Effect of gangliosides combined with hyperbaric oxygenation on neural functional recovery and oxidative stress injury after cerebral infarction intervention

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Objective: To explore the effect of gangliosides combined with hyperbaric oxygenation on neural functional recovery and oxidative stress injury after cerebral infarction intervention.

Methods: A total of 120 patients with cerebral infarction who received interventional therapy in our hospital between August 2013 and February 2016 were collected and divided into control group and observation group, 60 cases in each group. Control group received hyperbaric oxygenation after intervention, and the observation group received gangliosides combined with hyperbaric oxygenation after intervention. The differences in serum levels of neurotrophy indexes, nerve injury indexes and oxidative stress indexes were compared between two groups of patients before and after treatment. Results: Before intervention, differences in serum levels of neurotrophy indexes, nerve injury indexes and oxidative stress indexes were not statistically significant between two groups of patients. After intervention, serum neurotrophy indexes BDNF and NT-3 levels in observation group were higher than those in control group; serum nerve injury indexes S100B, NGB, NSE and GFAP levels were lower than those in control group; serum oxidative indexes MDA, MPO and LPO levels were lower than those in control group while antioxidant indexes SOD, GSH-Px, CAT and TAC levels were higher than those in control group. Conclusion: Gangliosides combined with hyperbaric oxygenation for patients with cerebral infarction after interventional therapy helps speed up the neural functional recovery and also reduce systemic inflammatory response.

1. Introduction

Acute cerebral infarction is caused by multiple factors-induced cerebral artery lumen stenosis or occlusion in a short period of time, it can lead to ischemic hypoxic injury of brain tissue in corresponding blood-supply area, and severe cases can lead to irreversible neuron apoptosis and permanent nerve dysfunction[1,2]. The cerebral vascular thrombosis and the cerebral blood circulation blocking make it difficult for normal intravenous treatment to achieve effective thrombolysis, so interventional thrombolysis has become one of the common methods for the treatment of acute cerebral infarction[3,4]. The main cause of nerve injury is the ischemia reperfusion injury after thrombolysis, and how to effectively protect the brain function after intervention has also become the focus of current clinical research. Hyperbaric oxygen is the common method to treat ischemic cerebral infarction, it can stimulate the ischemic neurons to recover normal function, but the hyperbaric oxygen therapy alone has some limitations in improving patients' brain function. Ganglioside is an important substance to maintain the stability of the neuron membrane, many scholars have currently recommended adding exogenous ganglioside to optimize the neuron function, and it is expected to become an effective auxiliary method for clinical treatment of acute cerebral infarction[5,6]. In this study, ganglioside combined with hyperbaric oxygen was added in the treatment of patients with cerebral infarction after interventional therapy, and the specific clinical value was explored from neural functional recovery, oxidative stress injury and other aspects.

2. Information and methods

2.1 Case information

A total of 120 patients with cerebral infarction who received interventional therapy in our hospital between August 2013 and February 2016 were selected as research subjects, and patients' families signed informed consent. Random number table was used to divide the enrolled patients into control group and observation...
group, 60 cases in each group. Control group included 33 men and 27 women that were 49-78 years old; observation group included 35 men and 25 women that were 51-79 years old. The differences in gender and age distribution were not significant between the both groups \( (P>0.05) \), and the hospital ethics committee approved the study.

### 2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with cerebral infarction by head MRI; (2) the interval between onset and hospitalization 6 h; (3) surviving after treatment. Exclusion criteria: (1) with history of cerebral infarction, brain hemorrhage and traumatic brain injury; (2) combined with cerebrovascular malformation, Alzheimer's disease, Parkinson's disease and other neurological disorders; (3) combined with systemic infectious diseases.

### 2.3 Therapy

Control group of patients received hyperbaric oxygen therapy after intervention, specifically as follows: mask was used for oxygen uptake, the pressure was set to 0.1-0.2 MPa, the pressure was increased for 15 min, they received oxygen uptake for 20min each of three time periods under stable voltage, they took rest for 5 min after single oxygen uptake under stable voltage, the pressure was decreased for 15 min, and three times of oxygen uptake lasted for a total of 100 min, 1 time/d, for continuous treatment of 10 d.

Observation group of patients received ganglioside combined with hyperbaric oxygen therapy after intervention, specifically as follows: hyperbaric oxygen therapy was the same as that of control group of patients, they received intravenous drip of GM1 Ganglioside (Qilu Pharmaceutical Co., Ltd., approved by H20046213) at the same time, 40 mg was added in saline 250 mL and mixed, 1 time/d, for consecutive 14 d.

### 2.4 Nerve function indexes

Before and after treatment, 3.0 mL of cubital venous blood was extracted from two groups of patients, anti-coagulated and then centrifuged at low speed to take the supernatant, enzyme-linked immunosorbent assay (ELISA) was used to determine the neurotrophy indicators brain-derived neurotrophic factor (BDNF) and neurotrophic factor 3 (NT-3) levels as well as nerve injury indicators brain-derived neurotrophic factor (BDNF), catalase (CAT), and total antioxidant capacity (TAC).

