Effect of lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill on the endothelial function and serum biochemical indexes in patients with hypertension and carotid atherosclerosis

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ARTICLE INFO

Article history:
Received 7 Jul 2016
Received in revised form 17 Jul 2016
Accepted 12 Jul 2016
Available online 24 Jul 2016

Keywords:
Carotid atherosclerosis
Compound danshen dropping pill
Endothelial function
Adipocytokine

ABSTRACT

Objective: To study the effect of lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill on the endothelial function and serum biochemical indexes in patients with hypertension and carotid atherosclerosis. Methods: 98 patients with hypertension and carotid atherosclerosis treated in our hospital between June 2014 and July 2016 were selected as the research subjects and randomly divided into the research group who received lipid-lowering anticoagulant therapy combined with compound Danshen and the control group who received conventional lipid-lowering anticoagulant therapy. After 4 weeks of treatment, endothelial injury indexes and lipid metabolism indexes in serum were determined. Results: After 4 weeks of treatment, serum endothelin-1 (ET-1), thromboxane B2 (TXB2), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), oxidized low density lipoprotein (ox-LDL), lipoprotein (a) [Lp(a)], leptin, resistin and chemerin levels of research group were significantly lower than those of control group (P<0.05) while nitric oxide (NO), 6-Keto-PGF1α, high-density lipoprotein cholesterol (HDL-C), adiponectin and visfatin levels were significantly higher than those of control group (P<0.05). Conclusion: Lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill can improve the endothelial function and lipid metabolism in patients with hypertension and carotid atherosclerosis.

1. Introduction

The incidence of cardiovascular and cerebrovascular diseases is rising year by year, which causes adverse effect on patients’ quality of life and life safety. Carotid atherosclerosis and hypertension are the independent risk factors for cardiovascular and cerebrovascular diseases, routine lipid-lowering anticoagulant drugs can stabilize the properties of atherosclerotic plaques, restrain the activation of blood coagulation process and reduce the risk of cardiovascular and cerebrovascular diseases[1,2]. However, patients with hypertension and carotid atherosclerosis still have a high risk of cardiovascular and cerebrovascular diseases, and after conventional lipid-lowering anticoagulant therapy, there are still some patients who will develop cardiovascular and cerebrovascular diseases[3]. Compound Danshen dropping pill is the common TCM preparation for the treatment of cardiovascular and cerebrovascular diseases, its active ingredients include tanshinol, notoginseng and borneol, it is with the pharmacological effects such as improving circulation, protecting endothelium, inhibiting platelet adhesion and aggregation and scavenging oxygen free radicals, and it is used for the treatment of coronary heart disease angina pectoris and has exact curative effect[4,5]. At present, there is no report about the value of compound Danshen dropping pill for treatment of hypertension combined with carotid atherosclerosis. In the following study, the effect of lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill on the endothelial function and serum biochemical indexes in patients with hypertension and carotid atherosclerosis was analyzed.
2. Materials and methods

2.1. Research subjects

98 patients with hypertension and carotid atherosclerosis treated in our hospital between June 2014 and July 2016 were selected as the research subjects, all patients were with clear history of essential hypertension as well as the carotid atherosclerosis confirmed by the carotid artery ultrasonography, and the patients with secondary hypertension and those with previous history of myocardial infarction and cerebral infarction were excluded. After the patients signed informed consent, random number table was used to divide the included patients into two groups, 49 cases in each group. Research group received compound Danshen dropping pill combined with lipid-lowering anticoagulant therapy, including 29 male cases and 20 female cases that were 39–57 years old; control group received routine lipid-lowering anticoagulant therapy, including 31 male cases and 18 female cases that were 37–58 years old. The two groups of patients were not significantly different in general data ($P>0.05$).

2.2. Treatment methods

Both groups of patients received conventional oral antihypertensive drug therapy, and the target blood pressure value was $\leq 130/80$ mmHg. On the basis of oral antihypertensive drug therapy, control group of patients received conventional lipid-lowering anticoagulant drugs, which was as follows: oral atorvastatin 20 mg 1/d, and oral aspirin enteric-coated tablets 100 mg 1/d; on the basis of oral antihypertensive drug therapy, research group received compound Danshen dropping pill combined with conventional lipid-lowering anticoagulant drugs, which was as follows: oral compound Danshen dropping pill 10 pills 3/d, oral atorvastatin 20 mg 1/d and oral aspirin enteric-coated tablets 100 mg 1/d.

