Correlation of anxiety with nerve injury and oxidative stress response in patients with acute cerebral infarction complicated by type 2 diabetes mellitus

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ABSTRACT

Objective: To study the correlation of anxiety with nerve injury and oxidative stress response in patients with acute cerebral infarction complicated by type 2 diabetes mellitus. Methods: Patients with acute cerebral infarction complicated by type 2 diabetes mellitus that were treated in Jingzhou First People’s Hospital between March 2015 and April 2017 were selected and divided into anxiety group and non-anxiety group according to HAMA score; the healthy subjects who received physical examination during the same period were selected as the control group. The serum contents of nerve injury markers, oxidative stress indexes and apoptosis indexes of three groups of subjects were measured. Results: Serum NSE, Glu, \(\beta\)-actin, NF155, sTM, MDA, ox-LDL, AOPP, sFas, sFasL and Caspase-3 levels of anxiety group and non-anxiety group were significantly higher than those of control group whereas GPx, SOD, Bcl-2 and Livin contents were lower than those of control group; serum NSE, Glu, \(\beta\)-actin, NF155, sTM, MDA, ox-LDL, AOPP, sFas, sFasL and Caspase-3 contents of anxiety group were significantly higher than those of non-anxiety group whereas GPx, SOD, Bcl-2 and Livin contents were lower than those of non-anxiety group. Conclusion: The anxiety in patients with acute cerebral infarction complicated by type 2 diabetes mellitus can aggravate the degree of nerve injury and oxidative stress response.

1. Introduction

Acute cerebral infarction is a common cerebrovascular disease in our country, the pathological basis is atherosclerosis and lumen occlusion, and the ischemic hypoxic injury occurs in the diseased brain tissue and causes damage to the nerve function. Patients with type 2 diabetes mellitus are the high-risk group for acute cerebral infarction, and the endothelial damage, inflammation, oxidative stress and other pathological factors in the course of diabetes can accelerate the process of atherosclerosis and increase the occurrence risk of cerebral infarction\(^1,2\). In recent years, the studies about the development and change of type 2 diabetes mellitus combined with acute brain infarction have shown that the negative psychological status after disease onset will influence multiple pathophysiological links of cerebral infarction and then cause the changes in nerve damage and oxidative stress reaction extent. Among the many negative psychological states, anxiety is with the most significant effect on nerve damage and oxidative stress\(^3\), and the present study specifically analyzed the correlation of anxiety with nerve injury and oxidative stress response in patients with acute cerebral infarction complicated by type 2 diabetes mellitus.

2. Materials and methods

2.1. Research subjects

Patients with acute cerebral infarction complicated by type 2 diabetes mellitus who were treated in Jingzhou First People’s Hospital between March 2015 and April 2017 were selected, all patients had the history of type 2 diabetes mellitus and were admitted into hospital due to acute cerebral infarction this time, they were diagnosed with acute cerebral infarction by the combination...
of clinical symptoms, signs and imageological examination, the
patients with the history of cerebrovascular disease, brain trauma or
brain tumor and the patients combined with autoimmune diseases
or infectious diseases were ruled out, and the enrolled patients
were divided into anxiety group and non-anxiety group according
to HAMA score. The healthy subjects who received physical
examination in Jingzhou First People's Hospital during the same
period were selected as the control group, and they were without
nervous system diseases, autoimmune system diseases or infectious
diseases. There were 38 cases in the anxiety group, including 22
males and 16 females who were 42-64 years old; there were 52
cases in the non-anxiety group, including 32 males and 20 females
who were 40-66 years old; there were 80 cases in the control group,
including 46 males and 34 females who were 39-65 years old. There
was no significant difference in the general data among the three
groups (P>0.05).

2.2. Research methods

2.2.1. Anxiety evaluation

The HAMA scale was used for the evaluation of anxiety, and there
was anxiety if the HAMA score was > 14 points.