### 2.5 Oxidative stress indexes

Before and after treatment, peripheral blood serum was obtained from two groups of patients in the same way, and ELISA was used to detect the contents of oxidative stress indicators, including oxidation indicators malondialdehyde (MDA), myeloperoxidase (MPO) and lipid peroxide (LPO) as well as anti-oxidation indexes superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), catalase (CAT) and total antioxidant capacity (TAC).

### 2.6 Statistical processing

Statistical software was SPSS 21.0, and the statisticians passed the professional exam. Nerve protection indexes, nerve injury indexes and oxidative stress indexes belong to measurement data and were in terms of mean ± standard deviation, and the comparison was by t test. Statistics \( P<0.05 \) was the standard of statistical significance in differences.

### 3. Results

#### 3.1 Neurotrophy indicators

Comparison of serum neurotrophy indicators BDNF and NT-3 levels between two groups of patients before and after treatment was as follows: differences in serum BDNF and NT-3 levels were not statistically significant between two groups of patients before \( (P>0.05) \); after treatment, serum BDNF and NT-3 levels in both groups increased, serum BDNF and NT-3 levels in observation group were higher than those in control group, and the differences were statistically significant \( (P<0.05) \), shown in Table 1.

#### 3.2 Nerve injury indexes

Comparison of serum nerve injury indexes S100B (pg/mL), NGB (pg/mL), NSE (ng/mL) and GFAP (pg/mL) levels between two groups of patients before and after treatment was as follows: differences in serum S100B, NGB, NSE and GFAP levels were not statistically significant between two groups of patients before treatment \( (P>0.05) \); after treatment, serum S100B, NGB, NSE and specific enolase (NSE) and glial fibrillary acidic protein (GFAP) levels.

### Table 1.

Comparison of serum nerve injury index levels between two groups of patients before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>S100B</th>
<th>NGB</th>
<th>NSE</th>
<th>GFAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>1.26±0.18</td>
<td>231.84±27.95</td>
<td>28.94±3.37</td>
<td>23.71±2.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.89±0.09</td>
<td>129.37±15.88</td>
<td>17.63±2.18</td>
<td>16.53±2.11</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>1.24±0.17</td>
<td>230.66±28.61</td>
<td>28.65±3.19</td>
<td>23.52±2.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.47±0.06*</td>
<td>71.64±8.99*</td>
<td>11.57±1.94*</td>
<td>9.73±1.04*</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \(^* P<0.05 \); compared with control group after treatment, \(^* P<0.05 \).

### Table 2.

Comparison of serum neurotrophy indicator levels between two groups of patients before and after treatment (pg/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>BDNF</th>
<th>NT-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before treatment</td>
<td>21.37±2.88</td>
<td>3.28±0.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>30.68±3.52</td>
<td>4.71±0.52</td>
</tr>
<tr>
<td>Observation group</td>
<td>60</td>
<td>Before treatment</td>
<td>21.64±2.79</td>
<td>3.26±0.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>41.37±4.96*</td>
<td>5.88±0.73*</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \(^* P<0.05 \); compared with control group after treatment, \(^* P<0.05 \).
and GFAP levels in both groups decreased, serum S100B, NGB, NSE and GFAP levels in observation group were lower than those in control group, and the differences were statistically significant (P<0.05), shown in Table 2.

### 3.3 Oxidative stress indexes

Comparison of serum oxidative stress indexes MDA (nmol/mL), MPO (μmol/L), LPO (μmol/L), SOD (U/mL), GSH-Px (U/mL), CAT (U/mL) and TAC (U/mL) levels between two groups of patients before and after treatment was as follows: differences in serum MDA, MPO, LPO, SOD, GSH-Px, CAT and TAC levels were not statistically significant between two groups of patients before treatment (P>0.05); after treatment, serum oxidation indexes MDA, MPO and LPO levels in both groups decreased while anti-oxidation indexes SOD, GSH-Px, CAT and TAC levels increased, serum oxidation indexes MDA, MPO and LPO levels in observation group were lower than those in control group while anti-oxidation indexes SOD, GSH-Px, CAT and TAC levels were higher than those in control group, and differences were statistically significant (P<0.05), shown in Table 3.

### 4. Discussion

Interventional thrombolysis is one of the most reliable ways to treat patients with acute cerebral infarction within time window, it can effectively recanalize infarction vessel and restore blood supply of ischemic foci, but there is the problem of nerve tissue ischemia-reperfusion injury after recanalization. When cerebral ischemia reperfusion occurs, the suddenly increased oxygen infusion can lead to massive generation of oxygen free radicals, lead to oxidation reaction of unsaturated fatty acid on cell membrane, phospholipid degradation denaturation, concentrate, and finally end up with cell necrosis[7,8]. How to reduce the ischemia reperfusion injury of the brain tissue after intervention and positively protect nerve function is the focus and difficulty of current clinical research.

