The evaluation value of the quantitative electroencephalogram for the prognosis of neonatal hypoxic ischemic encephalopathy and its relationship with serological indicators

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Objective: To study the evaluation value of the quantitative electroencephalogram (qEEG) for the prognosis of neonatal hypoxic ischemic encephalopathy (HIE) and its relationship with serological indicators.

Methods: 76 children with HIE who were born and treated in our hospital between April 2013 and February 2017 were collected as observation group, and 50 healthy newborns who were born in our hospital during the same period were collected as normal control group. qEEG parameter values of two groups of children were determined, serum levels of nerve injury indexes, nerve apoptosis indexes and oxidative stress indexes were compared between the two groups, and Pearson test was used to evaluate the inner link between qEEG parameter values and disease severity in children with HIE.

Results: qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values of observation group were significantly lower than those of normal control group. Serum NSE, NPY, S-100B and MBP contents in observation group were higher than those in normal control group; nerve apoptosis indexes sFas, sFasL and Caspase-3 contents were higher than those in normal control group while Bcl-2 content was lower than that in normal control group; serum oxidative stress indexes AOPP and MDA contents were higher than those in normal control group while SOD content was lower than that in normal control group. Pearson test showed that qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values in children with HIE were directly correlated with the contents of nerve injury indexes, nerve apoptosis indexes and oxidative stress indexes.

Conclusion: The qEEG parameter values in children with HIE are lower than those in normal children, and the specific values are closely related to the severity of the disease.

1. Introduction

Neonatal hypoxic ischemic encephalopathy (HIE) is the perinatal cerebral ischemic injury caused by asphyxia due to hypoxia, and it is currently the primary cause of neonatal cerebral palsy and mental retardation[1,2]. HIE severity is difficult to identify, which makes some children unable to receive effective treatment and is one of the important causes of poor prognosis. Quantitative electroencephalogram (qEEG) combines the mathematics and computer technology, quantizes the original EEG data, and is finally expressed in EEG power, frequency and other digital information. Previous studies have confirmed that qEEG parameter levels can be used for auxiliary judgment of the severity of Alzheimer’s disease, schizophrenia, depression and other neuropsychiatric diseases, and it has high accuracy and sensitivity[3,4]. In the study, qEEG was introduced in the detection of children with HIE, and the inner link between qEEG parameters and HIE severity was further determined in order to find more reliable way for subsequent HIE illness judgment, now reported as follows.
2. Information and methods

2.1 Case information

A total of 76 children with HIE who were born and treated in our hospital between April 2013 and February 2017 were collected as observation group, 50 healthy newborns who were born in our hospital during the same period were collected as normal control group, and family members of both groups of newborns signed informed consent. The gestational age at delivery of observation group was 38-41 weeks and (39.21±0.64) weeks in average, and the body mass at birth was 2.41-3.49 kg and (2.83±0.41) kg in average; the gestational age at delivery of control group was 37-41 weeks and (39.18±0.73) weeks in average, and the body mass at birth was 2.38-3.54 kg and (2.85±0.44) kg in average. The difference in gestational age at delivery and body mass at birth were not statistically significant between between the two groups of newborns (P>0.05), and the hospital ethics committee approved the study.

2.2 Diagnostic criteria for HIE

(1) with clear history of asphyxia due to hypoxia; (2) with severe asphyxia at birth; (3) with neurological symptoms such as awareness disorder, muscular tone change and abnormal primitive reflex; (4) frequent convulsions in severe cases.

2.3 Quantitative EEG examination

Routine EEG examination was performed before qEEG examination, the unipolar and bipolar of newborns were traced in the natural sleep, the international 10/20 lead was referred to install eight electrodes of Fp1, Fp2, C3, C4, T3, T4, O1 and O2, the display speed was 30 mm/s, and the tracing time was 20 min. On the basis of EEG, the brain electrical activity data of above electrode area were selected, the non-artifact segments of electroencephalogram (EEG) were selected and 30 s was as one sampling unit to calculate the mean power spectrum.

2.4 Serum indexes

0.5-1.0 mL of peripheral blood was extracted from the two groups of newborns, anti-coagulated and then centrifuged to get supernatant, which was frozen in a deep cryogenic freezer (Jinan Bohua Instrument Co., Ltd., article number MDF-1156ATN) for test. Electrochemiluminescence immunoassay was used to determine serum levels of nerve injury indexes, including neuron-specific enolase (NSE), neuropeptide Y (NPY), S-100B protein (S-100B) and myelin basic protein (MBP). Enzyme-linked immunosorbent assay was used to determine serum levels of nerve apoptosis indexes and oxidative stress indexes, including nerve apoptosis indexes Bcl-2, sFas, sFasL and Caspase-3 as well as oxidative stress indexes advanced oxidation protein products (AOPP), superoxide dismutase (SOD) and propionaldehydes (MDA).