2.3. Serum sample collection and index detection methods

After 4 weeks of treatment, 5 mL of fasting peripheral venous blood was collected from two groups of patients and centrifuged to separate serum specimens, enzyme-linked immunosorbent assay kits were used to determine endothelin-1 (ET-1), nitric oxide (NO), 6-Keto-PGF$\alpha$, thromboxane B2 (TXB2), oxidized low density lipoprotein (ox-LDL), adiponectin, visfatin, leptin, resistin and chemerin levels, and TOSHIBA TBA-120FR automatic biochemical analyzer was used to detect the levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and lipoprotein (a) [Lp(a)].

2.4. Statistical analysis

SPSS20.0 software was used to input data and statistically analyze the differences in data between groups, measurement analysis between two groups was by two independent-samples $t$ test and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1. Serum endothelial function indexes of two groups of patients

After 4 weeks of treatment, analysis of serum endothelial function indexes ET-1, NO, 6-Keto-PGF$\alpha$, and TXB2 between two groups of patients was shown in Table 1: serum ET-1 and TXB2 levels of research group were significantly lower than those of control group while NO and 6-Keto-PGF$\alpha$ levels were significantly higher than those of control group. Differences in serum ET-1, NO, 6-Keto-PGF$\alpha$, and TXB2 levels were statistically significant between two groups of patients after 4 weeks of treatment ($P<0.05$).

3.2. Serum lipid metabolism indexes of two groups of patients

After 4 weeks of treatment, analysis of serum blood lipid indexes TC, LDL-C, ox-LDL, HDL-C and Lp(a) between two groups of patients was shown in Table 2: serum TC, LDL-C, ox-LDL and Lp(a) levels of research group were significantly lower than those of control group while HDL-C level was significantly higher than that of control group. Analysis of serum adipocytokines adiponectin, visfatin, leptin, resistin and chemerin between two groups of patients was shown in Table 3: serum adiponectin and visfatin levels of research group were significantly higher than those of control group while leptin, resistin and chemerin levels were significantly lower than those of control group. Differences in serum TC, LDL-C, ox-

Table 1
Comparison of serum endothelial function indexes between two groups of patients ($n=49, \bar{x} \pm s$).

<table>
<thead>
<tr>
<th>Groups</th>
<th>ET-1 (μg/mL)</th>
<th>NO (μmol/L)</th>
<th>6-Keto-PGF$\alpha$ (pg/mL)</th>
<th>TXB2 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>114.22±15.64</td>
<td>136.54±18.72</td>
<td>89.35±10.23</td>
<td>56.23±8.25</td>
</tr>
<tr>
<td>Control group</td>
<td>178.65±22.35</td>
<td>83.47±10.36</td>
<td>58.65±7.61</td>
<td>77.89±9.31</td>
</tr>
<tr>
<td>$t$</td>
<td>7.584</td>
<td>8.208</td>
<td>8.981</td>
<td>7.216</td>
</tr>
<tr>
<td>$P$</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
LDL, HDL-C, Lp(a), adiponectin, visfatin, leptin, resistin and chemerin levels were statistically significant between two groups of patients after 4 weeks of treatment (P<0.05).

4. Discussion

Hypertension and carotid atherosclerosis are the independent factors to assess the risk of cardiovascular and cerebrovascular diseases, and hypertension combined with carotid atherosclerosis can greatly increase the risk of myocardial infarction, cerebral infarction and other cardiovascular and cerebrovascular events. In clinical practice, using antihypertensive drugs to reasonably control the blood pressure and using anticoagulant lipid-lowering drugs to stabilize plaques can reduce the occurrence risk of cardiovascular and cerebrovascular events in patients with hypertension and carotid atherosclerosis to a certain extent, but there are still some patients who are with significant endothelial dysfunction, abnormal platelet activation, lipid metabolism disorder and so on, and still have a higher risk of cardiovascular and cerebrovascular diseases[6,7]. In recent years, the compound Danshen dropping pill is the traditional Chinese medicine preparation that has been used in the adjacent treatment of cardiovascular and cerebrovascular diseases in recent years, and its active ingredients including tanshinol, notoginseng and borneol. Modern pharmacological studies have proved that compound Danshen dropping pill has the effect of inhibiting platelet activation, reducing endothelial function injury, scavenging oxygen free radicals and regulating lipid metabolism, and can improve the microcirculation perfusion and endothelial function in the development and change of cardiovascular and cerebrovascular diseases[8,9]. Study has shown that compound Danshen dropping pill treatment of coronary heart disease angina pectoris can achieve positive effect[10], but it is not yet clear about the value of the drug for treatment of hypertension combined with carotid atherosclerosis.

Table 2
Comparison of serum blood lipid compositions between two groups of patients (n=49, \( \bar{x} \pm s \)).

