Effects of hyperbaric oxygen intervention on cerebral oxygen metabolism, cerebral injury and oxidative stress response in patients with craniocerebral injury

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ARTICLE INFO

Objective: To investigate the effects of hyperbaric oxygen intervention on cerebral oxygen metabolism, cerebral injury and oxidative stress response in patients with craniocerebral injury.

Methods: A total of 78 patients with traumatic craniocerebral injury who were treated in our hospital between September 2015 and January 2018 were selected as the research subjects and divided into control group (n=39) and hyperbaric oxygen group (n=39) by random number table method. Control group received clinical routine intervention for patients with traumatic craniocerebral injury, hyperbaric oxygen group received hyperbaric oxygen intervention on the basis of routine intervention, and the intervention lasted for one month. The differences in the cerebral oxygen metabolism indexes, cerebral injury-related indexes and oxidative stress indexes were compared between the two groups of patients immediately after admission and after 1 month of treatment.

Results: Immediately after admission, the levels of cerebral oxygen metabolism indexes as well as the contents of cerebral injury-related indexes and oxidative stress indexes were not significantly different between the two groups. After 1 month of treatment, cerebral oxygen metabolism indexes SjvO2 and CERO2 levels in hyperbaric oxygen group were higher than those in control group whereas A-vDO2 level was lower than that in control group; serum cerebral injury-related indexes GFAP, MBP, RBP4, SAA and NSE contents were lower than those of control group; serum oxidative stress indexes CAT and T-AOC contents were higher than those of control group whereas ROS and LHP contents were lower than those of control group.

Conclusion: Hyperbaric oxygen intervention can effectively optimize the cerebral oxygen metabolism, reduce the cerebral injury and inhibit the systemic oxidative stress response in patients with craniocerebral injury.

1. Introduction

Traumatic brain injury is very common in clinical practice, the patients can be manifested as damaged local cerebral hemorrhage and corresponding cerebral ischemic hypoxic injury, and serious cases may endanger the patients’ life[1,2]. Acute decompressive craniectomy is the first choice for clinical treatment of traumatic brain injury, it can actively remove intracranial congestion and reduce the incidence of secondary brain edema, but some patients still develop serious nerve dysfunction after postoperative conventional neurotrophy and other drug intervention, which directly affects their future life and work ability. Hyperbaric oxygen is a physical therapy method that can improve the oxygen content in brain tissue and reduce the neural hypoxic state, and has been successfully applied in cerebral hemorrhage, cerebral infarction and other cerebrovascular diseases[3,4]. In this study, hyperbaric oxygen intervention was used in patients with traumatic craniocerebral injury, and the effect of the therapy on patients’ condition was discussed from cerebral oxygen metabolism, cerebral injury and oxidative stress response in order to lay the foundation for further clinical practice.

2. Information and methods

2.1 Case information

A total of 78 patients with traumatic craniocerebral injury who were treated in our hospital between September 2015 and January 2018 were chosen as the research subjects and divided into the
control group (n=39) and the hyperbaric oxygen group (n=39) by random number table method. There were 22 males and 17 females in the control group, and they were 21-67 years old; there were 21 males and 18 females in the hyperbaric oxygen group, and they were 22-69 years old. There was no significant difference in the above data distribution between groups, and the follow-up study plan was approved by the ethics committee of our hospital.

Inclusion criteria: (1) diagnosed with traumatic craniocerebral injury; (2) without history of cerebral trauma, cerebral hemorrhage or cerebral infarction; (3) without history of surgery within 6 months after admission; (4) without history of hyperbaric oxygen therapy; (5) with family members' informed consent.

Exclusion criteria: (1) combined with basic cognitive dysfunction; (2) combined with intracranial infection; (3) combined with systemic infectious diseases such as pneumonia; (4) ≥80 years old; (5) pregnant or breastfeeding women.

2.2 Intervention

Control group received routine clinical intervention from patients with traumatic craniocerebral injury, including oxygen uptake, mannitol for lowering intracranial pressure, neurotrophy, water electrolyte balance regulation and so on. On the basis of conventional intervention, hyperbaric oxygen group received hyperbaric oxygen intervention, which was as follows: the hyperbaric oxygen chamber pressure was set to 0.25 MPa, the patients entered the chamber after the pressure was stable, they wore a mask to inhale oxygen for 30 min and inhale oxygen again for 20 min with 10 min interval, and the intervention lasted for a total of 60 min and was done once/d for continuous 1 month of treatment.

