The influence of immunomodulator on the immunoglobulin and T cell subsets in children with intractable epilepsy

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ABSTRACT

Objective: To observe the influence of immunomodulator on the immunoglobulin and T cell subsets in children with intractable epilepsy. Method: A total of 82 children with intractable epilepsy in our hospital were selected and randomly divided into 2 groups: the control group (41 cases) and the observation group (41 cases). Routine antiepileptic drugs were given to the control group (41 cases) and the observation group (41 cases). The medication regimen was that more than 2 kinds of antiepileptic drugs were combined used. But the immunomodulator wasn't used. Treatment of immune globulin was given to the control group on the basis of observation group. By taking the 400 mg/kg/d as the standard of dosage, for 5 d every course of treatment. One course of treatment was carried out every month, 3 months in total. The changes of IgA, IgG, IgM and CD3+, CD4+, CD8+, CD4+/CD8+ were compared in 2 groups before and after treatment. Result: The comparison of IgA, IgG, IgM in the two groups before treatment was not statistically significant. After treatment, IgA, IgG in observation group were significantly higher than that before treatment and the difference was statistically significant. However, there was no significant difference on the IgM. There was no significant difference on the IgA, IgG in the control group compared with that before treatment. IgA, IgG in observation group was significant higher than that in the control group. The comparison of IgM between 2 groups was not statistically significant. The comparison of CD3+, CD4+, CD8+, CD4+/CD8+ in the two groups before treatment was not statistically significant. After treatment, CD3+, CD4+, CD8+, CD4+/CD8+ in observation group were significantly higher than that before treatment; CD8+ in observation group was significantly lower than that before treatment. The difference was statistically significant. Conclusion: Compared with using routine antiepileptic drugs, application of immune globulin as an immunomodulator combined with conventional antiepileptic drug in children with refractory epilepsy can effectively improve the expression of IgA, IgG, IgM and T cell subsets, which has a positive effect on the immune function of the children.

1. Introduction

Epilepsy is a chronic disease of the nervous system, which is also a common disease in children when their nervous system development[1,2]. Although the standard treatment can effectively alleviate and control the majority of children's condition[3]. There are still about 20%-30% of children with poor epilepsy drug response and treatment effect. This situation is called intractable epilepsy[4]. Because of the own disease and their long term use of anti epileptic drugs, children with intractable epilepsy often has abnormal immune function[5,6]. Related studies have confirmed the feasibility
of immunoglobulin therapy in epilepsy[7]. Therefore, this study used immunoglobulin in the treatment of children with refractory epilepsy. Then, we observe its effect on the immune function of the children. The result was satisfied, which was reported as follow.

2. Objects and methods

2.1 Object

A total of 82 cases of children with intractable epilepsy in our hospital from June 2013 to June 2016 were selected as research objects. Inclusion criteria: (1) Meet the diagnostic criteria of refractory epilepsy in children[8]. (2) Non tumor and other neurodegenerative diseases were confirmed by CT or MRI examination. (3) Approved by the ethics committee of our hospital, and the children and their families signed the informed consent. Exclusion criteria: (1) With inherited metabolic diseases. (2) With immunodeficiency, asthma, nephrotic syndrome and other diseases that affect the immune system. (3) With recent infection or history of taking immunosuppressive drugs. There are 45 boys and 37 girls in the 82 children. They were 3-13 years old, with an average age of seven. Among them, there are 24 cases with generalized seizures, 20 cases with simple partial seizure, 19 cases with partial seizure generalization, 19 cases with complex partial seizures. According to the order number, we use SPSS 19.0 statistics software to generate random number, coding and assigning randomly. According to the proportion of 1:1, 82 cases were divided into observation group (41 cases) and control group (41 cases). Compared with the gender, age and other clinical data, we found no statistical difference.

2.2 Treatment method

Routine antiepileptic drugs were given to the control group. Medication regimen was that more than 2 kinds of anti epileptic drugs were be combined used. But the immunomodulator wasn’t used. Treatment of immunoglobulin (produced by Shanghai RAAS blood products Co., Ltd., 2.5 g/50 mL) was given to the control group on the basis of observation group. By taking the 400 mg/kg/d as the standard of dosage, for 5 d every course of treatment. One course of treatment was carried out every month, 3 months in total.

