Effect of adjuvant ginkgo–damole therapy on the plaque stability, apoptosis and coagulation indicators in patients with unstable angina

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ABSTRACT

Objective: To study the effect of adjuvant ginkgo-damole therapy on the plaque stability, apoptosis and coagulation indicators in patients with unstable angina. Methods: A total of 80 patients with unstable angina who received inpatient treatment in our hospital between July 2014 and July 2016 were collected and divided into control group (conventional therapy) and observation group (conventional therapy + ginkgo-damole) according to the random number table, 40 cases in each group. The plaque stability, apoptosis and coagulation indicator contents were compared between two groups of patients before and after treatment. Results: Before treatment, differences in serum levels of plaque stability, apoptosis and coagulation indicators were not statistically significant between two groups of patients; after treatment, serum plaque stability indicators PTX3, Lp-PLA2, sCD40 and sCD40L contents in observation group were lower than those in control group; pro-apoptosis indexes sFas and Bax contents were lower than those in control group, and anti-apoptosis index Bcl-2 content was higher than that in control group; coagulation indicators Fg and D-D contents were lower than those in control group while t-PA content was higher than that in control group. Conclusion: Adjuvant ginkgo-damole therapy helps to improve the plaque stability, inhibit myocardial apoptosis and also reduce the hypercoagulable state in patients with unstable angina.

1. Introduction

Unstable angina is the clinical symptom between the stable angina and acute myocardial infarction as well as sudden death, and without timely and reasonable treatment, it can progress into acute myocardial infarction in a short period of time, and cause serious consequences[1–3]. β agonist, angiotensin-converting enzyme inhibitors and calcium channel blockers are currently the routine drugs for unstable angina treatment, but many scholars suggest adding Chinese patent drug therapy in order to expand the overall curative effect from different mechanisms. Ginkgo-damole is the compound preparation containing gingkoflavone and dipyridamole, it is mostly used to prevent the occurrence of coronary heart disease and thromboembolic disease, it has the functions such as improving blood viscosity and myocardial blood supply, and there is not much research at present about the curative effect of the drug for treatment of unstable angina. In the study, on the basis of conventional treatment, ginkgo–damole was introduced as adjuvant drug to treat unstable angina, and its curative effect was elaborated from plaque stability, apoptosis, and coagulation indicators.

2. Information and methods

2.1 Case information

A total of 80 patients with unstable angina who received inpatient treatment in Nanchong Hospital of Traditional Chinese Medicine in Sichuan Province between July 2014 and July 2016 were selected as research subjects, and patients’ families signed informed consent. According to the random number table, the patients were divided into control group and observation group, 40 cases in each group. Control group included 22 men and 18 women that were 45-78 years old; observation group included 23 men and 17 women that...
were 46-79 years old. The differences in gender and age distribution were not significant between the two groups (P<0.05), and the study was approved by the ethics committee of Nanchong Hospital of Traditional Chinese Medicine in Sichuan Province.

The inclusion criteria were as follows: (1) in accordance with the diagnostic criteria for unstable angina; (2) cooperating with the whole treatment and examination, and with complete data that could be compared. Exclusion criteria: (1) with history of ginkgo-damole allergy; (3) combined with severe liver and kidney insufficiency; (4) associated with systemic infectious diseases; (5) associated with malignant tumor disease.

2.2 Therapy

Control group of patients received β agonist, angiotensin-converting enzyme inhibitors, calcium channel blockers and other general treatment for unstable angina. Observation group of patients, based on above conventional treatment, received adjuvant ginkgo-damole therapy, specifically as follows: ginkgo-damole injection (Tonghua Guhong Pharmaceutical Co., Ltd., approved by H22026140) 10-25 mL in 500 mL of 5% glucose liquid, by intravenous drip, 1 time/d, for continuous treatment of 1 month.

2.3 Observation indexes

Before and after treatment, 5.0 mL of fasting cubital venous blood was obtained from two groups of patients, anti-coagulated and then centrifuged at low speed to get upper serum, and enzyme-linked immunosorbent assay (ELISA) was used to detect serum levels of plaque stability indexes pentraxin 3 (PTX3), lipoprotein-associated phospholipase A2 (Lp-PLA2), soluble CD40 (sCD40) and soluble CD40 ligand (sCD40L). Serum levels of myocardial apoptosis indexes sFas, Bcl-2 and Bax were detected by radioimmunoassay. Coagulometer (Italy Minivolt S.N.C. Company, specifications BICO) was used to detect serum levels of coagulation function indexes fibrinogen (Fg), D dimer (D-D) and tissue-type plasminogen activator (t-PA).

