Clinical Research

Effects of purified herbal extract of Salvia miltiorrhiza on lipid profile in hyperlipidemic patients

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Background and Objective Hyperlipidemia is one of the most potent and best substantiated risk factors for coronary heart disease (CHD). Purified Salvia miltiorrhiza extract (PSME) had been shown to have hypolipidemic effect in animal experiments. This study aimed to evaluate its lipids modulating effects in hyperlipidemic patients. Methods In this single-blind, placebo controlled study, lipid profiles of 80 hyperlipidemic patients were checked at same conditions. They were divided into two equal groups randomly (each composing of 40 patients). They were given PSME tablet (800 mg) three times per day, or placebo tablet. All patients were put on NCEP type II diet and six weeks later, lipid profiles were checked. Results In PSME group, total cholesterol decreased by 27.32 mg/dl (12.3% reduction), LDL-cholesterol decreased by 23.13 mg/dl (16.8% reduction) and HDL-cholesterol increased by 9.06 mg/dl (11.1%), all were statistically significant. Although triglyceride dropped by 12.12 mg/dl (5.1%) but this was not significant statistically (P=0.34). There were no significant changes of lipids levels in the placebo group. Conclusions PSME has significant favorable effect on total cholesterol, LDL-cholesterol, and HDL-cholesterol and may be a potential agent for the treatment of atherogenic dyslipidemia. (J Geriatr Cardiol 2009; 6:99-101)

Key words Hyperlipidemia; Salvia miltiorrhiza; randomized trial

Introduction

Hyperlipidemia is one of the most potent and best substantiated risk factors for atherosclerotic diseases, particularly coronary heart disease (CHD).1 In China, due to the rapidly changing of lifestyle, the prevalence of dislipidemia is increasing dramatically.2 Proper recognition and management of dislipidemia can reduce cardiovascular and total mortality rates.2 Danshen (Salvia miltiorrhiza) is a Chinese herbal medicine that has been used for hundreds of years in the treatment of numerous ailments including cardiovascular diseases.3 The lipids lowering effects of danshen had been reported in Chinese in dozens of animal experiments and clinical studies in the mainland of China. A total of 20 major ingredients in S miltiorrhiza have been identified.4 Purified S miltiorrhiza extract (PSME) is an extract consisting of 4 active water-soluble compounds from the 20 major ingredients. PSME had demonstrated its effectiveness on prevention of ischemic heart disease.5 A recent study by Ji and Gong6 showed that PSME significantly lowered the concentrations of plasma total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides, as well as concentrations of liver total cholesterol and triglycerides in rats fed on high-fat/high-cholesterol diet. In this randomized study, we evaluated the effects of PSME on lipid profile in hyperlipidemic patients with CHD.

Patients and methods

Patients and study protocol

A single-blind, randomized, placebo-controlled intervention study was conducted on patients with coronary artery disease with newly diagnosed hyperlipidemia. A total of 80 patients were selected from Department of Traditional Chinese Medicine, China Coal General Hospital. Exclusion criteria included: 1) having significant hepatic, renal and gastrointestinal tract disease; 2) acute myocardial infarction; 3) uncontrolled diabetes; and 4) underlying previous therapies for hyperlipidemia. Twenty two cases were excluded. All patients had total cholesterol level ≥ 200 mg/dl and/or LDL-cholesterol ≥ 100 mg/dl after 12 hours of fasting. Also, we checked HDL-cholesterol and triglyceride. Written informed consent was obtained from each patient before any study-specific procedure.

We randomly divided patients into two groups, each composing of 40 cases. PSME group received PSME tablet (800 mg, purchased from Shanghai Materia Medica Bioengineering Institute) three times per day. Placebo group was given placebo. Demographic information of different groups is shown in Table 1. After 6 weeks, we checked again the
total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglyceride after 12 hours of fasting.

Table 1  Demographic characteristics of the 2 groups

<table>
<thead>
<tr>
<th></th>
<th>PSME group (n=40)</th>
<th>Placebo group(n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>30</td>
</tr>
<tr>
<td>Male</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Age (year)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>55</td>
<td>56.5</td>
</tr>
<tr>
<td>Minimum</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Maximum</td>
<td>78</td>
<td>74</td>
</tr>
</tbody>
</table>

All patients were given National Cholesterol Enducation program(NCEP) type II, i.e. protein about 0.6 g/kg desirable body weight per day, 55 % of total calories from carbohydrate, no more than 30 % of total energy intake be derived from dietary fat, polyunsaturated fats to <10 %, saturated fat and trans-fat should be limited to <10 % of calories, throughout the study.