2.3 Observation indexes

Immediately after admission and after 1 month of treatment, 5.0 mL of peripheral blood samples were obtained from the two groups of patients at the same time point to separate and freeze the serum, and 2.0 mL of radial artery blood samples were also collected. Blood gas analyzer was adopted to determine the levels of cerebral oxygen metabolism indexes, including venous oxygen saturation (SjvO2), arterio-venous oxygen content difference (A-vDO2) and cerebral oxygen extraction rate (CERO2). Ria kit was used to determine the serum contents of cerebral injury-related indexes, including glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), retinol binding protein (RBP4), amyloid A (SAA) and neuron-specific enolase (NSE); Elisa kit was used to determine the serum contents of oxidative stress indexes, including catalase (CAT), total antioxidant capacity (T-AOC), reactive oxygen species (ROS) and lipid hydroperoxide (LHP).

2.4 Statistical processing

The specific values of cerebral oxygen metabolism index levels, cerebral injury-related index contents and oxidative stress index contents were all input in the selected statistical software SPSS 25.0 to calculate the statistic P (P<0.05 indicated statistical significance in differences in the study).

3. Results

3.1 Cerebral oxygen metabolism indexes

Comparison of cerebral oxygen metabolism indexes SjvO2 (%), A-vDO2 (mL/L) and CERO2 (%) levels in the two groups at different time points was as follows: immediately after admission, SjvO2, A-vDO2 and CERO2 levels were not significantly different between the two groups (P>0.05); after 1 month of treatment, SjvO2 and CERO2 levels in both groups were higher than those immediately after admission whereas A-vDO2 levels were lower than those immediately after admission (P<0.05). After 1 month of treatment, SjvO2 and CERO2 levels in hyperbaric oxygen group were higher than those in control group whereas A-vDO2 level was lower than that in control group (P<0.05), shown in Table 1.

3.2 Cerebral injury–related indexes

Comparison of cerebral injury-related indexes GFAP (pg/mL), MBP (ng/mL), RBP4 (mg/L), SAA (mg/L) and NSE (ng/mL) contents in the two groups at different time points was as follows: immediately after admission, serum GFAP, MBP, RBP4, SAA and NSE contents were not significantly different between the two groups (P>0.05), after 1 month of treatment, serum GFAP, MBP, RBP4, SAA and NSE contents of both groups were lower than those immediately after admission (P<0.05). After 1 month of treatment, serum GFAP, MBP, RBP4, SAA and NSE contents of hyperbaric oxygen group were lower than those of control group (P<0.05), shown in Table 2.

Table 1.
Comparison of cerebral oxygen metabolism index levels in the two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>SjvO2</th>
<th>A-vDO2</th>
<th>CERO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>Immediately</td>
<td>48.23±5.71</td>
<td>67.23±7.09</td>
<td>33.87±4.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>after admission</td>
<td>54.48±7.06</td>
<td>54.71±6.42</td>
<td>39.23±4.52</td>
</tr>
<tr>
<td>Hyperbaric oxygen</td>
<td>39</td>
<td>Immediately</td>
<td>48.15±5.46</td>
<td>66.94±8.43</td>
<td>33.79±4.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td>after admission</td>
<td>62.13±7.45*</td>
<td>45.23±6.18*</td>
<td>44.12±5.09*</td>
</tr>
</tbody>
</table>

Note: vs. control group immediately after admission, P<0.05; vs. hyperbaric oxygen group after 1 month of treatment, P<0.05.

Table 2.
Comparison of cerebral injury–related index contents in the two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>GFAP</th>
<th>MBP</th>
<th>RBP4</th>
<th>SAA</th>
<th>NSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>39</td>
<td>Immediately</td>
<td>20.49±2.81</td>
<td>64.18±7.53</td>
<td>32.42±5.19</td>
<td>10.26±1.74</td>
<td>9.23±1.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>after treatment</td>
<td>12.48±1.63*</td>
<td>45.21±6.59*</td>
<td>18.34±2.09*</td>
<td>6.38±0.81*</td>
<td>4.02±0.48*</td>
</tr>
<tr>
<td>Hyperbaric oxygen</td>
<td>39</td>
<td>Immediately</td>
<td>20.31±2.56</td>
<td>63.95±8.12</td>
<td>33.07±4.85</td>
<td>10.34±1.62</td>
<td>9.18±1.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>after treatment</td>
<td>7.59±0.85*</td>
<td>24.75±3.09*</td>
<td>11.21±1.63*</td>
<td>3.22±0.41*</td>
<td>1.84±0.23*</td>
</tr>
</tbody>
</table>

Note: vs. control group immediately after admission, P<0.05; vs. hyperbaric oxygen group after 1 month of treatment, P<0.05.
A-vDO2 reflects the equilibrium state of cerebral oxygen supply and demand, the lower level of SjvO2, and CERO2 reflects the utilization of oxygen in brain tissue, and the higher its level, the higher the cerebral oxygen utilization. The study results showed that SjvO2 and CERO2 levels in both groups were higher whereas A-vDO2 levels were lower after treatment, which shows that the cerebral oxygen metabolism has been improved to varying degrees under different treatments; further comparison showed that SjvO2 and CERO2 levels in hyperbaric oxygen group after treatment were higher than those in control group whereas A-vDO2 level was lower than that in control group, which confirms that hyperbaric oxygen intervention can further optimize the cerebral oxygen metabolism in patients with craniocerebral injury and lay foundation for neural functional recovery.