2.5 Statistical processing

Personnel (one) who had statistical background recorded and calculated the data in the study, qEEG parameters, nerve injury indexes, nerve apoptosis indexes, oxidative stress indexes and other measurement data were in terms of mean ± standard deviation, and the comparison between groups was by grouping t test. Correlation analysis was by Pearson test. P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Quantitative electroencephalogram parameters

Comparison of qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values between two groups of newborns was as follows: qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values of observation group were significantly lower than those of normal control group. Differences in qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values were statistically significant between two groups of newborns (P<0.05), shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Fp1</th>
<th>Fp2</th>
<th>C3</th>
<th>C4</th>
<th>T3</th>
<th>T4</th>
<th>O1</th>
<th>O2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control group</td>
<td>50</td>
<td>502.13±67.92</td>
<td>472.82±53.69</td>
<td>459.37±52.17</td>
<td>463.28±51.28</td>
<td>409.26±48.12</td>
<td>388.28±42.17</td>
<td>509.28±63.27</td>
<td>512.47±59.66</td>
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<tr>
<td>Observation group</td>
<td>76</td>
<td>154.38±20.18</td>
<td>168.93±21.27</td>
<td>151.24±18.66</td>
<td>160.42±18.93</td>
<td>131.17±16.88</td>
<td>134.86±17.24</td>
<td>167.93±20.52</td>
<td>153.28±17.61</td>
</tr>
<tr>
<td>P</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>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 1.
Comparison of qEEG parameters between two groups of newborns.
3.2 Nerve injury indexes

Comparison of serum nerve injury indexes NSE (ng/mL), NPY (ng/L), S-100B (pg/mL) and MBP (μg/L) contents between two groups of newborns was as follows: serum NSE, NPY, S-100B and MBP contents in observation group were significantly higher than those in normal control group. Differences in serum nerve injury indexes NSE, NPY, S-100B and MBP contents were statistically significant between two groups of newborns (P<0.05), shown in Table 2.

Table 2.
Comparison of serum nerve injury index contents between two groups of newborns.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>NSE</th>
<th>NPY</th>
<th>S-100B</th>
<th>MBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>50</td>
<td>6.28±0.71</td>
<td>14.38±2.09</td>
<td>0.31±0.05</td>
<td>0.28±0.03</td>
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<tr>
<td>Observation group</td>
<td>76</td>
<td>25.91±3.45</td>
<td>117.69±14.73</td>
<td>1.76±0.27</td>
<td>1.37±0.19</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>10.982</td>
<td>14.382</td>
<td>8.392</td>
<td>7.948</td>
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<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
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</tbody>
</table>

3.3 Nerve apoptosis indexes

Comparison of serum nerve apoptosis indexes Bcl-2, sFas, sFasL and Caspase-3 contents between two groups of newborns was as follows: serum sFas, sFasL and Caspase-3 contents in observation group were significantly higher than those in normal control group while Bcl-2 content was significantly lower than that in normal control group. Differences in serum nerve apoptosis indexes Bcl-2, sFas, sFasL and Caspase-3 contents were statistically significant between two groups of newborns (P<0.05), shown in Table 3.

Table 3.
Comparison of serum nerve apoptosis index contents between two groups of newborns (ng/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Bcl-2</th>
<th>sFas</th>
<th>sFasL</th>
<th>Caspase-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>50</td>
<td>12.71±0.68</td>
<td>11.28±2.74</td>
<td>2.18±0.35</td>
<td>2.31±0.27</td>
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<tr>
<td>Observation group</td>
<td>76</td>
<td>7.92±0.75</td>
<td>36.47±4.52</td>
<td>4.29±0.56</td>
<td>5.19±0.68</td>
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<tr>
<td>T</td>
<td></td>
<td>7.281</td>
<td>16.397</td>
<td>8.398</td>
<td>7.983</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
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</tr>
</tbody>
</table>

3.4 Oxidative stress indexes

Comparison of serum oxidative stress indexes AOPP (μmol/L), SOD (nU/mL) and MDA (mmol/L) contents between two groups of newborns was as follows: serum AOPP and MDA contents in observation group were higher than those in normal control group while SOD content was lower than that in normal control group. Differences in serum oxidative stress indexes AOPP, SOD and MDA contents were statistically significant between two groups of newborns (P<0.05), shown in Table 4.

Table 4.
Comparison of serum oxidative stress index contents between two groups of newborns.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>AOPP</th>
<th>SOD</th>
<th>MDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>50</td>
<td>50.38±7.19</td>
<td>68.38±7.52</td>
<td>1.72±0.25</td>
</tr>
<tr>
<td>Observation group</td>
<td>76</td>
<td>139.46±17.53</td>
<td>30.17±4.36</td>
<td>4.09±0.53</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>20.938</td>
<td>16.716</td>
<td>8.932</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
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</tbody>
</table>

3.5 Correlation analysis

Pearson test showed that qEEG parameter values in children with HIE were negatively correlated with nerve injury indexes NSE, NPY, S-100B and MBP contents; they were negatively correlated with nerve apoptosis indexes sFas, sFasL and Caspase-3 contents, and positively correlated with Bcl-2 content; they were negatively correlated with oxidative stress indexes AOPP and MDA contents, and positively correlated with SOD content (P<0.05).

