Effects of propofol anesthesia on oxidative stress, neurological function and inflammatory cytokines in patients with craniocerebral trauma

Yan Liu\(^1\), Jie Xia\(^1\), Zong-Jun Peng\(^2\), Yu-Feng Ma\(^1\)

\(^1\) Department of Anesthesiology, Sichuan Friendship Hospital, Sichuan, Chengdu 610066, China
\(^2\) Department of Neurosurgery, Sichuan Friendship Hospital, Sichuan, Chengdu 610066, China

ARTICLE INFO

Article history:
Received 28 Nov 2017
Received in revised form 2 Dec 2017
Accepted 7 Dec 2017
Available online 14 Dec 2017

Objective: To investigate the effect of propofol anesthesia on oxidative stress, neurological function and inflammatory cytokines in patients with craniocerebral trauma. Methods: A total of 102 patients with craniocerebral trauma who underwent surgery in our hospital from December 2014 to January 2017 were randomly divided into control group and observation group, each contained 51 cases. The control group was given 1%-2% of sevoflurane and 0.1-0.2 μg/kg/min of remifentanil and 20-30 μg/kg/h of vecuronium for anesthesia maintenance. The observation group was given propofol 4-6 mg/kg/h, remifentanil 0.1-0.2 μg/kg/min and vecuronium 20-30 μg/kg/h for anesthesia maintenance. The levels of oxidative stress, neurological function, and inflammatory factors were assessed in both groups. Results: Compared with before treatment, the levels of SOD and HO-1 in the two groups were significantly increased and the levels of MDA were significantly decreased, the difference was significant, and the levels of SOD and HO-1 in the observation group were significantly higher than control group, the level of MDA was significantly lower than that of the control group, the difference was significant. Compared with before treatment, the levels of NSE, GFAP and Tau level were significantly decreased in the two groups after treatment, and level in observation group was lower than control group, the difference was statistically significant. Compared with before treatment, the levels of IL-6, TNF-α and CRP in the two groups after treatment were significantly lower than those in the control group, the difference was statistically significant. Conclusion: Propofol anesthesia can significantly reduce the oxidative stress injury, inhibit the inflammatory reaction and protect the neurological function of patients. The effect is better than isoflurane anesthesia, and it is worthy of clinical application.

1. Introduction

Craniocerebral trauma is one of the most common critical diseases in neurosurgery. The incidence is acute and with high mortality\(^1\). Craniotomy for decreasing pressure and removal of cerebral hematoma are commonly used means, but craniotomy in reducing the lesion at the same time will increase the incidence of brain injury in patients\(^2\). Therefore, it requires a reasonable anesthetic method to protect the patient’s brain function, reduce damage during operation. Propofol and sevoflurane are commonly used in clinical anesthesia, with rapid onset, low toxicity, easy recovery and other characteristics, has been widely used in clinic\(^3,4\). It has been reported that propofol has a significantly better protective effect on brain cells than sevoflurane\(^5\), but the impact of propofol on other aspects of brain trauma is less reported. In view of this, this article explored the effect of two different anesthesia methods on neurological function, inflammatory factors and oxidative stress levels, reported as following.

2. Data and methods

2.1 General data

A total of 102 patients with craniocerebral trauma undergoing surgery in our hospital from December 2014 to January 2017 were selected. Inclusion criteria: (1) All patients had craniocerebral trauma and met the surgical characteristics through CT scan; (2)
Glasgow Coma Scale (GCS) score of all patients was <9 points; (3) All patients were informed and had signed informed consent. Exclusion criteria: (1) heart, liver, kidney and blood system diseases; (2) cardio-cerebrovascular diseases, stroke and myocardial infarction patients; (3) allergic to drugs used in this experiment or with contraindications. All patients were randomly divided into control group and observation group, 51 cases in each group, in the control group 28 males and 23 females, aged from 35-67 years old, type of trauma: injury from car accident in 16 cases, falling injury in 17 cases, hitting injury in 10 cases, the other injury 8 cases; in the observation group 27 males and 24 females, aged from 34-66 years old, type of trauma: car accident in 17 cases, falling injury in 15 cases, hitting injury in 9 cases, the other injury 10 cases; There was no significant difference in the two groups of patients with gender, age, type of trauma and other general information, it was comparable.

2.2 Methods

All patients were opened venous access after entered the operating room, maintaining airway patency, monitoring blood pressure and ECG, followed by midazolam 1-2 mg, vecuronium 0.1-0.15 mg/kg, sufentanil 0.2-0.3 μg/kg, etomidate 0.2-0.3 mg/kg intravenous injection and anesthesia induction. Control group was given 1%-2% sevoflurane inhalation and remifentanil 0.1-0.2 μg/kg/min, vecuronium 20-30 μg/kg/h for anesthesia maintenance; the observation group was given propofol 4-6 mg/kg/h, remifentanil 0.1-0.2 μg/kg/min and vecuronium 20-30 μg/kg/h for anesthesia maintenance. Two groups of patients returned to the ICU after operation.