<table>
<thead>
<tr>
<th>Groups</th>
<th>TC (mmol/L)</th>
<th>LDL-C (mmol/L)</th>
<th>ox-LDL (μg/L)</th>
<th>HDL-C (mmol/L)</th>
<th>Lp(a) (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research group</td>
<td>3.55±0.52</td>
<td>2.21±0.36</td>
<td>10.58±1.65</td>
<td>1.39±0.17</td>
<td>0.16±0.02</td>
</tr>
<tr>
<td>Control group</td>
<td>4.87±0.49</td>
<td>2.89±0.38</td>
<td>17.44±2.26</td>
<td>1.14±0.13</td>
<td>0.28±0.05</td>
</tr>
<tr>
<td>t</td>
<td>6.918</td>
<td>7.283</td>
<td>8.485</td>
<td>6.383</td>
<td>9.381</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 3
Comparison of serum adipocytokine levels between two groups of patients (n=49, \( \bar{x} \pm s \)).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Protective adipocytokines</th>
<th>Damaging adipocytokines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adiponectin (μg/mL)</td>
<td>Visfatin (μg/mL)</td>
</tr>
<tr>
<td>Research group</td>
<td>16.76±2.03</td>
<td>38.21±4.65</td>
</tr>
<tr>
<td>Control group</td>
<td>11.35±1.33</td>
<td>22.36±3.26</td>
</tr>
<tr>
<td>t</td>
<td>7.928</td>
<td>7.182</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Endothelial function damage is an important pathological feature of patients with cardiovascular and cerebrovascular diseases. Under physiological conditions, vascular endothelial cells locate between the vascular subcutaneous tissue and blood, and can regulate vasomotion state, prevent platelet aggregation and adhesion in local area and inhibit micro-thrombosis. Endothelial cell structure and function injury can cause the subendothelial collagen exposure, platelet aggregation and activation as well as micro-thrombosis, and then result in ischemic hypoxic diseases. Endothelial cells can synthesize NO, ET-1, TXA2, PGI2 and a variety of other endogenous factors, and endothelial function damage will cause the changes in the contents of above endogenous factors. TXA2 and ET-1 are the endogenous factors with significant vasoconstrictor and pro-platelet aggregation effect, and can cause endothelial function damage; NO and PGI2 are the endogenous factors with significant vasodilatory effect, and can protect the endothelial function. In the development and change of atherosclerosis as well as cardiovascular and cerebrovascular diseases, TXA2 and ET-1 generation significantly increase while NO and PGI2 generation is significantly suppressed[11,12]. 6-Keto-PGF1α and TXB2 are the PGI2 and TXA2 metabolites in the body respectively, they are with relatively stable nature and content, and they can reflect PGI2 and TXA2 generation. In the study, analysis of serum endothelial function indexes between two groups of patients showed that serum ET-1 and TXB2 levels of research group were significantly lower than those of control group (P<0.05) while NO and 6-Keto-PGF1α levels were significantly higher than those of control group (P<0.05). This means that lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill can effectively improve the endothelial function in patients with hypertension and carotid atherosclerosis.

In the process of atherosclerosis, the main lipid composition within plaques is cholesterol, and cholesterol metabolism disorder in the body is closely related to the formation of arterial plaques. The cholesterol within carotid plaques is mainly from LDL-C, the LDL-C infiltrating in the arterial intima will be oxidized and
modified into ox-LDL, which is absorbed by macrophages to become foam cells, accumulates constantly and forms atheromatous plaque; HDL-C is the lipid composition that promotes cholesterol metabolism, and it can inhibit the formation of atheromatous plaque and is the protective factor of atherosclerosis, Lp(a) has the lipid compositions similar to those of LDL, is connected to apolipoprotein B and can promote the formation of atheromatous plaque[13,14]. In the study, analysis of the contents of above lipid compositions showed that serum TC, LDL-C, ox-LDL and Lp(a) levels of research group were significantly lower than those of control group ($P<0.05$) while HDL-C level was significantly higher than that of control group ($P<0.05$). The lipid metabolism disorder will not only cause the changes of lipid compositions, but can also cause the changes in contents of various adipocytokines[15,16]. Adiponectin and visfatin are the protective adipocytokines that can promote lipid metabolism and improve endothelial function, and leptin, resistin and chemerin are the damaging adipocytokines that can worsen insulin resistance, damage endothelial function and promote atheromatous plaque formation[17,18]. In the study, analysis of the contents of above adipocytokines showed that serum adiponectin and visfatin levels of research group were significantly higher than those of control group while leptin, resistin and chemerin levels were significantly lower than those of control group. It means that lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill can effectively regulate the blood lipid metabolism and improve the endothelial function and adipocytokine disorder in patients with hypertension and carotid atherosclerosis.

To sum up, it can be concluded in the study that lipid-lowering anticoagulant therapy combined with compound Danshen dropping pill treatment of patients with hypertension and carotid atherosclerosis can improve the endothelial function and regulate blood lipid metabolism and adipocytokine secretion.

References


