Effects of lipid-lowering anticoagulant antihypertensive drugs combined with ginkgo capsule on endothelial injury and plaque stability in patients with carotid atherosclerosis

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ABSTRACT

Objective: To investigate the effects of lipid-lowering anticoagulant antihypertensive drugs combined with ginkgo capsule on endothelial injury and plaque stability in patients with carotid atherosclerosis. Methods: A total of 114 patients with carotid atherosclerosis who were treated in Songzi People’s Hospital between April 2016 and January 2017 were collected and divided into control group (n=57) and ginkgo capsule group (n=57) by random number table. Control group received conventional lipid-lowering anticoagulant antihypertensive drug therapy and ginkgo capsule group received lipid-lowering anticoagulant antihypertensive drugs combined with ginkgo capsule therapy. The differences in endothelial injury and plaque stability were compared between the two groups before and after treatment. Results: There was no statistically significant difference in serum levels of endothelial function indexes and plaque stability-related indexes between the two groups before treatment. After 1 month of treatment and after 6 months of treatment, serum endothelial injury indexes sVCAM-1, vWF and ET-1 levels of ginkgo capsule group were lower than those of control group at corresponding points in time whereas NO and 6-Reto-PGF1α levels were higher than those of control group at corresponding points in time; serum plaque stability-related indexes LEP, RETN, Hcy, PTX3 and Lp-PLA2 levels were lower than those of control group at corresponding points in time whereas APN levels were higher than those of control group at corresponding points in time. Conclusions: Lipid-lowering anticoagulant antihypertensive drugs combined with ginkgo capsule therapy can effectively protect the vascular endothelial function and stabilize the atherosclerotic plaque in patients with carotid atherosclerosis.

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1. Introduction

Carotid atherosclerosis is the carotid expression of systemic atherosclerosis, its condition is aggravated with the increase of age, the carotid atherosclerosis progresses more rapidly in those combined with hypertension and hyperlipidemia, and it is considered to be one of the important factors for stroke in the elderly[1,2]. Patients with carotid atherosclerosis should receive active treatment to suppress the progress of the disease and avoid the occurrence of cerebrovascular accident. For carotid atherosclerosis patients combined with hypertension, hyperlipidemia and other significant causes, lipid-lowering, anticoagulant and blood pressure-lowering are the routine therapies, but current studies have shown that these routine therapies have limitations in delaying the carotid atherosclerosis progression, and other drugs are needed for combination therapy. Ginkgo capsule is made from high-quality ginkgo biloba extract ginkgo flavonol and total terpene lactones, which has the effects such as lowing blood pressure, regulating blood lipid and softening blood vessels, and is the highly praised Chinese patent medicine for cardiovascular system[3,4]. In this study, ginkgo capsule was used as adjuvant medicine for the treatment of patients with carotid atherosclerosis, and its effect on the disease progression after application was discussed.
2. Materials and methods

2.1. Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with carotid atherosclerosis by ultrasound; (2) combined with hypertension and hyperlipidemia; (3) without previous systematic treatment; (4) cooperating with the treatment and laboratory examination.

Exclusion criteria: (1) with history of cerebral hemorrhage and cerebral infarction; (2) combined with gingko capsule allergy; (3) combined with systemic infectious diseases; (4) combined with severe liver and kidney insufficiency.

2.2. Case information

A total of 114 patients with carotid atherosclerosis who were treated in this hospital between April 2016 and January 2017 were divided into control group (n=57) and ginkgo capsule group (n=57) by random number table. Control group included 31 males and 26 females who were 43-71 years old; ginkgo capsule group included 32 males and 25 females who were 45-72 years old. The differences in the above gender and age distribution were not significant between group, and the research plan was approved by the hospital ethics committee.

2.3. Therapy

Control group were treated with conventional lipid-lowering, anticoagulant and blood pressure-lowering drugs. Ginkgo capsule group were treated with ginkgo capsules on the basis of lipid-lowering, anticoagulant and blood pressure-lowering treatment, which was as follows: oral ginkgo capsules, 2 capsules/time, 2 times/d, for continuous 6 months of treatment.