2.3 Monitoring indicators

Venous blood of all patients were collected before and 24 h after operation. Serum was collected by centrifugation. Later the levels of interleukin-6 (IL-6), tumor necrosis factor-α and C-reactive protein (CRP) were measured by radioimmunoassay. The contents of hemoglobin (Hb), neuron specific enolase enzyme (NSE), glial fibrillary acidic protein (GFAP) and Tau protein (Tau) levels were detected by enzyme linked immunosorbent assay (ELISA). The neuron specific enolase enzyme (NSE), glial fibrillary acidic protein (GFAP) and Tau protein (Tau) levels were detected by enzyme linked immunosorbent assay kits.

2.4 Statistical methods

SPSS 17.0 was used for statistical analysis of the data obtained in the research, measurement data using t test, presented by Mean ± SD, P<0.05 indicated the difference was statistically significant.

3. Results

3.1 Comparison of oxidative stress levels before and after treatment in both groups

Table 1 showed that, before treatment, SOD, MDA and HO-1 levels in both groups were no significant difference (P>0.05); after treatment, SOD and HO-1 levels in both groups were significantly increased, MDA significantly decreased, in control group after treatment SOD, MDA and HO-1 levels were respectively (90.24 ± 1.11) U/L, (7.54 ± 0.09) μmol/L and (75.72 ± 0.57) U/L. After treatment, the SOD, MDA and HO-1 levels in observation group were (115.4 ± 1.21) U/L, (4.48 ± 0.09) μmol/L and (94.23 ± 0.99) U/L respectively. The SOD and HO-1 levels in the observation group were significantly higher than those in the control group, MDA level was significantly lower than the control group, the difference was statistically significant (P<0.05).

3.2 Comparison of neurological changes before and after treatment in both groups

Table 2 showed that, before treatment, NSE, GFAP and Tau levels were not significantly different between the two groups (P>0.05); after treatment, NSE, GFAP and Tau levels were significantly decreased in both groups. NSE, GFAP and Tau levels in control group after treatment were (35.29 ± 0.12) μg/L, (0.24 ± 0.03) ng/L and (4.53 ± 0.14) ng/L, respectively. The NSE, GFAP and Tau levels in the observation group were (28.95 ± 0.52) μg/L, (0.16 ± 0.03) ng/L and (3.88 ± 0.10) ng/L, respectively, which were significantly lower than those in the control group the difference was significant (P<0.05).

Table 1.
Comparison of oxidative stress levels before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>SOD (U/L)</th>
<th>MDA (μmol/L)</th>
<th>HO-1 (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before</td>
<td>58.01±0.78</td>
<td>14.73±0.4</td>
<td>44.89±0.53</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>90.24±1.11*</td>
<td>7.54±0.09*</td>
<td>75.72±0.57*</td>
</tr>
<tr>
<td>Observation</td>
<td>Before</td>
<td>57.90±0.55</td>
<td>14.77±0.5</td>
<td>43.94±0.68</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>115.40±1.21*</td>
<td>4.48±0.09*</td>
<td>94.23±0.99*</td>
</tr>
</tbody>
</table>

Note: *Compared with before treatment, P<0.05; †Compared with the control group after treatment, P<0.05.

Table 2.
Comparison of neurological changes before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>NSE (μg/L)</th>
<th>GFAP (ng/L)</th>
<th>Tau (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before</td>
<td>59.26±0.10</td>
<td>0.47±0.02</td>
<td>7.73±0.09</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>35.29±0.12*</td>
<td>0.24±0.03*</td>
<td>4.53±0.14*</td>
</tr>
<tr>
<td>Observation</td>
<td>Before</td>
<td>59.30±0.15</td>
<td>0.49±0.04</td>
<td>7.77±0.08</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>28.95±0.52*</td>
<td>0.16±0.03*</td>
<td>3.88±0.10*</td>
</tr>
</tbody>
</table>

Note: *Compared with before treatment, P<0.05; †Compared with the control group after treatment, P<0.05.
Comparison of inflammatory cytokines levels before and after treatment in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>IL-6 (kU/L)</th>
<th>TNF-α (pg/mL)</th>
<th>CRP (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>59.37±2.67</td>
<td>1.46±0.06</td>
<td>2 019.24±58.89</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>54.12±2.31</td>
<td>1.21±0.05*</td>
<td>1 805.49±41.37</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>58.87±2.45</td>
<td>1.49±0.04</td>
<td>2 019.64±50.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>50.57±1.84*</td>
<td>1.07±0.06*</td>
<td>1 523.19±41.03</td>
</tr>
</tbody>
</table>

Note: *Compared with before treatment, P<0.05; #Compared with the control group after treatment, P<0.05.

3.3 Comparison of inflammatory cytokines levels before and after treatment in both groups

Table 3 showed that before treatment, IL-6, TNF-α and CRP levels in both groups were no significant difference (P>0.05); after treatment, IL-6, TNF-α and CRP levels in both groups decreased obviously, IL-6, TNF-α and CRP levels in control group after treatment were respectively (54.12 ± 2.31) kU/L, (1.21 ± 0.05) pg/mL, and (1805.49 ± 41.37) pg/mL, and IL-6, TNF-α and CRP levels in observation group were (50.57 ± 0.80) kU/L, (1.07 ± 0.06) pg/mL and (1523.19 ± 11.03) pg/mL respectively, which was significantly lower than control group, the difference was significant (P<0.05).

