Study on the effect of urinary kallidinogenase after thrombolytic treatment for acute cerebral infarction


Department of Neurology, Tianjin Huanhu Hospital, Tianjin Key Laboratory of Cerebral Vascular and Neurodegenerative Diseases, Tianjin, China

Abstract. – OBJECTIVE: To evaluate the safety and efficacy of urinary kallidinogenase for recombinant tissue-type plasminogen activator (rt-PA) intravenous thrombolytic treatment in patients with acute cerebral infarction.

PATIENTS AND METHODS: All 200 patients with acute cerebral infarction were randomized 1:1 into an experimental group (100 cases) and a control group (100 cases). Patients in the control group were administered rt-PA (0.9 mg/kg) while patients in the experimental group were given urinary kallidinogenase by intravenous drip (0.15 PNAU/d, for 7 days) after rt-PA intravenous thrombolytic treatment (0.9 mg/kg). The main evaluation index was NIHSS and BI.

RESULTS: Compared to the control group, the NIHSS scores were significantly lower 7 and 90 days after thrombolytic therapy \((t = 2.391, 2.714; p < 0.05)\). BI scores were obviously higher at 90 days after thrombolytic therapy in the experimental group \((t = 2.675, p < 0.05)\).

CONCLUSIONS: Urinary kallidinogenase may improve the treatment effect for rt-PA intravenous thrombolytic treatment in patients with acute cerebral infarction.

Key Words:
Tissue plasminogen activator, Human urinary kallikrein, Acute cerebral infarction.

Introduction

The most effective treatment of acute cerebral infarction is thrombolytic therapy\(^1,2\). Recombinant tissue plasminogen activator, rt-PA was approved for thrombolytic therapy by the US Food and Drug Administration in 1996. Human urinary kallikrein, namely kallikrein, is a glycoprotein extracted from urine\(^3\). Clinical studies have confirmed that it can activate its kallikrein-kinin system, expand arterioles of the cerebral ischemia area and aggregate anti-platelet. Currently, clinical studies about the combination of thrombolytic and kallikrein are rare\(^4\). The purpose of this study is to observe the efficacy of thrombolytic and kallikrein on acute cerebral infarction.

Patients and Methods

Two hundred patients receiving thrombolytic therapy between June 2012 and January 2014 were selected for this study. Of all the patients, 109 are men and 91 women with an age between 35 and 80 years old and an average age of 63 (5 ± 8.7 years old). The thrombolysis inclusion criteria are: (1) Age not more than 80; (2) Diagnosed as ACI and the NIHSS is between 4 and 25; (3) No intracranial hemorrhage and obvious low density shadow found by head CT scan; (4) Time of onset is not more than four and half hours; (5) Thrombolytic informed consent signed by family members or patients. Exclusion criteria are: (1) History of intracranial hemorrhage including suspicious subarachnoid hemorrhage, head trauma in the last three months, bleeding in gastrointestinal or urinary system in the last three weeks, major surgery in the last two weeks and arterial puncture of oppression-forbidden area in the last week; (2) History of cerebral or myocardial infarction in the last three weeks with exception of patients with no neurological function signs left in old locule gaps; (3) Severe heart, kidney, liver dysfunction or severe diabetes patients; (4) Active bleeding or trauma found at examination; (5) Oral anticoagulation and the INR is over 1.5, heparin treatment within 48 hours (aPTT time outside the normal range); (6) Blood platelets less than 100×10^9/L, blood sugar less than 2.7 mmol/L; (7) Blood pressure:
systolic blood pressure over 180 mmHg and diastolic blood pressure over 100 mmHg; (8) Gestation; (9) Non-cooperation.

**Patients and Methods**

The patients included in the treatment program were divided into the control group and the experimental group. All patients received rt-PA thrombolytic therapy with 0.9 mg/kg (total amount less than 90 mg), 10% by intravenous injection in one minute and 90% by intravenous drip in 60 minutes. The experimental group received kallikrein (0.15 PNA/d, continuous for 7 d) after thrombolytic therapy. It was forbidden to use angiotensin-converting enzyme inhibitors in the treatment. The control group received blood platelets treatment after 24 hours with aspirin of 300 mg QD. At the same time, hypotensive, hypoglycemic, lipid-lowering, anti-atherosclerosis, and plaque stability treatments were administered for complications like diabetes mellitus, hypertension, carotid artery plaque, and hyperlipidemia.

