Observation on the therapeutic effect of aspirin in combined with ozagrel sodium in the treatment of acute cerebral infarction

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ABSTRACT

Objective: To evaluate the changes in serum index levels after monosialoganglioside injection combined with conventional treatment of neonatal hypoxic ischemic encephalopathy. Methods: A total of 70 children with neonatal hypoxic ischemic encephalopathy treated in our hospital between February 2013 and February 2016 were selected and randomly divided into observation group and control group, control group received clinical routine treatment and observation group accepted monosialoganglioside injection combined with conventional treatment. After 1 week of treatment, serum levels of apoptosis factors, nerve function indexes, oxidation/anti-oxidation indexes and disease severity indexes of two groups of patients were detected. Results: Serum PDCD5, sFas, sFasL, NSE, S100-β, MDA, NO, NOS, H-FABP, NPY, caspase-1 and ET-1 levels of observation group were lower than those of control group while BDNF, NGF, SOD, GSH-PX, IGF-1 and GH levels were higher than those of control group. Conclusion: Monosialoganglioside injection can enhance the overall treatment effect and promote the realization of homeostasis in children with HIE.

1. Introduction

Neonatal hypoxic ischemic encephalopathy (HIE) is with serious consequences, relevant statistics show that the disease mortality rates is as high as 10%-20%, and about 25% of survived children can develop permanent nerve hypoplasia[1,2]. How to improve the effect of HIE treatment and optimize treatment outcome has been the key point of the clinical pediatrics research, the current "three maintenance" and "three symptomatic" therapy has been used as routine means in the treatment of HIE, but many scholars suggest that the targeted drugs should be added to further protect the brain function and inhibit nerve cell apoptosis. It is found after monosialoganglioside application in rat models with brain injury that the drug can play a positive role in brain protection and homeostasis, and even help to promote the regeneration of the damaged neurons, and therefore, many scholars recommend it as auxiliary drug for HIE treatment at present[3,4]. In order to clear the effect of monosialoganglioside on the conditions of children with HIE, it was combined with conventional treatment, added the treatment of children with HIE in our hospital, and mainly studied from the serum levels of apoptosis factors, nerve function indexes, oxidation/anti-oxidation indexes and disease severity indexes.

2. Information and methods

2.1 General information

Inclusion criteria: (1) With brain damage confirmed by CT examination, and complying with the diagnostic criteria for neonatal hypoxic ischemic encephalopathy (HIE) established by world health organization (WHO); (2) Not associated with other severe congenital viscera dysfunction; (3) Children’s families understood the research process and signed informed consent; (4) Approved by the hospital ethics committee. Exclusion criteria: (1) With congenital cerebral vascular dysfunction; (2) Children dropped out of treatment or family members voluntarily gave up treatment; (3) With incomplete clinical information. 70 children with neonatal
hypoxic ischemic encephalopathy treated in our hospital between February 2013 and February 2016 conformed to the above criteria and were divided into observation group and control group (n=35) according to random number table. Control group included 19 male cases and 16 female cases, the gestational age was 35-41 weeks and (37±3) weeks in average, the birth weight was 2.31-3.87 kg and (2.78±0.41) kg in average, and the disease grading was: 12 cases with mild degree, 17 cases with moderate degree and 6 cases with severe degree; observation group included 18 male cases and 17 female cases, the gestational age was 34-42 weeks and (37±3) weeks in average, the birth weight was 2.35-3.81 kg and (2.76±0.45) kg in average, and the disease grading was: 14 cases with mild degree, 16 cases with moderate degree and 5 cases with severe degree. Two groups of children were not statistically different in the distribution of gender, gestational age, birth weight and disease severity (P>0.05), and they were comparable.

2.2 Treatment methods

Control group received routine clinical HIE therapy, including controlling convulsion, reducing intracranial pressure, maintaining blood glucose and normal ventilation, etc. Observation group accepted regular + monosialoganglioside injection treatment, which was as follows: monosialoganglioside 20 mg was dissolved in 20 mL of 10% glucose liquid, the solution was by slow intravenous drip, 1 time/d and 7 d was a course of treatment.

2.3 Serum indexes

After 1 week of treatment, 1 ml of umbilical venous blood was collected from both groups at the same time and date to get supernatant, and the specific detection indexes were as follows: (1) The apoptosis factors: ELISA double-antibody sandwich method was used to determine programmed cell death 5 (PCDC5), soluble Fas (sFas) and soluble Fas ligand (sFasL) levels; (2) The nerve function indexes: brain-derived neurotrophic factor (BDNF), neuron-specific enolase (NSE), S100-β protein (S100-β) and nerve growth factor (NGF); (3) The oxidation/anti-oxidation indexes: superoxide dismutase (SOD), malondialdehyde (MDA), nitric oxide (NO), nitric oxide synthase (NOS) and superoxide dismutase (GSH-PX); (4) The disease severity indexes: heart-type fatty acid-binding protein (H-FABP), neuropeptide Y (NPY), insulin growth factor 1 (IGF-1), growth hormone (GH), cysteine protease-1 (caspase-1) and endothelin-1 (ET-1).