2.4. Endothelial injury indexes

Before treatment (T0), after 1 month of treatment (T1) and after 6 months of treatment (T2), the peripheral blood samples were collected respectively to separate and freeze serum. Enzyme-linked immunosorbent assay method was adopted to detect the contents of endothelial function indexes soluble vascular cell adhesion molecule 1 (sVCAM-1), von willebrand factor (vWF), nitric oxide (NO), endothelin-1 (ET-1) and 6-ketone prostaglandin (6-Reto-PGF1α).

2.5. Plaque stability–related indexes

Before treatment (T0), after 1 month of treatment (T1) and after 6 months of treatment (T2), the peripheral blood serum was also obtained from two groups of patients respectively, immunoturbidimetry was adopted to determine the contents of plaque stability-related parameters leptin (LEP), adiponectin (APN), resistin (RETN), homocysteine (Hcy), pentraxin 3 (PTX3) and lipoprotein-associated phospholipase A2 (Lp-PLA2).

2.6. Statistical analysis

Endothelial function indexes and plaque stability-related indexes were all input in statistical software SPSS 23.0, the P value was calculated and $P<0.05$ was set as the standard of statistical significance in differences.

3. Results

3.1. Endothelial function indexes

At T0, the differences in serum sVCAM-1, vWF, ET-1 and 6-Reto-PGF1α levels were not statistically significant between the two groups ($P>0.05$). At T1 and T2, serum sVCAM-1, vWF and ET-1 levels of both groups were lower than those at T0 whereas NO and 6-Reto-PGF1α levels were higher than those at T0; serum sVCAM-1, vWF and ET-1 levels of ginkgo capsule group were lower than those of control group at corresponding points in time whereas NO and 6-Reto-PGF1α levels were higher than those of control group at corresponding points in time ($P<0.05$), shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time point</th>
<th>sVCAM-1 (pg/mL)</th>
<th>vWF (μmol/L)</th>
<th>NO (μmol/L)</th>
<th>ET-1 (pg/mL)</th>
<th>6-Reto-PGF1α (pg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>57</td>
<td>T0</td>
<td>1 983.62±254.77</td>
<td>41.92±4.76</td>
<td>45.27±5.11</td>
<td>72.18±8.54</td>
<td>58.23±6.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>1 621.48±190.53</td>
<td>35.71±4.03</td>
<td>48.64±4.93</td>
<td>67.53±7.09</td>
<td>62.41±6.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>1 326.74±153.29</td>
<td>28.95±3.42</td>
<td>53.16±5.88</td>
<td>60.21±6.57</td>
<td>65.72±6.84</td>
</tr>
<tr>
<td>Ginkgo capsule group</td>
<td>57</td>
<td>T0</td>
<td>1 975.94±243.81</td>
<td>41.67±4.85</td>
<td>45.23±5.95</td>
<td>72.34±7.99</td>
<td>58.45±5.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>1 157.03±124.66</td>
<td>29.68±3.24</td>
<td>52.04±5.76</td>
<td>54.17±6.14</td>
<td>68.24±7.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>750.92±86.45</td>
<td>17.15±2.04</td>
<td>59.22±6.43</td>
<td>47.12±5.03</td>
<td>71.61±7.50</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, $P<0.05$. 

and the specific contents are positively correlated with endothelial damage, also increase, both of them are the markers of endothelial damage, released after endothelial cell damage, the content of sVCAM-1 may also increase, both of them are the markers of endothelial damage, and the specific contents are positively correlated with endothelial damage degree[10,11]. NO is the strongest vasodilatory factor, ET-1 has vasoconstrictive function, and the NO synthesis reduces while the ET-1 is massively secreted after vascular endothelial injury, which cause vasomotor dysfunction and further endothelial injury progression[12,13]. 6-Reto-PGF1α also has vasodilatory function, it has been found that the 6-Reto-PGF1α content in plasma of patients with atherosclerosis decreases, and it is the protective factor of coronary heart disease and so on[14]. The study found that compared with those at T0, serum sVCAM-1, vWF and ET-1 levels of both groups decreased whereas NO and 6-Reto-PGF1α levels increased at T1 and T2, indicating that both therapies can protect vascular endothelial function; further compared with those of control group, serum sVCAM-1, vWF and ET-1 levels of ginkgo capsule group were lower whereas NO and 6-Reto-PGF1α levels were higher, it shows that adding ginkgo capsule in the overall treatment can further optimize the endothelial function and reduce vascular endothelial damage, and this is one of the visual evidences of it to optimize the carotid atherosclerosis.