2.2.2. Serum index detection

3-5 mL of cubital venous blood was collected from the three
groups of subjects and centrifuged to separate serum, enzyme-linked
immunosorbent assay kit was used to determine the contents of NSE,
Glu, β -actin, NF155 and sTM, ox-LDL, sFas, sFasL, Caspase-3, Bcl-2
and Livin, and radioimmunoprecipitation kit was adopted to detect
the MDA, AOPP, GPx and SOD contents.

2.3. Statistical methods

SPSS 21.0 was used for variance analysis of the differences in
measurement data among three groups, and the differences in
analysis results were statistically significant if P<0.05.

3. Results

3.1. Serum nerve injury marker levels

Analysis of serum nerve injury markers NSE (ng/mL), Glu (nmol/
ml), β -actin (ng/mL), NF155 (pg/mL) and sTM (ng/mL) levels
among three groups of subjects was as follows: serum NSE, Glu,
β -actin, NF155 and sTM levels of anxiety group and non-anxiety
group were significantly higher than those of control group, and
serum NSE, Glu, β -actin, NF155 and sTM levels of anxiety
group were significantly higher than those of non-anxiety group.
Differences in pair-wise comparison of serum NSE, Glu, β -actin,
NF155 and sTM levels were statistically significant among three
groups of subjects (P<0.05), Shown in Table 1.

3.2. Serum oxidative stress index levels

Analysis of serum oxidative stress indexes MDA (μmol/L), ox-
LDL (μmol/L), AOPP (μmol/mL), GPx (U/L) and SOD (U/L) levels
among three groups of subjects was as follows: serum MDA, ox-
LDL and AOPP levels of anxiety group and non-anxiety group were
significantly higher than those of control group whereas GPx and
SOD levels were lower than those of control group; serum MDA,
ox-LDL and AOPP levels of anxiety group were significantly higher
than those of non-anxiety group whereas GPx and SOD levels
were lower than those of non-anxiety group. Differences in pair-
wise comparison of serum MDA, ox-LDL, AOPP, GPx and SOD
levels were statistically significant among three groups of subjects
(P<0.05), shown in Table 2.

3.3. Serum apoptosis index levels

Analysis of serum apoptosis indexes sFas (pg/mL), sFasL (pg/mL),
Caspase-3 (ng/mL), Bcl-2 (nmol/mL) and Livin (nmol/mL) levels
among three groups of subjects was as follows: serum sFas, sFasL
and Caspase-3 levels of anxiety group and non-anxiety group were
significantly higher than those of control group whereas Bcl-2 and
Livin levels were lower than those of control group; serum sFas,
sFasL and Caspase-3 levels of anxiety group were significantly

Table 1.

Comparison of serum nerve injury markers among three groups of subjects.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>NSE</th>
<th>Glu</th>
<th>β -actin</th>
<th>NF155</th>
<th>sTM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety group</td>
<td>38</td>
<td>36.51±5.96</td>
<td>132.6±16.8</td>
<td>4.89±0.61</td>
<td>1.51±0.18</td>
<td>18.41±2.25</td>
</tr>
<tr>
<td>Non-anxiety group</td>
<td>52</td>
<td>22.32±3.89</td>
<td>85.5±11.4</td>
<td>2.66±0.36</td>
<td>0.92±0.12</td>
<td>12.14±1.76</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>8.39±1.03</td>
<td>42.5±6.8</td>
<td>1.02±0.16</td>
<td>0.38±0.06</td>
<td>4.82±0.75</td>
</tr>
</tbody>
</table>

*: compared with control group, P<0.05; #: compared with non-anxiety group, P<0.05.

Table 2.