2.4 Statistical processing

Statistical software was SPSS 20.0, and the statisticians received professional training and passed the examination. Plaque stability indicators, myocardial apoptosis indicators, coagulation indicators and so on belong to measurement data and were in terms of (Mean ± SD), and the comparison was by t test. Statistics P<0.05 was set the boundary of statistical significance in differences between groups in the study.

3. Results

3.1 Plaque stability indicators

Comparison of serum plaque stability indicators PTX3 (ng/mL), Lp-PLA2 (μg/L), sCD40 (pg/mL) and sCD40L (pg/mL) contents between two groups of patients was as follows: before treatment, differences in serum PTX3, Lp-PLA2, sCD40 and sCD40L contents were not significant between two groups of patients (P>0.05); after treatment, serum PTX3, Lp-PLA2, sCD40 and sCD40L contents in both groups were lower than those before treatment, and serum PTX3, Lp-PLA2, sCD40 and sCD40L contents in observation group were lower than those in control group (P<0.05), shown in Table 1.

3.2 Myocardial apoptosis indicators

Comparison of serum myocardial apoptosis indicators sFas (μg/L), Bcl-2 (pg/mL) and Bax (pg/mL) contents between two groups of patients was as follows: before treatment, differences in serum sFas, Bcl-2 and Bax contents were not significant between two groups of patients (P>0.05); after treatment, serum pro-apoptosis indexes sFas and Bax contents in both groups were lower than those before treatment while anti-apoptosis index Bcl-2 contents were higher than those before treatment, and serum pro-apoptosis indexes sFas and Bax contents in observation group were lower than those in control group while anti-apoptosis index Bcl-2 content was higher than that in control group (P<0.05), shown in Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>PTX3</th>
<th>Lp-PLA2</th>
<th>sCD40</th>
<th>sCD40L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>2.94±0.31</td>
<td>59.83±7.15</td>
<td>45.28±5.19</td>
<td>28.45±3.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.61±0.28'</td>
<td>34.61±4.52'</td>
<td>31.66±4.06'</td>
<td>19.61±2.43'</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>2.93±0.34</td>
<td>59.27±7.09</td>
<td>45.61±5.07</td>
<td>27.94±3.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.12±0.26''</td>
<td>18.45±2.11''</td>
<td>17.45±2.05''</td>
<td>11.58±1.94''</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after treatment, †P<0.05.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>sFas</th>
<th>Bcl-2</th>
<th>Bax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>2.93±0.34</td>
<td>0.73±0.09</td>
<td>6.38±0.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.17±0.25'</td>
<td>1.25±0.16'</td>
<td>4.11±0.45'</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>2.92±0.33</td>
<td>0.76±0.08</td>
<td>6.34±0.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>1.36±0.17''</td>
<td>1.87±0.21''</td>
<td>3.09±0.41''</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after treatment, †P<0.05.
Table 3.
Comparison of serum coagulation indicator contents between two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>Fg</th>
<th>D-D</th>
<th>t-PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>4.38±0.51</td>
<td>0.67±0.08</td>
<td>0.23±0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>3.61±0.39*</td>
<td>0.55±0.06*</td>
<td>0.34±0.04*</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>4.35±0.49</td>
<td>0.65±0.07</td>
<td>0.22±0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.75±0.33*</td>
<td>0.41±0.05*</td>
<td>0.45±0.07*</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after treatment, #P<0.05.

3.3 Coagulation indicators

Comparison of serum coagulation indicators Fg (g/L), D-D (g/L) and t-PA (IU/mL) contents between two groups of patients was as follows: before treatment, differences in serum Fg, D-D and t-PA contents were not significant between two groups of patients (P>0.05); after treatment, serum Fg and D-D contents in both groups were lower than those before treatment while t-PA contents were higher than those before treatment, and serum Fg and D-D contents in observation group were lower than those in control group while t-PA content was higher than that in control group (P<0.05), shown in Table 3.