4. Discussion

HIE is a brain lesion caused by hypoxia in the perinatal period, the children are characterized by abnormal consciousness, changes in muscular tone, frequent convulsions and so on, and severe cases may die within one week. Clarifying HIE severity and choosing reasonable treatment is the key to optimize the treatment outcome in HIE children, but the newborns are without autonomous expression capability, and the changes in consciousness, muscular tone and so on cannot become the objective indexes to judge the disease, so looking for convenient and accurate way to judge HIE illness is a hot spot in current clinical research[5,6]. qEEG can quantifiably reflect changes in the brain electrical activity, it has been successfully applied in the diagnosis of a variety of neuropsychiatric diseases, and some scholars have also pointed out that qEEG parameters have high research value for the judgment of the change in brain function of children with HIE[7]. The brain electrical change in children with HIE is mainly based on background activity, which is characterized by low voltage, low amplitude and low peak power spectrum values. In the study, qEEG parameter values were compared between newborns with HIE and normal newborns, and it was found that qEEG Fp1, Fp2, C3, C4, T3, T4, O1 and O2 loci power spectrum values of observation group were significantly lower than those of normal control group, this is consistent with the brain lesion characteristics of HIE and confirms that qEEG parameters can accurately reflect the brain lesions in children with HIE, but the intrinsic relation between parameter value and the severity of HIE remains to be confirmed in following study.

Ischemic hypoxic nerve injury is the pathological basis of HIE, neuron damage can lead to changes in the production and secretion of a variety of factors, and it can indirectly reflect the degree of nerve damage[9]. NSE is a sensitive marker of central nerve injury, which can be released into the blood after nerve damage and myelin disintegration and detected to be increase in serum level[10]. NPY is a bioactive polypeptide, and the sympathetic excitability increases after ischemic hypoxic nerve injury, which promotes NPY release. S-100B belongs to the acid calcium binding protein, it can not easily penetrate the blood brain barrier because of the damage of blood brain barrier in children with HIE, therefore, high level of S-100B can be detected[11,12]. MBP is a single stranded polypeptide that is closely associated with the function of the nervous system, and nerve injury can increase its secretion and eventually releases it into the peripheral blood. In the study, serum content of nerve damage indexes were compared between two groups of newborns, and it was found that serum NSE, NPY, S-100B and MBP contents in observation group were significantly higher than those in normal control group, it confirms that there is obvious nerve damage in
children with HIE, Pearson test confirms that each qEEG parameter value was negatively correlated with the contents of NSE, NPY, S-100B and MBP, and it further illustrates that qEEG detection can reflect the degree of nerve injury in children with HIE.

Severe ischemic hypoxic injury can eventually lead to the apoptosis of neurons, and cause irreversible pathological changes in children. The degree of hypoxia can affect the expression of apoptotic molecules, and then affect the apoptosis process[13]. Bcl-2 is an important mechanism for the self-protection of nerve cells, and the Bcl-2 expression decreases with the extension of the neural ischaemia-reperfusion. SFas, sFasL and Caspase-3 all have the pro-apoptotic effect, which can be massively released after neuron damage and promote its apoptosis[14,15]. It was found in the study that serum SFas, sFasL and Caspase-3 contents in observation group were significantly higher than those in normal control group while Bcl-2 content was significantly lower than that in normal control group, and the combination with the physiological effects of each molecules shows that the neuron apoptosis is activated in HIE children. Pearson test showed that the qEEG parameter values of HIE were directly correlated with the contents of above apoptotic molecules, and it confirms that the qEEG parameters could indirectly reflect the nerve apoptosis of HIE children.

There is local and systemic oxidative stress in brain tissue of children with HIE, and therefore, many studies have chosen the mild hypothermia, hyperbaric oxygen and other ways that can reduce oxidative stress to treat HIE, and have made outstanding achievements[16]. The AOPP and MDA are the oxidative metabolites, they have strong oxidative properties and their levels are consistent with the degree of oxidative stress in the body[17]. SOD is an antioxidant molecule, and its serum content is low when oxidative stress reaction is strong and SOD is consumed excessively[18]. In the study, serum contents of oxidative stress indexes were compared between two groups of newborns, and it was found that serum AOPP and MDA contents in observation group were higher than those in normal control group while SOD content was lower than that in normal control group, which indicates that the oxygen free radicals increase, the antioxidants decrease, and the overall level of oxidative stress is higher in children with HIE. Further Pearson test showed that qEEG parameter values of children with HIE were negatively correlated with AOPP and MDA contents, and positively correlated with SOD content, confirming that qEEG parameters can objectively reflect the extent of systemic oxidative stress in children with HIE.

To sum up, it is concluded that the qEEG parameter values are abnormal in children with HIE, and the abnormal degree is closely related to the severity of the disease. Detecting qEEG parameters in children with HIE can objectively and accurately reflect the severity of the disease, and can be the reliable means for the treatment guidance of the long-term similar diseases and the judgment of prognosis.

References