4. Discussion

Surgery is currently the main treatment method for craniocerebral trauma, the main purpose is to reduce intracranial pressure, clear the hematoma, improve brain cell metabolism, to prevent re-injury of brain cells caused by hematoma[6]. However, the operations of brain surgery are complicated and the anastomosis is difficult, and the requirements for perioperative operation and anesthesia are particularly high, which is a more difficult operation in the entire surgical operation[7]. Therefore, a reasonable method of anesthesia not only to meet the surgical needs, but also protect the brain cells of patients and reduce the occurrence of brain injury. Propofol is a new type of anesthetics commonly used in clinic, study found that it cannot only play a role in sedation and analgesia, but also reduce intracranial pressure, protect brain tissue, studies have confirmed that brain protection function of propofol was related to anti-free radical activity, regulating γ-amino acid content, inhibiting intracellular calcium overload and other mechanisms[8-10], in addition to it can regulate macrophages, inhibit the body's inflammatory response[11]; sevoflurane is an inhaled anesthetics commonly used in clinic, also has a protective effect of the brain[10], some studies have found that sevoflurane can effectively relax microvascular smooth muscle, reduce brain edema, improve brain injury caused by ischemic hypoperfusion, effectively protect the brain[12].

Both traumatic brain injury and hematoma oppression can affect the function of neurons in the lesion area, resulting in the abnormalities of brain cells and blood-brain barrier function, releasing a large number of nerve injury factors to the blood[13]. NSE is a type of enolase involved in the glycolytic pathway, widely present in nerve tissue and neuroendocrine tissues, less in serum, cerebrospinal fluid and other non-neurological tissues. When neurons are damaged or dysfunction, it can penetrate the blood-brain barrier into the peripheral blood[14]; GFAP is a specific acidic protein in the astrocytes in central nervous system, when the nervous system damage occurred, it can overflow from glial cells into the blood[15,16]; Tau protein is a phosphoprotein, presents in the axon of nerve cells, when the brain cells appeared lesions, the level will be significantly increased[17]. The study found that propofol has a good protective effect on brain tissue, which can effectively reduce the spillover of GFAP and NSE, reduce the synthesis and release of excitatory amino acids, and reduce their damage to brain tissue[1,18].

In this study, after propofol anesthesia, serum NSE, GFAP and Tau protein levels were significantly lower than the preoperative, and the observation group was lower than the control group. Which indicated that brain surgery can clear the lesion to a certain extent, reduce the degree of nerve injury in patients, and use of propofol anesthesia during operation can be more effective to decrease the release of nerve injury mediators than sevoflurane, protect the brain tissue.

Both anesthesia and trauma can cause stress in the patient, resulting in stress damage[19]. In the process of brain injury, the hematoma press will cause the ischemia and hypoxia of the brain tissue, together with the release and stimulation of excitatory amino acids, will lead to oxidative stress and destruction of cell function. MDA is the product of lipid peroxidation, and its content in the body reflects the extent of the body's degree of peroxidation[20]; SOD is an antioxidant enzyme, its level reflects the antioxidant capacity of body and can effectively scavenges oxygen free radicals and neutralizes the oxidative products and reduces the damage of oxidative stress[21]. HO-1 is a peroxidase regulated by Nrf2 and has a good scavenging effect on reactive oxygen and peroxidation products[22]. The study found that a large number of oxygen free radicals generated during traumatic brain injury will over-consume antioxidant enzymes, leading to a serious reduction in its level, resulting in reduced antioxidant capacity[23], while reports have shown that propofol can effectively inhibit lipid peroxidation mediated by free radicals, enhance the ability of cells to resist peroxide damage, and play a role in protecting the body[24]. In this study, propofol anesthesia, MDA level was significantly lower than the before operation, SOD and HO-1 levels increased significantly compared with before operation, and the effect of observation group was significantly better than the control group. It showed that brain surgery to some extent reduced the stress damage caused by traumatic brain injury, and use of propofol anesthesia during operation can be more effective to raise the level of antioxidant enzymes, reduce the level of free radicals,
the effect was significantly better than Sevoflurane anesthesia. Trauma and pain will also increase the release of inflammatory mediators, aggregating the patient's condition and increasing the risk of postoperative infection. TNF-α, IL-6 and CRP are important participant in the inflammatory response. TNF-α is one of the inflammatory factors in the early stage of injury. It plays a role in initiating and triggering inflammatory reaction. Excessive level of inflammatory factors in the early stage of injury. It plays a role in a sharp increase in stress response liver, its serum levels in normal human are extremely low, appears a sharp increase in stress response.Int 154; 2013;

References


18] Zhang Yue. Protection of propofol derivative 6-naphthol on cerebral ischemia-reperfusion injury and its effect on glial cells. Chongqing: Chongqing Medical University; 2013.