Cerebral oxygen metabolism condition is consistent with the specific brain injury in patients, there are many factors in the serum of patients that are closely related to brain damage, the change of their expression is closely related to the degree of neuronal dysfunction, and their contents are mostly used as the indirect means in clinical practice to evaluate the disease severity and reflect the therapeutic effect. GFAP is the main factor that forms astrocytes, it is the cytoskeletal protein specific in central nervous system, it plays an important role in the pathological physiological processes of the nervous system, and it is known in brain trauma, brain tumors and other mechanical damage that MBP, as a part of the myelin sheath, can be dissociated to enter into the blood stream[16,17]. RBP4 is considered to be an independent risk factor for the occurrence of cardiovascular diseases, and RBP4 content in circulating blood may increase within 24 h after craniocerebral injury; SAA is closely related to the occurrence and development of cerebral stroke, and the content of SAA in serum further increases with the development of nerve function injury. NSE is one of the most thoroughly studied brain injury-related indicators in clinic, its levels is the highest in the brain tissue cells, and it is highly expressed in the brain injury and nerve tumor diseases, and can be used as the reliable index to evaluate the disease severity and reflect the therapeutic effect. GFAP is the main factor that forms astrocytes, it is the cytoskeletal protein specific in central nervous system, it plays an important role in the pathological physiological processes of the nervous system, and it is known in brain trauma, brain tumors and other mechanical damage that MBP, as a part of the myelin sheath, can be dissociated to enter into the blood stream[16,17]. RBP4 is considered to be an independent risk factor for the occurrence of cardiovascular diseases, and RBP4 content in circulating blood may increase within 24 h after craniocerebral injury; SAA is closely related to the occurrence and development of cerebral stroke, and the content of SAA in serum further increases with the development of nerve function injury. NSE is one of the most thoroughly studied brain injury-related indicators in clinic, its levels is the highest in the brain tissue cells, and it is highly expressed in the brain injury and nerve tumor diseases, and can be used as the reliable index to early diagnose the existence of neurological dysfunction[18]. The study results showed that serum GFAP, MBP, RBP4, SAA and NSE contents of both groups were lower after treatment, indicating that both treatment regimens could reduce the degree of brain injury in patients with craniocerebral injury; further comparison showed that serum GFAP, MBP, RBP4, SAA and NSE contents of hyperbaric oxygen group after 1 month of treatment were lower than those of control group, confirming that hyperbaric oxygen intervention can further optimize the neural function and reduce the brain damage in patients with craniocerebral injury.

More and more studies have confirmed that oxidative stress plays an important role in the pathological physiological processes after craniocerebral injury, and the excessively produced free radicals and peroxidation products in brain tissue can activate lipid peroxidation, nucleic acid and protein oxidation, inflammation and other processes, and cause secondary damage to nerve cells. Meanwhile, oxidative stress can mediate mitochondria, nuclear
transcription factors and other pathways to indirectly damage neuron function[19,20]. The contents of indexes such as CAT and T-AOC intuitively reflect the body's antioxidant capacity, ROS and LHP are positively correlated with the oxidative stress degree in the body, and the equilibrium state between the two can indirectly reflect the present situation and disease outcome trend of patients with craniocerebral injury[21,22]. The study results showed that serum CAT and T-AOC contents of both groups increased whereas ROS and LHP contents decreased after treatment; further comparison showed that serum CAT and T-AOC contents of hyperbaric oxygen group after 1 month of treatment were higher than those of control group whereas ROS and LHP contents were lower than those of control group, it confirms that hyperbaric oxygen intervention can effectively relieve the oxidative stress reaction, and this is also one of the internal mechanisms for it to improve the patients' cerebral oxygen metabolism and reduce brain damage.

To sum up, it is concluded that hyperbaric oxygen intervention after emergency surgery can effectively optimize the cerebral oxygen metabolism status, reduce the brain damage and suppress the oxidative stress reaction in patients with craniocerebral injury, it is one of the reliable ways to improve the treatment outcome of patients with craniocerebral injury, and it is worthy of popularization and application in clinical practice in the future.

References


[9] Zaretsky DV, Romanovsky AA, Zaretkskaia MV, Molkov YI. Tissue oxidative metabolism can increase the difference between local temperature and arterial blood temperature by up to 1.3 °C: Implications for brain, brown adipose tissue, and muscle physiology. Temperature (Austin) 2018; 5(1): 22-35.


