The Effect of lumbrokinase capsules on plasma endothelin and calcitonin gene-related peptide levels in cerebral infarction patients with Qi deficiency and Blood stagnation

Gui-Lan Leng, Xue-Li Weng, Yu-Bo Hua
The Second People’s Hospital, Hangzhou, Zhejiang (Hangzhou 310015)
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Abstract

Purpose  To examine the therapeutic effect of lumbrokinase on acute cerebral infarction patients with Qi deficiency and Blood stagnation.
Method  64 patients were assigned randomly to either treatment group or control group. Both groups were treated with conventional medical care guidelines, and the treatment group was additionally given lumbrokinase. The plasma endothelin (ET) and calcitonin gene-related peptide (CGRP) levels were measured at the beginning and the end of the study.
Result  The levels of ET and CGRP in the treatment group improved more significantly compared to the control group.
Conclusion  Lumbrokinase capsules are an effective treatment for acute cerebral infarction patients with Qi deficiency and Blood stagnation.

Keywords
Cerebral infarction, Qi deficiency and Blood stagnation, lumbrokinase, endothelin, calcitonin gene-related peptide

1. Information and Method

1.1 General Information
All 64 subjects were patients who were admitted to the hospital during 2002 and 2003. Patients were all diagnosed as acute cerebral infarction according to current standards (1.2), and as “Wind Stroke” of Qi deficiency and Blood stagnation subtype according to Traditional Chinese Medicine (TCM). All cases were confirmed by cerebral CT scan or MRI. Subjects were randomly assigned into two groups. The treatment group consisted of 32 subjects with 27 males and 5 females all between the ages of 39 to 77. The average age was 65.15 and the duration of the illness was between 1 to 5 days with the average being 3.02 days. The control group consisted of 32 subjects with 24 males and 8 females all between the ages of 40 to 75. The average age was 63.48 and the duration of the illness was between 1 to 4 days with the average being
2.91 days. There was no significant difference between the patients of both groups. (P >0.05)

1.2 Treatment Method
Both groups were treated with standard conventional medicine, intravenous injectable Dan Shen (Salvia miltiorrhiza) compound formula 250ml twice daily, and nimodipine 20mg orally three times daily. The treatment group was also given two lumbrokinase capsules three times daily (manufactured by Beijing Baiao Pharmaceuticals Co., Ltd.). After 15 days, the treatment results of the two groups were compared.

1.3 Observation and Method
The changes in plasma ET ad CGRP were measured before and after the treatment. Each time, 4ml of fasting venous blood sample was obtained and added into a test tube with 5ml of 10% sodium EDTA and 50ml of aprotinin. The sample was then centrifuged at 3000r/min for 10 minutes in 4°C, and the plasma portion was also stored at 4°C. Radioimmunoassay was used for measuring ET and CGRP. All reagents were provided by the Dongye Immune Research Institute.

1.4 Statistical Analysis
Information and data were calculated and expressed using mean and standard deviation (x±s) and t values.

2. Results
Please refer to table 1. Prior to the treatment, ET and CGRP levels were comparable for both groups. After the treatment, both groups showed different levels of improvement (P<0.05 or 0.01), but improvement in the treatment group was much more pronounced (P<0.01).

Table 1 Comparison of ET and CGRP prior and after treatment (mg/ml, x±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>Prior Treatment</th>
<th>ET</th>
<th>CGRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>After Treatment</td>
<td>52.03±10.08**Δ</td>
<td>45.62±12.00**Δ</td>
</tr>
<tr>
<td>(n=32)</td>
<td></td>
<td>83.01±12.12</td>
<td>29.90±8.12</td>
</tr>
<tr>
<td>Control</td>
<td>Prior Treatment</td>
<td>82.01±11.73</td>
<td>28.41±9.26</td>
</tr>
<tr>
<td>(n=32)</td>
<td></td>
<td>70.02±13.22*</td>
<td>37.60±7.33*</td>
</tr>
</tbody>
</table>

Compared within the group prior to treatment, * P<0.05, ** P<0.01
Compared with the control group after treatment, Δ P<0.01
3. Discussion
It has been observed clinically that stroke patients with Qi deficiency and Blood stagnation should be treated with medications that tonify Qi and invigorate blood, and the earlier the treatment starts the better the prognosis. Medicines that control bleeding should only be used with discretion. Early treatment with Qi tonifying and Blood invigorating medicine would help maintain the free flow in the meridians and prevent Jin (津) from leaking out and becoming Phlegm (痰), thus avoiding the inter-blocking between Phlegm and Stagnant Blood (瘀) that is often seen in the late stage of illness. In addition, early correct treatment can facilitate the resolution/resorption of thrombosis and edema, minimize compression of adjacent nerve tissues thus preventing brain edema, promote peripheral circulation at thrombosed site to improve perfusion to the brain, restore brain cell function and contribute to the overall prognosis. Research has shown that after experiencing local ischemia-reperfusion injury, rat brains would produce significantly higher level of ET (3); ET is a major contributing factor in the pathophysiology of brain ischemia and is the most potent vasoconstrictor known at this time. On the other hand, CGRP is a strong vasodilator and can counter the effects of ET. During cerebral infarction, CGRP can protect the brain tissues by reducing the severity of ischemia. ET level increases significantly in cerebral infarction while CGRP level decreases. Without adequate level of CGRP to keep ET under check the arterioles would go into spasm, further aggravating the ischemic state of the brain. Lumbokinase is the active ingredient extracted from Di Long (earthworms) and has the effects of decreasing ET and increasing CGRP, therefore improving endothelium function and cerebral ischemic state. In TCM terms, lumbrokinase can effectively “invigorate the Blood and resolve Blood Stasis”, and should be promoted clinically for treating brain ischemia conditions.

References: