Effects of hyperbaric oxygen on serum inflammatory factors, oxidative stress, endothelin and intracranial pressure in patients with severe head injury

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ABSTRACT

Objective: To investigate the effect of hyperbaric oxygen (HBO) on serum inflammatory factors, oxidative stress status, endothelial cell function and intracranial pressure in patients with severe craniocerebral injury (STBI), and to provide scientific basis for clinical treatment of patients with severe craniocerebral injury. Methods: 110 cases of STBI were selected and divided into control group and treatment group according to the random data table, 55 cases in each group. The control group received conventional combined therapy, the observation group were given HBO treatment on the base of the control group, the inflammatory factors [C reactive protein (CRP), tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and interleukin-10 (IL-10)] and oxidative stress [malondialdehyde (MDA) and superoxide dismutase-1 (SOD-1)], endothelin (ET) and intracranial pressure (ICP) level changes of the two groups were observed and compared before and after treatment for 10 d in patients. Results: The levels of CRP, TNF-α, IL-6, MDA, ET and ICP in the treatment group and the control group were significantly lower than those in the same group before treatment, the difference was statistically significant (P<0.05), the CRP, TNF-α, IL-6, MDA, ET and ICP levels of the observation group after treatment were significantly lower than the control group after treatment (P<0.05); After treatment, IL-10 and SOD-1 levels of the two groups of patients were significantly increased than the same group before treatment (P<0.05), and both levels in the observation group after treatment was significantly higher than the control group after treatment (P<0.05). Conclusions: HBO treatment of severe brain injury patients with significant effect, can effectively reduce oxidative stress damage and inflammation, improve patients’ endothelial cell function, reduce intracranial pressure, and has a certain clinical value.

1. Introduction

Traumatic brain injury (TBI) is a severe disease with high death rate and disability rate, which is caused by the direct or indirect effect on the head by brain tissue injury. Among which 18% to 20% are severe traumatic brain injury (STBI), and the mortality rate is 30% to 50%[1,2]. STBI patients with cerebral microcirculation disorder is the main cause of death, although conventional surgical treatment can stabilize the disease, but its efficacy is limited, and its effect on the STBI-induced endothelial dysfunction is limited. Hyperbaric oxygen (HBO) therapy as a new treatment, can effectively improve the body’s hypoxic state[3]. The aim of this study was to investigate the effect of HBO therapy on STBI and its influence on biochemical parameters.

2. Materials and methods

2.1. General Information

110 patients with STBI from June 2015 to August 2016 in our hospital were selected, and all of them met the diagnostic criteria of STBI[4]. They were randomly divided into control group and
observation group according to digital table method, each group of 55 patients. In the control group, there were 32 males and 23 females; the age ranged from 22 to 64 years; Causes of injury: 26 cases of car accidents, 18 cases of blunt objects, 8 cases in the falls and 3 cases of fall hurt; 15 cases of upper and lower extremity fractures, 4 cases of rib fractures and 3 cases of pneumothorax; Admission Glasgow coma (GCS) score was (6.0±1.2) points. In the observation group, there were 35 males and 20 females; the age ranged from 21 to 62 years old. The causes of injury were: 28 cases of car accidents, 17 cases of blunt objects, 8 cases in the falls and 2 cases of fall hurt; 7 cases of rib fractures, pneumothorax in 3 cases; Admission GCS score (6.1±1.3) points. There were no significant differences in age, sex, comorbidity, cause of injury and GCS score between the two groups (P>0.05). The study was approved by the ethics committee of the hospital, and the patients and their families signed informed consent and agreed to cooperate with the study.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) all patients were admitted to the hospital within 24 h after injury, with obvious history of traumatic brain injury; (2) the brain MRI or CT diagnosis with STBI diagnostic criteria (GCS score 3–8); (3) brain CT imaging studies show that patients can endure HBO treatment.

Exclusion criteria: (1) with other parts of serious damage, at the same time to other parts of the rescue operation; (2) the bleeding shock; (3) the other with severe tracheal disorders (heart, lung and kidney damage or dysfunction); (4) died within 2–3 d after admission; (5) the incomplete data.

2.3. Treatment methods

Control group: According to the severity of patients, patients were treated with conservative treatment or surgical treatment. Clinical routine treatment, including oxygen, reducing intracranial pressure, protect brain cells, anti-infection, neurotrophic and maintain electrolyte balance.

The observation group: on the basis of the control group, the patient’s condition was relatively stable after the treatment of hyperbaric oxygen, with three class seven door hyperbaric oxygen (Shandong Yantai moon hyperbaric oxygen limited production), the treatment pressure is 0.2 Mpa, slow increase the pressure in the hyperbaric oxygen chamber of 20 min, after continuous treatment of 1 h, rest 15 min (inhaled air), after the treatment of slow blood pressure (20 min), 1 times/d, 10 d for a course of treatment, a total of 4 courses of treatment, the interval between 3 d.

2.4. Detection indicators and detection methods

Extraction of all patients with fasting elbow vein blood 4–5 mL before and after 10 d treatment, with 3 000 r/min centrifuge 10 min, extracted serum, placed in -80 °C refrigerator preservation to detect serum biochemical indicators. Biochemical parameters include: inflammatory factors, oxidative stress and endothelin. Using enzyme-linked immunosorbent assay for the detection of C reactive protein (CRP), tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) and interleukin-10 (IL-10) level, kit provided by Beijing Jingmei biotech Co. Ltd.; The malondialdehyde (MDA) was detected by thiobarbituric acid method, provided by Shanghai Jining Biotechnology Co., the superoxide dismutase-1 (SOD-1) and endothelin (ET) levels were detected by radioimmunoassay (RIA), the kit was provided by Shenzhen crystal beauty Biological Engineering Co., Ltd., the operation was strictly in accordance with the instructions. At the same time using transcranial Doppler analyzer for monitoring intracranial pressure (ICP).

2.5. Statistical analysis

The data were analyzed by SPSS 17.0, and the data were expressed as mean±standard deviation (SD). Two samples were compared by independent sample t test, chi-square analysis was used for count data, P<0.05 indicated that there was a significant difference.

3. Results

3.1. Comparison of inflammatory factor levels in the two groups before and after treatment

The levels of serum CRP, TNF-α, IL-6 and IL-10 in both groups before and after treatment are shown in Table 1. There were no significant differences in the levels of CRP, TNF-α, IL-6 and IL-10 between the two groups before treatment (P>0.05). The levels of CRP, TNF-α and IL-6 in the two groups were significantly lower than those before treatment in the same group (P<0.05). After treatment, three levels of the observation group compared with the control group decreased significantly (P<0.05); After treatment, the IL-10 levels of two groups were compared with the same group before treatment were significantly higher (P<0.05), and the observation group was significantly higher than the control group.

![Table 1](attachment:image)

Comparison of inflammatory factor levels in the two groups before and after treatment (n=55±5±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CRP (mg/L)</th>
<th>TNF-α (ng/L)</th>
<th>IL-6 (ng/L)</th>
<th>IL-10 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The control group</td>
<td>Before treatment</td>
<td>28.46±3.18</td>
<td>36.34±6.67</td>
<td>138.14±10.57</td>
<td>10.43±3.37</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>13.87±2.24</td>
<td>22.41±3.74</td>
<td>99.73±9.82</td>
<td>10.79±4.15</td>
</tr>
<tr>
<td>The observation group</td>
<td>Before treatment</td>
<td>28.62±3.47</td>
<td>35.72±4.59</td>
<td>137.92±10.62</td>
<td>10.42±3.81</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>10.73±1.86</td>
<td>16.82±4.17</td>
<td>92.06±8.89</td>
<td>10.98±4.31</td>
</tr>
</tbody>
</table>

* compared with the control group after treatment, P<0.05; † compared with the same group before treatment, P<0.05.
The control group after treatment, the control group after treatment, (P<0.05).

3.2. Comparison of oxidative stress-related indicators changes in the two groups before and after treatment

Oxidative stress related indicators MDA and SOD-1 level changed in two groups of patients before treatment and after treatment, and the results are shown in Table 2. MDA and SOD-1 levels of two groups of patients before treatment were no significant difference (P>0.05); After treatment, MDA levels of the two groups were significantly decreased compared with the same group before treatment (P<0.05), and the observation group after treatment was significantly lower than the control group (P<0.05); After treatment, SOD-1 levels of two groups were significantly increased compared with the same group before treatment (P<0.05). And the levels of SOD-1 in the observation group after treatment was significantly higher than that in the control group (P<0.05).

Table 2
Comparison of oxidative stress-related indicators changes in the two groups before and after treatment (n=55±7±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>MDA (µmol/L)</th>
<th>SOD-1 (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The control group</td>
<td>Before treatment</td>
<td>4.97±0.54</td>
<td>261.57±31.36</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>3.73±0.47</td>
<td>297.41±24.09</td>
</tr>
<tr>
<td>The observation group</td>
<td>Before treatment</td>
<td>4.92±0.59</td>
<td>262.03±32.49</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>3.08±0.32</td>
<td>328.74±28.96</td>
</tr>
</tbody>
</table>

* compared with the same group before treatment, P<0.05; * compared with the control group after treatment, P<0.05.

3.3. Comparison of ET and ICP levels in the two groups before and after treatment

The ET and ICP levels of two groups of patients before treatment and after treatment changed (Table 3). Before treatment, ET and ICP levels of the two groups was not statistically significant (P>0.05); Both levels were significantly decreased compared with the same group before treatment (P<0.05). After treatment, the ET and ICP levels of observation group were significantly lower than those of the control group (P<0.05).

Table 3
Comparison of ET and ICP levels in the two groups before and after treatment (n=55±7±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>ET (ng/L)</th>
<th>ICP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The control group</td>
<td>Before treatment</td>
<td>75.34±7.92</td>
<td>16.04±3.11</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>61.15±6.35</td>
<td>14.83±3.17</td>
</tr>
<tr>
<td>The observation group</td>
<td>Before treatment</td>
<td>74.85±7.23</td>
<td>15.97±3.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>54.32±6.55</td>
<td>11.19±3.24</td>
</tr>
</tbody>
</table>

* compared with the same group before treatment, P<0.05; * compared with the control group after treatment, P<0.05.

4. Discussion

STBI is a common clinical neurosurgery disease with high mortality and morbidity, often accompanied by the occurrence of intracranial hematoma, cerebral contusion and other complications, which oppressed brain tissue, leading to blood-brain barrier damage, microcirculation disorder, cerebral hypoxia ischemia, intracranial pressure increased sharply, secondary cerebral hernia caused life-threatening. The cerebral microcirculation state depends mainly on the cerebral vascular resistance, including thromboxane and ET vascular endothelial cells, inflammatory factors and local brain chemical factors and nerve regulation other factors are all involved in the process of microcirculation after injury[5,6]. In recent years, studies have shown that, after the occurrence of STBI, a large number of inflammatory factors in the brain gathered, the level of proinflammatory cytokines increased dramatically, induced intracranial inflammatory response, thereby exacerbating brain damage or induce secondary brain injury[7-9]. STBI treatment is mainly for secondary injury, such as the use of hypothermia, free radical scavengers and antioxidants and other means, the mechanism is the inhibition of oxygen free radicals and pro-inflammatory factors, reduce oxidative stress, so as to achieve the purpose of reducing the secondary brain injury[10]. Therefore, the control of inflammatory factors, oxidative stress, endothelin and intracranial pressure and other indicator levels is an important part of STBI treatment. HBO, as a new treatment therapy, has been widely used in the treatment of clinical diseases, including the treatment of TBI[11,12]. In this study, the effect of HBO therapy on STBI and the changes of serum inflammatory factors, oxidative stress related indexes, endothelin and intracranial pressure were observed and the effect of HBO treatment on STBI was discussed, providing the reference for clinical application.

A large number of studies have indicated that the degree of damage is positively related to the content of CRP in the serum of the body, so it is often used as an early diagnosis and evaluation of therapeutic efficacy by CRP level. The mechanism may be the role of CRP to stimulate cells to release TNF-α, IL-6 and other inflammatory mediators, which play a proinflammatory effect[13]. In addition to the release of pro-inflammatory factors IL-6 and TNF-α, but also to release the IL-10 anti inflammatory factor. IL-10 release can inhibit the activation and aggregation of proinflammatory cytokines, reduce the level of proinflammatory cytokines, and thus improve the immune recovery function of the body to combat excessive inflammation in brain tissue[14,15]. The results showed that the levels of inflammatory cytokines were significantly improved in both groups after treatment, and serum inflammatory factor levels in STBI patients after HBO treatment were significantly better than conventional clinical treatment, mainly, it can effectively increase the level of anti-inflammatory factor IL-10, reduce CRP and pro-inflammatory cytokines TNF-α, IL-6 levels. The results suggest that HBO treatment can inhibit the level of proinflammatory cytokines and increase the expression of antiinflammatory cytokines in patients with STBI. It can help to relieve the inflammatory reaction, protect the damaged brain tissue and reduce the secondary brain injury of STBI. The results were consistent with those reported in the literature[16,17].

Oxidative stress plays an important role in the development and progression of STBI, and is closely related to the apoptosis of nerve cells. The level of MDA reflects the degree of free radical attack by
the cells, while SOD-1 has a strong antioxidant effect, and it can scavenge superoxide anion free radicals, thereby protecting cells from damage, which is the body's antioxidant capacity index\[18\]. ET is the strongest and longest vasoactive peptide known to be involved in the pathogenesis of secondary brain injury after craniocerebral injury. ET over-expression and release is an important factor in the development of secondary brain injury. The main mechanism for the role of endothelium in blood vessels lasting strong contraction increase brain tissue hypoxia-ischemia and neuronal damage, and then lead to brain damage\[19\]. Studies have confirmed that HBO treatment can protect the early injury of the edge of the neurons, enhance the blood supply function of brainstem reticular activation system, reduce platelet aggregation, increase the level of oxygen metabolism in brain tissue, reduce ICP, reduce cerebral edema, restore reversible damaged neurons, and improve brain function of severe craniocerebral injury\[20\]. The results of this study show that HBO treatment of severe craniocerebral injury patients with significant improvement in oxidative stress levels, mainly to reduce the level of MDA, increase SOD-1 levels, in addition, HBO treatment can also reduce the patients’ ET concentration, decrease ICP levels. This study also found that the efficacy in patients with severe brain injury after HBO treatment was significantly improved. The mechanism may be through improving the ability of SOD to remove oxygen free radicals, and then accelerate the excretion of ET, reduce the level of ET, which has achieved a more satisfactory curative effect. The results of the study are consistent with the previous reports\[21,22\].

In summary, a significant clinical effect of HBO therapy in patients with STBI, can effectively alleviate the oxidative stress and inflammatory reaction, improve vascular endothelial cell function of the patients, reduce the intracranial pressure, has certain clinical value.

References