2.4 Statistical methods

Data in the study was input in software SPSS 23.0, measurement data was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Apoptosis factors

After 1 week of treatment, comparison of serum apoptosis factors PDCD5, sFas and sFasL levels between two groups of patients was as follows: serum PDCD5, sFas and sFasL levels of observation group were significantly lower than those of control group. Differences in serum apoptosis factors PDCD5, sFas and sFasL levels were statistically significant between two groups of patients after 1 week of treatment (P<0.05), shown in Table 1.

Table 1.

Comparison of serum apoptosis factor levels between two groups of patients after treatment (μg/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>PDCD5</th>
<th>sFas</th>
<th>sFasL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>35</td>
<td>6.12±0.72</td>
<td>11.37±1.74</td>
<td>2.16±0.28</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>11.89±1.66</td>
<td>19.68±2.42</td>
<td>4.05±0.53</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>8.293</td>
<td>7.475</td>
<td>5.861</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.2 Nerve function indexes

After 1 week of treatment, comparison of serum nerve function indexes BDNF (ng/L), NSE (ng/L), S100-β (μg/L) and NGF (μg/L) between two groups of patients was as follows: serum BDNF and NGF levels of observation group were significantly higher than those of control group while NSE and S100-β levels were significantly lower than those of control group. Differences in serum nerve function indexes BDNF, NSE, S100-β and NGF levels were statistically significant between two groups of patients after 1 week of treatment (P<0.05), shown in Table 2.

Table 2.

Comparison of serum nerve function index levels between two groups of patients after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>BDNF</th>
<th>NSE</th>
<th>S100-β</th>
<th>NGF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>35</td>
<td>1 823.85±201.77</td>
<td>9.34±0.91</td>
<td>1.18±0.19</td>
<td>143.28±15.09</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>1 396.21±150.65</td>
<td>14.57±1.98</td>
<td>2.37±0.31</td>
<td>121.45±13.28</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>12.843</td>
<td>7.392</td>
<td>5.382</td>
<td>8.093</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.3 Oxidation/anti-oxidation indexes

After 1 week of treatment, comparison of serum oxidation/anti-oxidation indexes SOD (U/L), MDA (mol/L), NO (μmol/L), NOS (U/mL) and GSH-PX (U/mL) between two groups of patients was as follows: serum SOD and GSH-PX levels of observation group were significantly higher than those of control group while MDA, NO and NOS levels were significantly lower than those of control group.
Comparison of serum disease severity index levels between two groups of patients after treatment.

Table 4.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>H-FABP (μg/L)</th>
<th>NPY (ng/L)</th>
<th>IGF-1 (μg/L)</th>
<th>GH (μg/L)</th>
<th>caspase-1 (μg/L)</th>
<th>ET-1 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>35</td>
<td>284.93±40.12</td>
<td>63.28±7.01</td>
<td>85.38±9.01</td>
<td>11.03±1.76</td>
<td>8.84±0.93</td>
<td>70.27±8.05</td>
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<tr>
<td>Control</td>
<td>35</td>
<td>341.85±40.17</td>
<td>88.59±9.12</td>
<td>72.45±8.11</td>
<td>9.63±0.97</td>
<td>12.01±1.87</td>
<td>82.16±8.05</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Differences in serum oxidation/anti-oxidation indexes SOD, MDA, NO, NOS and GSH-PX levels were statistically significant between two groups of patients after 1 week of treatment (P<0.05), shown in Table 3.

3.4 Disease severity indexes

After 1 week of treatment, comparison of serum disease severity indexes H-FABP (ng/L), NPY (ng/L), IGF-1 (μg/L), GH (μg/L), caspase-1 (μg/L) and ET-1(ng/L) levels between two groups of patients was as follows: serum H-FABP, NPY, caspase-1 and ET-1 levels of observation group were significantly lower than those of control group while IGF-1 and GH levels were significantly higher than those of control group. Differences in serum disease severity indexes H-FABP, NPY, IGF-1, GH, caspase-1 and ET-1 levels were statistically significant between two groups of patients after 1 week of treatment (P<0.05), shown in Table 4.

