.2/1 million, which is one specific form of liver disease [13, 14]. Although the liver damage caused by statin treatment has no obvious features, transaminases levels of the patients are elevated, which mostly occur within 3 months after the drug administration. Abnormal expression of ALT, AST, TBIL were found and further damage to liver function such as liver fibrosis and liver failure will also occur [15]. Therefore, most patients are forced to stop lipid-lowering treatment, which greatly increases the risk of MACE and is not conducive to patient prognosis.

NSTE ACS is a symptom of chest paralysis and heartache in Traditional Chinese medicine (TCM). Its main pathogenesis includes qi deficiency, blood stasis, phlegm turbidity, and stagnation, of which blood stasis and phlegm turbidity are the main causes. Thus, NSTE ACS should be treated by removing blood stasis and
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

Table 3. Comparison of the incidence of cardiovascular events between the two groups [n (%)]

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Myocardial infarction</th>
<th>Angina pectoris</th>
<th>Heart failure</th>
<th>Malignant arrhythmia</th>
<th>All-cause death</th>
<th>Total incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>52</td>
<td>0 (0.00)</td>
<td>2 (3.85)</td>
<td>2 (3.85)</td>
<td>1 (1.92)</td>
<td>0</td>
<td>9.62(^{1})</td>
</tr>
<tr>
<td>Control group</td>
<td>51</td>
<td>1 (1.96)</td>
<td>6 (11.76)</td>
<td>5 (9.80)</td>
<td>5 (9.80)</td>
<td>0</td>
<td>33.33</td>
</tr>
</tbody>
</table>

\(\chi^2\) -

\(P\) -

\(8.623\)

\(0.003\)

\(^{1}\) Compared with control group, \(P<0.05\).

Turnd by [16]. It was believed in TCM that liver damage caused by statins was related to qi stagnation while the phlegm turbidity and blood stasis are further blocked in the liver, resulting in liver stagnation, meridian obstruction, and distortion of liver function. It will eventually lead to blockade of static blood, impaired meridians, and impaired liver function over time. Therefore, the treatment should be based on the principle of protecting liver and benefiting qi, activating blood circulation, and removing stasis as well as turbidity.

In view of the above pathogenesis, the OG was treated with a self-made BSD. BSD is a prescription in the treatment of acute coronary syndrome in our hospital. In the prescription, Astragalus invigorates spleen and replenishes qi; Codonopsis supplements the spleen and nourishes the lungs, qi, and the blood; Angelica sinensis stagnates the blood and dispenses blood stasis; Thorowax root relieves stagnation, nourishes Qi and protects the liver; Snakegourd fruit removes phlegm and dispels stasis; Szechuan Lovage Rhizome promotes blood circulation and relieves pain; Radix cyathulae promotes blood circulation; Both fructus aurantii and pinellia eliminate dampness and phlegm; Rehmannia glutinosa clears heat and cools blood, nourishes yin and regenerates blood; Safflower activates blood circulation, and relieves stasis and pain; Panax notoginseng powder disperses stasis. The whole prescription plays the function of protecting liver, benefiting qi and removing turbidity as well as blood stasis. Modern pharmacology found that astragalus has function of positive inotropic action and anti-heart failure, elimination of oxygen free radicals, regulation of blood pressure, expansion of coronary vessel, protection of toxic liver injury, etc. [17, 18]. Dangshen, dan-shen and angelica [19] play the role of regulating glucose and lipid metabolism. Thorowax root protects liver and gallbladder, lowers blood pressure, reduces fever and relieves the pain.

The active ingredients of Szechwan Lovage Rhizome can dilate blood vessels and enhance the contractility of myocardium [20]. Snakegourd fruit, adix cyathulae [21], and fructus aurantii [22] could scavenge oxygen free radicals, dilate blood vessels, inhibit platelet aggregation and prevent thrombosis. To sum up, the self-made BSD can increase blood flow of coronary artery, improve blood supply of myocardium, enhance contractility of myocardium, and reduce the occurrence of cardiovascular events by dilating blood vessels, while astragalus and Thorowax root can effectively improve the liver function of patients.

The results of present study revealed that the total effective rate of the OG after treatment was higher than that of the CG, and TC, TG, LDL-C, ALT, AST, TBiL, CK, and CK-MB of the both groups were significantly reduced after treatment. These indices in the OG were improved more positively than in the CG, and the total incidence of cardiovascular events in the OG was remarkably lower, suggesting that the self-made SBD can significantly improve degree of myocardial damage, reduces blood lipid levels, improves liver function, and reduces the occurrence of cardiovascular events.

In conclusion, self-made BSD can significantly improve myocardial damage, effectively regulate blood lipid levels, improve liver function and reduce cardiovascular events in patients with NSTE ACS and SEALS.

Disclosure of conflict of interest

None.

Address correspondence to: Mingli Zhou, The Second Ward of Cardiovascular Department, The Second Affiliated Hospital of Kunming Medical University, No. 374, Dianmian Avenue, Wuhua District, Kunming 650000, Yunnan, China. Tel: +86-13888163485; E-mail: minglizhou100@163.com
Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

References


Effect of self-made blood stasis-expelling decoction on liver function and cardiovascular events

with phlegm-heat interconnected viral myocarditis and its effects on immune function and oxygen free radicals. World Chinese Medicine 2019; 14: 154-158.