2.3 Observation indexes

Fasting peripheral venous blood of children in two groups were collected before and after treatment. And then, the sample was placed to 4 °C refrigerator to be measured. IgA, IgG, IgM were detected by immune turbidity method. CD3+, CD4+, CD8+, CD4+/CD8+ were detected by flow cytometry.

2.4 Statistical Methods

SPSS 19.0 statistical package was conducted for statistical analysis. Measurement data were described as Mean ± SD with variance analysis ,inter-group comparison was conducted by t test, values of P<0.05 were considered to be statistically significant.

3. Results

3.1 Comparison of immune globulin in the two groups

The comparison of IgA, IgG, IgM in the two groups before treatment was not statistically significant (P>0.05). After treatment, IgA, IgG in observation group were significantly higher than that before treatment and the difference was statistically significant (P<0.05). However, there was no significant difference on the IgM (P>0.05). There was no significant difference on the IgA, IgG, IgM in the control group compared with that before treatment (P>0.05). After treatment, the IgA, IgG of children in the observation group were (0.97±0.41) g/L and (8.63±2.41) g/L, which were higher than that in control group. The difference was statistically significant (P<0.05). The comparison of IgM between 2 groups was not statistically significant (P>0.05)

Table 1.
Comparison of immune globulin in the two groups (g/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>IgA</th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>0.52±0.21</td>
<td>5.68±2.21</td>
<td>1.05±0.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.97±0.41</td>
<td>8.63±2.41</td>
<td>1.06±0.35</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>0.51±0.20</td>
<td>5.69±2.16</td>
<td>1.07±0.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.54±0.19</td>
<td>5.65±2.17</td>
<td>1.07±0.34</td>
</tr>
</tbody>
</table>

Note: compared with control group before treatment, aP<0.05; compared with control group after treatment, bP<0.05.

3.2 Comparison of T cell subsets in the two groups

The comparison of CD3+, CD4+, CD8+, CD4+/CD8+ in the two groups before treatment was not statistically significant (P>0.05). After treatment , CD3+, CD4+, CD4+/CD8+ in observation group were significantly higher than that before treatment; CD8+ in observation group was significantly lower than that before treatment. The difference was statistically significant (P<0.05). There was no significant difference on the CD3+, CD4+, CD8+, CD4+/CD8+ in the control group compared with that before treatment (P>0.05). CD3+, CD4+, CD4+/CD8+ in observation group were (0.77±0.19), (0.52±0.21) and (1.70±0.31) which were significant higher than that in the control group. CD8+ in observation group was (0.27±0.16).
which was significant lower than that in the control group. The difference was statistically significant \( (P<0.05) \).

### 4. Discussion

Epilepsy is a chronic neurological disease. Its incidence in the general population is about 5\% \[9\]. Epilepsy is more common in children, which is a common disease that affects the development of nervous system in children \[10\]. The nature of epileptic seizures can be induced by excessive ultra synchronized discharges of neurons in the brain, which cause transient dysfunction of the brain \[11\]. Most children with epilepsy can be controlled and regulated by timely and standardized treatment \[3\]. There are still about 20%-30% of children with poor epilepsy drug response and treatment effect. This situation is called intractable epilepsy \[4\]. Children is in the key stage of growing, which makes pediatric epilepsy a special field \[12\]. The pathogenesis of refractory epilepsy is more complex \[13\]. The impact on the life, development and growth of children is more serious. So it is urgent to improve the treatment effect of children with refractory epilepsy.

Because of the own disease and their long term use of anti-epileptic drugs, children with intractable epilepsy often has abnormal immune function \[5,6\]. In epileptic seizure, excessive discharge of neurons in brain makes ischemia and hypoxia of brain tissues, leading to nerve endocrine system disorders. And then, the regulating effect of neuroendocrine system also be influenced. So, abnormal immune function has been caused. In addition, frequent refractory epilepsy makes the body in a state of stress, which makes the body's endocrine change and affects the immune function \[14\]. Also, using antiepileptic drugs has a great side effect, which destroy the immune system \[15\].