Comparison of serum oxidative stress indexes among three groups of subjects.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>MDA</th>
<th>ox-LDL</th>
<th>AOPP</th>
<th>GPx</th>
<th>SOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety group</td>
<td>38</td>
<td>15.85±1.89</td>
<td>479.1±59.4</td>
<td>62.83±8.69</td>
<td>28.48±3.85</td>
<td>52.83±7.91</td>
</tr>
<tr>
<td>Non-anxiety group</td>
<td>52</td>
<td>9.98±1.15</td>
<td>325.6±51.3</td>
<td>39.51±4.95</td>
<td>44.21±6.47</td>
<td>89.31±10.24</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>5.67±0.73</td>
<td>214.5±33.7</td>
<td>22.31±3.85</td>
<td>70.31±9.84</td>
<td>132.13±16.58</td>
</tr>
</tbody>
</table>

*: compared with control group, P<0.05; #: compared with non-anxiety group, P<0.05.
higher than those of non-anxiety group whereas Bcl-2 and Livin levels were lower than those of non-anxiety group. Differences in pair-wise comparison of serum sFas, sFasL, Caspase-3, Bcl-2 and Livin levels were statistically significant among three groups of subjects \( (P<0.05) \), shown in Table 3.

4. Discussion

Psychological status is an important factor that affects neural function, and in the course of acute cerebral infarction combined with type 2 diabetes mellitus, the changes of psychological state, especially the generation of anxiety in the patients can affect multiple pathological links in the disease and lead to the aggravation of nerve damage degree\([4,5]\). NSE is an enzyme that catalyzes glycolysis in neurons in the central nervous system and it can specifically reflect the damage of neurons\([6]\); Glu is a kind of excitatory amino acid, and hypoxic stimuli can cause increased generation of Glu, produce neurotoxicity and cause nerve damage\([7,8]\); \( \beta \)-actin is a kind of cytoskeletal protein widely distributed in the microvascular endothelial cells of the brain, and the damage of hypoxia to microcirculation can lead to the increased release of \( \beta \)-actin; NF155 belongs to the immunoglobulin superfamily and is located in the lateral area of Ranvier node, and the damage of myelin figure during cerebral infarction will increase the release of NF155\([9]\); sTM is the split product of thrombomodulin on endothelial cells, which is related to the injury of endothelial cells in the course of cerebral infarction\([10]\). The analysis of the changes in serum levels of above nerve injury markers in patients with acute cerebral infarction complicated by type 2 diabetes mellitus showed that serum NSE, Glu, \( \beta \)-actin, NF155 and sTM levels of anxiety group and non-anxiety group were significantly higher than those of control group. This indicates that various neural markers are massively released into the blood circulation in the process of acute cerebral infarction in patients with type 2 diabetes mellitus. Further analysis of the influence of anxiety on nerve injury degree in patients with acute cerebral infarction complicated by type 2 diabetes mellitus showed that serum NSE, Glu, \( \beta \)-actin, NF155 and sTM levels of anxiety group were significantly higher than those of non-anxiety group. This indicates that the release of nerve injury markers increases in patients combined with anxiety, showing that anxiety can aggravate the degree of nerve damage in patients with acute cerebral infarction complicated by type 2 diabetes mellitus.

Oxidative stress response is also involved in the pathological links of the occurrence of acute cerebral infarction and type 2 diabetes as well as the generation of anxiety, and the excessive generation of oxygen free radicals in the process of oxidative stress is closely related to the local cerebral ischemia hypoxia in patients with acute cerebral infarction, increased formation of glycation end products in patients with type 2 diabetes mellitus and the changes of neurotransmitters in patients with anxiety\([11,12]\). Oxygen free radicals have strong oxidizing property and can have oxidizing reaction with the lipids and proteins in a variety of tissue cells, which not only causes the changes in the biological functions of lipids and proteins and the damage to cellular structure, but also generates a lot of oxidation products MDA, ox-LDL and AOPP\([13,14]\). At the same time, the endogenous antioxidant mechanism in the local tissue will be reactively activated, antioxidant enzymes SOD and GPx are the important molecules involved in antioxidant mechanism composition, and they have reducibility and can scavenger free radicals to a certain extent; however, the excessively generated free radicals can significantly increase the consumption of GPx and SOD and weaken the antioxidant capacity\([15]\). The analysis of the changes in serum levels of above oxidative stress molecules in patients with acute cerebral infarction complicated by type 2 diabetes mellitus showed that serum MDA, ox-LDL and AOPP levels of anxiety group and non-anxiety group were significantly higher than those of control group whereas GPx and SOD levels were lower than those of control group. This indicates that the oxidative stress response is significantly activated during acute cerebral infarction in patients with type 2 diabetes mellitus. Further analysis of the influence of anxiety on oxidative stress response in patients with acute cerebral infarction complicated by type 2 diabetes mellitus showed that serum MDA, ox-LDL and AOPP levels of anxiety group were significantly higher than those of non-anxiety group, but GPx and SOD levels were lower than those of non-anxiety group. This shows that both the generation of oxidative stress products and the consumption of antioxidant enzymes increase in patients combined with anxiety, which indicates that anxiety can aggravate the oxidative stress in patients with acute cerebral infarction complicated by type 2 diabetes mellitus.