The NIHSS of the National Institutes of Health was used to assess the neurological functions of patients, seven days before treatment, and 90 days after treatment. The BI index was used to assess the daily living ability of patients 90 days after treatment.

**Statistical Analysis**

The SPSS for Windows 16.0 statistical package (SPSS Inc., Chicago, IL, USA) was used to process data. The measurement data was presented as $z \pm s$ and analyzed with $t$-test. Count data were tested with $\chi^2$. $p < 0.05$ was considered statistically significant.

### Results

The baseline data of the two groups were as follows: there was no evident difference (all over 0.05) in age, gender, and daily living ability, NIHSS of the National Institutes of Health, history of high blood pressure, coronary heart disease and diabetes scores (Table I).

Comparison of NIHSS before and after treatment between two groups. The NIHSS score has obviously improved (average $p$ less than 0.05) seven days and 90 days after treatment respectively. The experimental group is better than the control group ($p$ less than 0.05) (Table II).

Comparison of BI before and after treatment between two groups. The BI score has improved (average $p$ less than 0.05) 90 days after treatment. The experimental group is better than the control group ($p$ less than 0.05). (Table III).

### Discussion

The treatment of acute cerebral infarction has always been a hot research topic, and thrombolytic therapy is one of the few Class I recom-

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**Table I.** The baseline data of two groups.

<table>
<thead>
<tr>
<th></th>
<th><strong>Experimental group</strong></th>
<th><strong>Control group</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.8 ± 10.6</td>
<td>61.2 ± 9.7</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>54/46</td>
<td>55/45</td>
</tr>
<tr>
<td>ADL Score</td>
<td>46.3 ± 16.2</td>
<td>52.9 ± 17.6</td>
</tr>
<tr>
<td>NIHSS Score</td>
<td>13.8 ± 5.9</td>
<td>12.7 ± 6.2</td>
</tr>
<tr>
<td>History of high blood pressure (%)</td>
<td>68 (68)</td>
<td>72 (72)</td>
</tr>
<tr>
<td>History of coronary heart disease (%)</td>
<td>35 (35)</td>
<td>32 (32)</td>
</tr>
<tr>
<td>History of diabetes mellitus (%)</td>
<td>39 (39)</td>
<td>42 (42)</td>
</tr>
</tbody>
</table>

**Table II.** Different time NIHSS score with two groups of patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>NIHSS Score before Thrombolysis</th>
<th>NIHSS Score Seven Days Later</th>
<th>NIHSS Score 90 Days Later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental group</td>
<td>100</td>
<td>13.8 ± 5.9</td>
<td>4.2 ± 3.8</td>
<td>1.2 ± 2.6</td>
</tr>
<tr>
<td>Control group</td>
<td>100</td>
<td>12.7 ± 6.2</td>
<td>6.9 ± 5.9</td>
<td>3.9 ± 5.7</td>
</tr>
<tr>
<td>Value of $t$</td>
<td>0.952</td>
<td></td>
<td>2.391</td>
<td>2.714</td>
</tr>
<tr>
<td>Value of $p$</td>
<td>0.379</td>
<td></td>
<td>0.045</td>
<td>0.041</td>
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</table>
Table III. Different time BI score with two groups of patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>BI Score before Thrombolysis</th>
<th>BI Score 90 Days Later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental group</td>
<td>100</td>
<td>35.7 ± 12.9</td>
<td>89.2 ± 21.6</td>
</tr>
<tr>
<td>Control group</td>
<td>100</td>
<td>33.7 ± 16.2</td>
<td>63.9 ± 25.7</td>
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<tr>
<td>Value of $t$</td>
<td>0.832</td>
<td></td>
<td>2.675</td>
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<tr>
<td>Value of $p$</td>
<td>0.787</td>
<td></td>
<td>0.012</td>
</tr>
</tbody>
</table>

Urinary kallidinogenase after thrombolytic treatment for acute cerebral infarction

Inflammation, expansion of the tiny blood vessels and improvement of circulation and inhibition of apoptosis\(^{27,30}\).

Acknowledgements

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Conflict of Interest

The Authors declare that they have no conflict of interests.

References


