Effect of Tongxinluo Capsule (通心络胶囊) on Plasma Endothelin, Calcitonin Gene-related Peptide and Nitrogen Oxide of Acute Cerebral Infarction Patients

WANG Ning (王 宁), GU Xi-zhen (顾锡镇), DENG Ying (邓 颖), ZHANG Nan-jun (张南军), TAN You-fen (谭友芬), CAI Xin (蔡 新), and WANG Li-zhu (王丽珠)

Research of TCM shows that the chief pathological basis of acute cerebral infarction (ACI) is “blood stasis obstructing collateral”. Here the authors used Tongxinluo capsule (通心络胶囊, TX-LC) for replenishing qi, removing stasis and dredging collateral to treat qi deficiency-blood stasis type of ACI, and observed the change of plasma endothelin (ET), calcitonin gene-related peptide (CGRP) and nitrogen oxide (NO), aiming at exploring the effect of TXLC on vascular endothelial function and neurotransmitter.

METHODS

Inclusion and Exclusion Criteria

One hundred and two patients were all inpatients of the Neurological Department of the author's hospital, their modern medical diagnosis all conformed to the revised standard of the 4th National Cerebro-vascular Disease Conference, Chinese Medical Association held in 1995(1), and was confirmed by skull CT or MRI examination. With the TCM diagnosis based on the revised standard on “TCM diagnosis and efficacy evaluation of stroke disease” advocated by the Medical Society of Chinese National TCM Association issued in 1986(2), the ACI was all found to belong to internal carotid arterial system, with patients of atrial fibrillation and severe heart diseases excluded from the study.

Clinical Data

According to the randomized digital chart, the enrolled patients were randomly divided into odd number treated group (n=52) and even number control group (n=50). In the treated group, there were 29 male cases, 23 female cases; age ranging 45-78 years, mean 68.2±3.3 years; illness course 12-146 hrs. Control group included 28 male cases, 22 female cases; age ranging 46-76 years, mean 67.4±3.5 years; illness course 13-147 hrs. The nerve function deficit scores (NFDS) of the two groups were 24.81±1.18 and 23.76±2.24 respectively. The sex, age, illness course, and NFDS between the two groups showed no significant difference, (P>0.05), and so they were comparable.

Therapeutic Method

Conventional therapy was given to both groups, including naloxan hydroxide (produced by Beijing Tetracycle Pharmaceutic Co., Ltd., batch number 01110820), with 1.6 mg added into normal saline 250 ml, given through intravenous dripping, once a day, for altogether 3 weeks. Salvia injection (produced by Guizhou Shenqi Pharmaceutic Co., Ltd., batch number: 01120921) 250 ml, intravenous dripping, once daily, for 3 weeks. Entero-coated aspirin tablet (produced by Nanjing Hengsheng Pharmaceutical Factory, batch number 011001), 50-75 mg, once every evening, for altogether 3 weeks. When necessary, such treatment was given as adjusting blood pressure, lowering blood glucose, regulating blood lipid and dehydration, etc.

Treated group: Conventional treatment was given with TXLC (produced by Shijiazhuang Yiling Pharmaceutic Co., Ltd., batch number 01110910) added, its chief ingredients being ginseng, scorpion, ground beetle, centipede, cicada slough, etc., 0.3 g each capsule, 3 capsules each time, 3 times a day, taken orally, consecutively for 3 weeks.

Correspondence to: WANG Ning, Tel: 025-6617141 Ext. 43019
Observatory Parameters and Determination Methods

The clinical efficacy and NFDS would be observed 3 weeks after treatment in both groups, the parameter of ET, CGRP and NO etc. before and after treatment would be monitored.

ET and CGRP determination: Twenty-four hours after admission fasting cubital venous blood 4 ml was collected, filled in the test tube containing 10% EDTA sodium 30 μl and trasyol 40 μl, centrifuged at 3 000 r/min for 10 min under 4°C, and the plasma was isolated and preserved at -304°C. The automatic microgranule chemical luminous immune system monitor and ELISA assay were used for determination. The test kit was provided by the East Asia Immune Technical Institute, General Hospital of PLA.

NO determination: 24 hrs after admission fasting cubital venous blood 2 ml was collected, filled in common test tube and placed under room temperature for 1 hr, centrifuged at 2 000 r/min, with isolated blood serum awaiting further determination, and the Griess assay used for testing serum. Test kit was provided by Nanjing Jiancheng Institute of Bio-engineering.

Efficacy Assessment Standard

According to the stroke patients’ clinical nerve function deficit degree assessment standard worked out by the Fourth National Cerebro-vascular Diseases Conference held in 1995(3) and in the light of living ability status the efficacy was assessed and defined into 6 grades: Basically cured, markedly effective, effective, unchanged, aggravated and death.

Statistical Analysis

The measurement data was adopted paired t test, and enumeration data χ² test.

RESULTS

Comparison of Clinical Efficacy between the Two Groups

Three weeks after the treatment, in the treated group the basically cured was 6 cases, markedly effective 24 cases, effective 16 cases, unchanged 5 cases, aggravated 1 case, cured-markedly effective rate being 57.69%, and effective rate 88.46%. In the control group the basically cured was 5 cases, markedly effective 20 cases, effective 16 cases, unchanged 8 cases, aggravated 1 case, cured-markedly effective rate being 50.00%, and effective rate 82.00%. Comparison of cured-markedly effective rate between these two groups showed that the difference was significant (P<0.05), indicating the effect of removing stasis and dredging collateral in the treated group was obvious.

Comparison between NFDS of the Two Groups

Before treatment, it was 24.81±1.18 in the treated group, while in the control group 23.72±2.24; after treatment, it was 9.17±2.33 in the treated group, and in the control group 13.48±1.93. After treatment, the NFDS of both group lowered (P<0.01), but treated group lowered more than that of the control group (P<0.05), indicating that in the treated group the medicine exerted more obvious action in improving NFDS.

Comparison between ET, CGRP and NO of Both Groups

Before treatment, ET, CGRP and NO of both groups have insignificant difference, P>0.05. After treatment the hematopoietic parameters were improved, but the change in the treated group was obviously better than that in the control group (P<0.05), indicating that TXLC administration could effectively regulate vascular activity and obviously elevate NO level. See Table 1.

Table 1. Comparison between ET, CGRP, NO of the Two Groups before and after Treatment (x±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>ET(ng/L)</th>
<th>CGRP (ng/L)</th>
<th>NO(mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated</td>
<td>52</td>
<td>BT 43.62±8.04</td>
<td>42.86±6.37</td>
<td>58.64±7.82</td>
</tr>
<tr>
<td></td>
<td>AT 48.38±8.22</td>
<td>△</td>
<td>53.14±7.68</td>
<td>△</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>BT 42.70±8.87</td>
<td>43.28±6.43</td>
<td>56.79±8.74</td>
</tr>
<tr>
<td></td>
<td>AT 54.74±8.58</td>
<td>*</td>
<td>46.82±8.13</td>
<td>*</td>
</tr>
</tbody>
</table>

Notes: * P<0.05, ** P<0.01, compared with the same group before treatment; △ P<0.05, compared with the control group after treatment.

Toxic and Adverse Reaction

After treatment in both groups abnormality was not discovered in liver-kidney function. Only in 1 case of treated group after treatment appeared gastric distress, but after changing to after meal administering, the symptom got relieved by itself, and abnormality was not found in other cases.

DISCUSSION

Scholars abroad discovered at the beginning of nineteen nineties that ET and CGRP are bio-active polypeptide consisting of 21 and 37 amino-acids respectively, and mainly distributed in the cardiovas-