Measurement of serum lipids

After the bloods were put at room temperature for 1 h, serum was separated by centrifugation at 1,500 x g for 15 min. The levels of serum total cholesterol (total cholesterol), HDL-cholesterol, and triglycerides were measured by enzymatic methods (Roche, USA) with an automatic analyzer (7170, Hitachi, Japan). Serum LDL-cholesterol was calculated by the method of Friedewald et al.7

Statistical analysis

Data were analyzed by paired sample t test and non parameter 2 related sample test using SPSS 13.0 program for windows (SPSS Inc. Chicago, Ill,USA). A difference was considered statistically significant when the probability value (P-value) was < 0.05.

Results

All of the patients cooperated well during the study period and did not show any adverse effect of these herbal drugs.

Changes in lipid profiles after 6 weeks and results of paired t test are shown in Table 2. It was found that changes in triglyceride, total cholesterol, LDL-cholesterol, and HDL-cholesterol were significantly different between the 2 groups. Although levels of serum triglyceride, total cholesterol, and LDL-cholesterol showed tendency of increase and HDL-cholesterol a tendency of decrease, these changes, however, are not statistically significant (all P > 0.05).

At the end of the six-week intervention period, it was found that the mean total cholesterol concentration dropped in the PSME group by 27.32 mg/dl (P<0.01). Similarly, LDL-cholesterol was reduced in this group by 23.13 mg/dl and HDL-cholesterol was increased by 9.06 mg/dl (both P<0.01). Although triglyceride decreased by 12.12 mg/dl, this was not statistically significant (P=0.34).

Discussion

Our study suggests that PSME reduces total cholesterol and LDL-cholesterol. These results are of particular clinical relevance considering that Danshen is widely used in China as an herbal medicine for the treatment of cardiovascular disease. Elevated plasma cholesterol levels, especially the LDL- cholesterol, predispose to coronary atherosclerosis. Oxidation of LDL is related to oxygen free radicals; oxidized LDL is involved in the development of atherosclerosis. Both salvianolic acid A and magnesium tanshinoate B, two active compounds in Danshen, inhibit LDL oxidation, resulting in a decrease in the uptake of LDL by the macrophages. Such an effect is therapeutically relevant in protecting cells from lipid peroxidation in vascular disorders. Yang et al.10 in a study of 96 elderly patients with hyperlipidemia reported that, in addition to reduction of plasma total cholesterol and LDL, danshen also causes a reduction in the ratio of thrombaxone B2 to 6-keto-prostaglandin F alpha, D-dimer and fibrinogen, and thus improves the blood coagulation system as well as the various endothelial functions. In another study by Li and Wan,11 with experimental rabbit models produced by feeding high cholesterol diet, showed that the level of serum triglycerides in danshen treated rabbits was significantly lower than in the control group.

During the past decades, the hypolipidemic activities of many Chinese herbal medicines have been proved in well-designed animal experiments. Mixtures of interacting compounds produced by plants may provide important combination therapies that simultaneously affect multiple pharmacological targets and provide clinical efficacy beyond the reach of single compound-based drugs.12

A recent study showed that one of the mechanisms by which PSME regulating lipids metabolism might be activating farnesoid X receptor/liver X receptor α. In addition, PSME had the potential to increase biliary bile salt and phospholipid concentrations and restore normal biliary lipid physiology, thereby increasing the export of total cholesterol and bile acid in the liver.6

In conclusion we found that PSME tablet can reduce total cholesterol, LDL-cholesterol and increase HDL-cholesterol, with no effect on triglyceride. However, this is only a preliminary study with relatively small sample and short term follow-up, therefore the findings of our study should be confirmed by larger clinical trials.
Table 2  Changes in lipid profile after 6 weeks (mg/dl)

<table>
<thead>
<tr>
<th></th>
<th>PSME group</th>
<th>Placebo group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute change, mg/dl (%)</td>
<td>t value</td>
</tr>
<tr>
<td>TG</td>
<td>-12.12 (5.1)</td>
<td>1.242</td>
</tr>
<tr>
<td>TC</td>
<td>-27.32 (12.3)</td>
<td>5.665</td>
</tr>
<tr>
<td>LDL</td>
<td>-23.13 (16.8)</td>
<td>4.816</td>
</tr>
<tr>
<td>HDL</td>
<td>+ 9.06 (11.1)</td>
<td>-5.43</td>
</tr>
</tbody>
</table>

TG: triglyceride; TC: total cholesterol; LDL: low density lipoprotein cholesterol

References