The nerve function damage in the course of cerebral infarction is not only related to the direct damage effect of ischemia hypoxia, oxidative stress and other pathological links on the nerve cells, but is also associated with the excessive apoptosis induced by above pathological links\([16]\). Fas/FasL are the upstream molecules regulating death receptor apoptosis pathway, Fas is the tumor necrosis factor receptor superfamily member located in the cell membrane, which can identify and be combined with FasL to recruit the caspase family members through downstream FADD structural

### Table 3.

Comparison of serum apoptosis indexes among three groups of subjects.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>sFas</th>
<th>sFasL</th>
<th>Caspase-3</th>
<th>Bcl-2</th>
<th>Livin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety group</td>
<td>38</td>
<td>89.31±11.82 *</td>
<td>113.58±16.85 *</td>
<td>6.58±0.93 *</td>
<td>10.28±1.48 *</td>
<td>6.28±0.85 *</td>
</tr>
<tr>
<td>Non-anxiety group</td>
<td>52</td>
<td>68.62±8.47</td>
<td>76.59±9.38</td>
<td>3.57±0.52</td>
<td>18.68±2.32</td>
<td>9.39±1.13</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>22.47±3.85</td>
<td>35.12±4.86</td>
<td>1.02±0.15</td>
<td>32.36±5.82</td>
<td>15.47±1.93</td>
</tr>
</tbody>
</table>

*: compared with control group, \( P<0.05 \); *: compared with non-anxiety group, \( P<0.05 \).
domain, and then finally activate caspase-3 and cause apoptosis by caspase cascade reaction [17,18]. Bcl-2 and Livin are has anti-apoptotic molecules in the body, the former can reduce the release of mitochondrial cytochrome C to the cytoplasm so as to suppress the mitochondrial apoptosis pathways, and the latter can be combined with a variety of caspase and hinder their activation way to inhibit mitochondrial apoptosis pathways, and the latter can be combined with apoptotic molecules in the body, the former can reduce the release of sFas, sFasL and Caspase-3 levels of anxiety group and non-anxiety group were significantly higher than those of control group whereas Bcl-2 and Livin levels were lower than those of control group. This indicates that the apoptosis is significantly increased in the process of acute cerebral infarction in patients with type 2 diabetes mellitus. Further analysis of the influence of anxiety on apoptosis in patients with acute cerebral infarction complicated by type 2 diabetes mellitus showed that serum sFas, sFasL and Caspase-3 levels of anxiety group and non-anxiety group were significantly higher than those of non-anxiety group whereas Bcl-2 and Livin levels were lower than those of non-anxiety group. This indicates that the generation of pro-apoptotic molecules increases whereas the generation of anti-apoptotic molecules decreases in patients combined with anxiety, which indicates that anxiety can aggravate the apoptosis in patients with acute cerebral infarction complicated by type 2 diabetes mellitus.

Anxiety has aggravating effect on the nerve injury and oxidative stress response in patients with acute cerebral infarction complicated by type 2 diabetes mellitus, and causes adverse effect on the outcome of the disease.

References