Hyperbaric oxygen is the most common adjuvant therapy after acute cerebral infarction surgery, it has been confirmed to be able to reduce local cerebral edema, lower intracranial pressure, stimulate the ascending reticular activating system and so on, and the specific mechanisms are directly related to its effects on increasing oxygen metabolism, reducing acid metabolite formation, strengthening phagocyte function and so on. The effect of hyperbaric oxygen on recovering brain function has been confirmed, but it is also obvious that hyperbaric oxygen therapy alone has limitations in protecting brain function, so many scholars recommend adding other auxiliary treatments to enhance the overall curative effect. Endogenous ganglioside is the component of human body cell membrane, it shoulders the role for maintaining the nerve cell membrane Na+-K+-ATPase activity, ganglioside content decreases in patients with cerebral infarction, and it is one of the important causes of neuron damage[9,10]. Given the important function of endogenous ganglioside, adding exogenous ganglioside has become the reliable way to optimize nerve function.

In the study, exogenous ganglioside was added on the basis of postoperative hyperbaric oxygen therapy, and its application value was discussed from the nerve function, oxidative stress and other aspects. BDNF and NT-3 are both neurotrophic factors that contribute to the regeneration of injured myelin sheath, the repair of neuronal function and so on, and the levels of BDNF and NT-3 are closely related to patient's prognosis[11]. In the study, serum BDNF and NT-3 levels were compared between the two groups of patients, and it was found that compared with those before treatment, serum BDNF and NT-3 levels in both groups increased after treatment, indicating that both treatments are effective; further compared with control group, the observation group of patients were with higher serum BDNF and NT-3 levels after treatment, indicating that adding exogenous ganglioside on the basis of hyperbaric oxygen therapy can further increase contents of neurotrophic factors and accelerate nerve repair, and it is an important symbol of neural function optimization.

When nerve damage occurs, a variety of molecules that are specifically expressed in nerve tissue can abnormally appear in circulating blood and can be used to quantify the degree of nerve damage. Specific high expression of S100B is discovered in various nervous system disorders, and it recruits cellular inflammatory mediators to regulate extracellular signal[12]. NGB is a member of the oxyglobulin family, it is highly expressed in the brain and has extremely high oxygen affinity, and the experiment in vitro shows that NGB expression in the brain tissue increases in the case of hypoxia[12]. NSE and GFAP are specifically expressed in the myelin sheath, it is released into the extracellular area early after nerve injury and enters into the peripheral blood through the damaged blood brain barrier, and their levels are consistent with the degree of nerve injury[13,14]. In the study, serum levels of these nerve injury indexes were compared between two groups of patients, and it was found that compare with those before treatment, serum S100B, NGB, NSE and GFAP levels in both groups decreased after treatment; compared with the control group, the observation group were with lower serum
S100B, NGB, NSE and GFAP levels after treatment, and the results showed that adding exogenous ganglioside can effectively reduce the degree of nerve damage. Exogenous ganglioside can cross through the blood brain barrier and embedded in damaged neurons so as to stabilize cell membrane, inhibit calcium influx, reduce water content in nerve cells, block the neurotoxicity of excitatory amino acids, and so on, and this is also the core mechanism for it to inhibit further nerve damage and protect nerve function.

The core mechanism of ischemia-reperfusion injury is local cerebral and systemic oxidative stress response, the accumulation of a large number of oxide metabolites and the damage to the structure of neurons as well as the inhibition of antioxidant system function all lead to direct neuron dysfunction and further nerve injury[15,16]. MDA, MPO and LPO are all oxidative metabolites with strong oxidative destruction effect; SOD, GSH-Px, and CAT are the typical antioxidants that can neutralize excessive oxygen free radicals and reduce oxidative damage, and TAC represents the body's overall antioxidant capacity[17,18]. In the study, serum levels of oxidative stress indexes were compared between two groups of patients before and after treatment, and it was found that compared with those before treatment, serum oxidation indexes MDA, MPO and LPO in both groups were lower while anti-oxidation indexes SOD, GSH-Px, CAT and TAC level were higher after treatment; further compared with control group, the observation group of patients were with lower levels of serum oxidation indexes MDA, MPO and LPO, and higher levels of anti-oxidation indexes SOD, GSH-Px, CAT and TAC after treatment, confirming that adding exogenous ganglioside can effectively suppress the oxidative stress reaction, and this is also one of the important mechanisms for it to exert neuroprotective effect.

After cerebral infarction intervention, ganglioside combined with adjuvant hyperbaric oxygen therapy can effectively exert neuroprotective effect and also positively the oxidative stress injury of nerve tissue, it is expected to become the important way to optimize the long-term treatment outcome in patients with acute cerebral infarction, and it is worthy of popularization and application in clinical practice in the future.

References