4. Discussion

The occurrence of neonatal hypoxic ischemic encephalopathy (HIE) involves the excitatory amino acid toxicity effect, intracellular calcium overload, oxygen free radical damage, cell apoptosis and other links after local tissue ischemia hypoxia, maintaining ventilation, circulation and blood glucose levels, controlling convulsions, reducing intracranial pressure and other measures in conventional treatment can slow down disease progression, but they cannot reverse the existing nerve injury and dysfunction, and their role is limited in lowering long-term limb dysfunction, hypophrenia and other complications[5,6]. Looking for reasonable drugs to really improve the injured nervous tissue function and promote the nerve regeneration is the focus of current research and treatment of HIE, and monosialoganglioside is considered as a new way to enhance the curative effect of HIE for its role in stabilizing internal environment, optimizing neural function and so on[7]. Study of LOU Yu-xia[8] has confirmed that the monosialoganglioside can improve the CT imaging and improve the overall treatment effectiveness, the drug was used as an adjuvant drug in the study and applied in children with HIE in our hospital, and the effect of monosialoganglioside was specifically studied from the perspective of serological indexes.

Cell apoptosis and local nerve injury caused by ischemia hypoxia is the basis of the occurrence and development of HIE, programmed cell death 5 (PDCD5), soluble Fas (sFas) and soluble Fas ligand (sFasL) are the recognized pro-apoptotic factors, and it was found in the study that serum PDCD5, sFas and sFasL levels of observation group were lower after 1 week of treatment, indicating that the nerve cell apoptosis of the group declines after treatment, and monosialoganglioside has anti-nerve apoptosis effect. Many studies have shown that monosialoganglioside can reduce the release of excitatory amino acids, this type of amino acids can directly kill nerve cells, so it was speculated that that monosialoganglioside exerts the anti-nerve cell apoptosis effect through the pathway[9,10]. Nerve cell apoptosis will directly result in neural function damage in children with HIE, and serum levels of brain-derived neurotrophic factor (BDNF), neuron-specific enolase (NSE), S100- β protein (S100- β ), nerve growth factor (NGF) and other neural function-related parameters were further detected in the study. Both BDNF and NGF can nourish nerves, prompt neural axon growth, etc., and their levels significantly decrease in children with HIE and are the direct markers of nerve function injury[11,12]. Serum NSE and S100- β levels are very low in physiological state, they only exist in the nerve cells, they are released out of the cells in the case of neuron injury and enter into the peripheral blood through the blood brain barrier, and the content changes are detected[13]. It was found in the study that after 1 week of treatment, serum BDNF and NGF levels of observation group were higher while NSE and S100- β levels were lower, indicating that monosialoganglioside has neurotrophic effect, and it can promote nerve regeneration and reduce nerve cell damage.

Calcium overload within neurons as well as the resulting oxygen free radical damage has been one of the important causes of HIE.
aggravation and nerve injury expansion, and effectively removing the oxygen free radicals in children is one of the keys to HIE treatment[14]. It has been confirmed in a variety of other diseases that monosialoganglioside can scavenge oxygen free radicals, and oxidation/anti-oxidation index levels of two groups of children were tested in the study, and it was found that oxidation indexes MDA, NO and NOS levels of observation group were lower while anti-oxidation indexes SOD and GSH-PX levels were higher, indicating that the oxidation/anti-oxidation balance system is optimized after treatment. In addition to cell apoptosis, nerve injury and oxidation/anti-oxidation, there are also many factors directly correlated with the disease in children with HIE, including the heart-type fatty acid-binding protein (H-FABP), neuropeptide Y (NPY), insulin growth factor 1 (IGF-1), growth hormone (GH), cysteine protease-1 (caspase-1), endothelin 1 (ET-1), etc. H-FABP is involved in fatty acid transport inside the cells and it is immediately released from the inside of cells into the blood circulation after cell injury[15]. NPY exists in the sympathetic nerve endings, it can be massively released and exert vasoconstrictor effect when the body is in a stress state, and it can further aggravate ischemia hypoxia in children with HIE. IGF-1 and GH have protective effect on HIE damage, and can reduce cerebral vascular resistance, inhibit oxidase toxicity and prevent nerve cell apoptosis[16]. It is found that caspase-1 can increase I content rises. ET-1 can activate calcium channel and promote calcium influx. It is found in the study that monosialoganglioside can lower serum H-FABP, NPY, caspase-1 and ET-1 levels and significantly increase the IGF-1 and GH levels in children with HIE, and its effect is significant on optimizing the overall illness.

To sum up, it is concluded as follows: monosialoganglioside injection can enhance the overall treatment effect and promote the realization of homeostasis in children with HIE, and it’s worth popularization and application in clinical practice in the future.

References