Plaque stability is closely related to the ultimate outcome of patients with carotid atherosclerosis, the illness of patients with stable plaque can be basically maintained at stable level, and unstable plaques easily rupture, bleed and even occlude the coronary artery to cause acute myocardial infarction[15,16]. Various factors are involved in the formation of atheromatous plaque, so the stability of plaque is also regulated by many factors. LEP, APN, RETN, Hcy, PTX3 and Lp-PLA2 are all proven to be related to plaque stability in different studies. LEP can promote endothelin secretion, induce vascular smooth muscle hyperplasia, accelerate platelet aggregation and microthrombosis, and promote vascular calcification process[17]. APN can improve insulin resistance, affect vascular smooth muscle proliferation and migration, and regulate endothelial cell function, and it has protective effect on atherosclerosis progression[18]. RETN can counteract the insulin effect, promote blood glucose to rise, induce systemic vascular constriction and spasm, damage vascular endothelial cells, and promote atherosclerosis formation[19]. Hyperhomocysteinemia is an independent risk factor for coronary heart disease occurs, the research has confirmed that the content of Hcy in unstable plaques is higher than that in stable plaque, and Hcy levels are positively correlated with the degree of atherosclerosis. PTX3 is an acute phase protein that can reflect the local plaque and systemic inflammation, and the high expression of PTX3 can promote plaque rupture and reduce plaque stability[5]. Lp-PLA2 is a phospholipase secreted by macrophages and foam cells under inflammatory stimulation, and its

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time point</th>
<th>LEP (ng/mL)</th>
<th>APN (μg/mL)</th>
<th>RETN (ng/mL)</th>
<th>Hcy (mg/L)</th>
<th>PTX3 (ng/mL)</th>
<th>Lp-PLA2 (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>57</td>
<td>T0</td>
<td>3.28±0.35</td>
<td>1.77±0.23</td>
<td>4.95±0.52</td>
<td>20.38±2.75</td>
<td>3.52±0.39</td>
<td>62.19±7.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>2.76±0.29</td>
<td>2.54±0.27</td>
<td>4.03±0.45</td>
<td>17.62±1.88</td>
<td>2.87±0.31</td>
<td>54.02±5.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>2.28±0.23</td>
<td>3.07±0.35</td>
<td>3.28±0.37</td>
<td>11.59±1.64</td>
<td>2.04±0.25</td>
<td>43.28±5.19</td>
</tr>
<tr>
<td>Ginkgo capsule group</td>
<td>57</td>
<td>T0</td>
<td>3.24±0.33</td>
<td>1.76±0.24</td>
<td>4.92±0.51</td>
<td>20.41±2.68</td>
<td>3.49±0.37</td>
<td>62.31±7.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>1.98±0.24</td>
<td>2.99±0.34</td>
<td>3.17±0.34</td>
<td>12.05±1.74</td>
<td>2.16±0.24</td>
<td>46.39±5.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>1.26±0.15</td>
<td>4.12±0.45</td>
<td>1.64±0.21</td>
<td>6.88±0.73</td>
<td>1.28±0.15</td>
<td>30.77±3.84</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, *P*<0.05.
high expression has been found in the serum of patients with acute stroke and unstable plaque[20,21]. This study showed that compared with those at T0, serum LEP, RETN, Hcy, PTX3 and Lp-PLA2 levels of both groups decreased whereas APN levels increased at T1 and T2; further compared with those of control group, serum LEP, RETN, Hcy, PTX3 and Lp-PLA2 levels of ginkgo capsule group were lower whereas APN levels were higher at T1 and T2, proving that the adjuvant ginkgo capsule therapy can increase the atheromatous plaque stability.

Lipid-lowering, anticoagulant and blood pressure-lowering drugs combined with ginkgo capsule therapy can effectively protect the endothelial function and increase the atheromatous plaque stability in patients with carotid atherosclerosis, and it is worthy of popularization and application in clinical practice in the future.

References