4. Discussion

Unstable angina is the main cause of acute myocardial infarction and sudden death, and the early active intervention is needed to optimize the treatment outcome[4]. Ginkgo-damole is the compound preparation well concerned at present, its main compositions contain gingkoflavone and dipyridamole, gingkoflavone can resist oxidation, protect vascular endothelium and expand coronary blood vessels, and dipyridamole can inhibit platelet release, reduce the blood viscosity, improve the myocardial blood supply, and others[5,6]. At present, many scholars have believed that ginkgo-damole can expand the curative effect of β agonists, angiotensin-converting enzyme inhibitors, calcium channel blockers and other conventional western medicines, and help to further optimize the patients’ condition. In order to define the efficacy of adjuvant ginkgo-damole treatment, it was added to the overall treatment of patients with unstable angina in this study, and the application value was specifically explored from plaque stability, apoptosis and coagulation indexes.

Artery atheromatous plaque instability is the direct cause of the unstable angina, the plaque rupture can directly lead to the occurrence of acute myocardial infarction or sudden death, and therefore, to judge the plaque stability can intuitively reflect the disease severity in patients with unstable angina[7,8]. PTX3 is an acute phase protein that is involved in the body’s inflammatory response, and its serum content can accurately reflect the stability of the coronary atherosclerosis plaque[9]. Lp-PLA2 is secreted by macrophages and foamed cells, and its expression increases in patients with ischemic stroke and unstable carotid atheromatous plaques, indicating that the index is closely associated with ischemic disease[10]. SCD40 and sCD40L are the important molecular regulating inflammation and platelet activation, their serum levels in patients with acute myocardial infarction are significantly higher than those in normal people, and it is speculated that they accelerate the plaque formation and increase the plaque instability to prompt the occurrence of cardiovascular and cerebrovascular events[11]. In the study, serum contents of above plaque stability indicators were compared between the two groups, and it was found that compared with those before treatment, serum PTX3, Lp-PLA2, sCD40 and sCD40L contents in both groups were lower after treatment; further compared with those in control group, serum PTX3, Lp-PLA2, sCD40 and sCD40L contents in observation group were lower after treatment, confirming that adjuvant ginkgo-damole therapy can further increase the atheromatous plaque stability, and it is the intuitive evidence of it to stabilize patients’ condition.

There is myocardial ischemic hypoxic injury in patients with unstable angina, and severe cases can lead to myocardial apoptosis and leave behind irreversible cardiac dysfunction[12]. The imbalance of pro-apoptosis index/anti-apoptosis index expression is the root cause of myocardial apoptosis, and the measure of their specific expression can quantitatively reflect the extent of myocardial apoptosis. sFas and Bax are pro-apoptosis indicators, which are highly expressed in patients with acute myocardial infarction or sudden cardiac death[13,14]. Bcl-2 is a typical anti-apoptosis index, it is excessively expressed in a variety of malignant tumors, its expression reduces in patients with myocardial infarction, and it is also one of the important causes of cardiac insufficiency after myocardial infarction[15]. In the study, serum contents of above apoptosis indicators were compared between the two groups, and it was found that compared with those before treatment, serum pro-apoptosis indexes sFas and Bax contents in both groups were lower while anti-apoptosis index Bcl-2 contents were higher after treatment; further compared with the control group, the observation group of patients were with lower serum contents of pro-apoptosis indexes sFas and Bax, and higher content of anti-apoptosis index Bax after treatment, confirming that adjuvant ginkgo-damole therapy can effectively reduce myocardial apoptosis and protect heart function.
Increased blood viscosity and hypercoagulability are the important causes of unstable angina occurrence and progression into acute myocardial infarction, and the patients’ coagulation state can largely determine its clinical outcome[6]. The increase of Fg and D-D can both increase blood viscosity; t-PA is an important component of the fibrinolysis system, it has positive anticoagulation effect, and the joint detection of the three helps to determine the coagulation state in the body[17]. It was found in the study that compared with those before treatment, serum Fg and D-D contents in both groups were lower while t-PA contents were higher after treatment; further compared with control group, the observation group of patients were with lower serum Fg and D-D contents, and higher t-PA content after treatment, confirming that adjuvant ginkgo-damole therapy can effectively reduce blood viscosity and optimize the coagulation function.

To sum up, it can be concluded that adjuvant ginkgo-damole treatment of unstable angina and can effectively stabilize atheromatous plaque, inhibit myocardial apoptosis and improve the body’s hypercoagulability, and it helps optimize patients’ final treatment outcome.

References