The time of children with intractable epilepsy taking medicine is long, which makes a great harm of immune system.

Immune globulin is an important part of the immune system. They were generated by B lymphocytes. They can exert their immune function through exclusion of foreign antigens and specific antigen binding. IgA, IgG and IgM are the most typical immunoglobulin, which can reflect the immune function of the body \[16\]. In T cell subsets, CD3+ was whole blood mature T lymphocyte; CD4+ was assisted or induced T lymphocytes; CD8+ has a cytotoxic effect, which can kill the corresponding target cells. The decrease of CD4+/CD8+ indicates that the body is in the state of immune suppression. So the balance of CD4+/CD8+ ratio is the key to maintain the balance of the immune system \[17\]. Related studies have confirmed that immunoglobulin can treat epilepsy \[7\]. In this study, immunoglobulin was used as immune modulators for adjunctive therapy in the observation group. While conventional antiepileptic drug therapy was performed on the control group. The results showed that: before treatment, the comparison of IgA, IgG, IgM and CD3+, CD4+, CD8+ in the two groups before treatment was not statistically significant \( (P>0.05) \). After treatment, IgA, IgG in observation group were significantly higher than that before treatment; CD3+, CD4+, CD8+ in observation group were significantly higher than that before treatment. CD8+ in observation group was significantly lower than that before treatment. The differences were all statistically significant \( (P<0.05) \). So, we can see that the immune globulin can significantly improve the immune function in children with refractory epilepsy; There was no significant difference on the IgA, IgG, IgM and CD3+, CD4+, CD8+, CD4+/CD8+ in control group compared with that before treatment \( (P>0.05) \). So, we can see that antiepileptic drugs didn't have an obvious effect on the immune function of children with refractory epilepsy. IgA, IgG and CD3+, CD4+, CD8+, CD4+/CD8+ in observation group was significantly higher than that in the control group. CD8+ in observation group was significantly lower than that before treatment. The difference was statistically significant \( (P<0.05) \). It showed that the immune function of the observation group was significantly better than that of the control group after the application of immunoglobulin, and the above conclusions were consistent with the research of Zhou Xiaohong. The mechanism of antiepilepsy and improving immunity of immunoglobulin are as follows. Immunoglobulin, which induced the generation of cytokines or other humoral factors, has effect on the function of central nervous system and EEG. It regulates the response of central nervous system and the expression of III-2R in hippocampus and maintain the balance of immune neuro endocrine network by IL-2. So, the intensity of immune response in patients with epilepsy is reduced. Because of its good effect, quick effect and no damage to the immune system, it has been widely used in the medical field \[19,20\].

Compared with using routine antiepileptic drugs, application of immune globulin as an immunomodulator combined with

### Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CD3+</th>
<th>CD4+</th>
<th>CD8+</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>41</td>
<td>Before</td>
<td>0.48±0.16</td>
<td>0.31±0.13</td>
<td>0.37±0.09</td>
<td>0.92±0.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>After</td>
<td>0.77±0.19</td>
<td>0.52±0.21</td>
<td>0.27±0.16</td>
<td>1.70±0.31</td>
</tr>
<tr>
<td>Observation</td>
<td></td>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before</td>
<td>0.49±0.17</td>
<td>0.30±0.18</td>
<td>0.36±0.10</td>
<td>0.93±0.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: compared with control group before treatment, \( P<0.05 \); compared with control group after treatment, \( P<0.05 \).
conventional antiepileptic drug in children with refractory epilepsy can effectively improve the expression of IgA, IgG, IgM and T cell subsets, which has a positive effect on the immune function of the children. However, the sample of the study is small and the understanding of the immune modulator in the treatment of epilepsy is relatively simple. In the future, we should expand the sample size, and further explore the correlation between the immune system and the brain function.

Reference


