Effects of propofol pretreatment on serum NSE and S100β protein content in elderly patients undergoing laparoscopic surgery

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Propofol
Laparoscopic surgery
NSE
S100β protein

ABSTRACT

Objective: To investigate the effects of propofol pretreatment on serum NSE and S100β protein content in elderly patients undergoing laparoscopic surgery. Methods: A total of 60 elderly patients of scheduled for elective laparoscopic gastrointestinal surgery were randomly divided into 3 groups with 20 cases each: propofol pretreatment group (Group S1), propofol pretreatment group (Group S2) and observation group (Group C). Blood samples were respectively taken from internal jugular vein simultaneously before pneumoperitoneum (H1); pneumoperitoneum was established after 1 h (H2); pneumoperitoneum was terminated immediately (H3); pneumoperitoneum was terminated after 1 h (H4). Meanwhile, blood samples (0.5mL) was immediately taken from transradial artery and jugular veins bulb at 4 time-point (heparin anticoagulant and cut off the air), venous blood gas analysis, blood glucose, blood lactic acid, Serum NSE and S100β protein concentration were detected. Results: The concentration of serum NSE and S100β protein in two groups of patients at H2-H4 was significantly higher than H1. The concentration of serum NSE and S100β protein at H3 and concentration of serum NSE at H4 were increased significantly than H2 in three groups. The concentration of NES and S100β protein at H4 was significantly lower than H3; The concentration of serum NSE and S100β protein have no statistical significance at difference time-point between 2 groups. Conclusion: The pneumoperitoneum can cause brain damage in elderly patients undergoing laparoscopic surgery and different dosage of pump injection of propofol has no obviously effect on this kind of damage.

1. Introduction

Compared to traditional surgery, laparoscopic surgery was performed without the operation of abdomen sectioning, which can diagnose various celiac disease. This kind of surgery can operate immediately for some patients who need this kind of treatment to avoid some unnecessary injury from laparotomy. Laparoscopic surgery receives more and more favors by clinicians due to its characteristics of minimal trauma, resume fast after the operation, less painful and less influence on nervous system, digestive system and immune system. With the expansion of indications of laparoscopic surgery, the ratios of elderly patients received laparoscopic surgery also increase annually.

Clear pneumoperitoneum is the prerequisite of laparoscopic surgery operation for surgeons. CO₂ is the most common inflatable gas use in clinic as it could not explode easily and have high solubility in blood. However, a large number of clinical researches showed that CO₂ can change the cerebral blood flow, and result in cerebral ischemia–hypoxia damage[1-3]. Therefore, in the process of operation, cerebral prevention and protection in elderly patients become one of research task for clinical anesthesia to solve urgently.

Propofol is the most commonly used of intravenous
anesthetics in clinic. There are some studies showed that propofol pretreatment can provide cerebral protection no matter in vitro culture of cell, or reversible focal cerebral in vivo or approximate complete cerebral ischemia in animal models[4-7]. Serum neuron specific enolase (NSE) and S100 β protein were two kind of effectively and strong specificity of cerebral injury biochemical criterion which was widely used in experimental studies of cerebral injury, clinical diagnosis and prognosis evaluation. Therefore, this study was aimed to investigate the cerebral protection effects of propofol pretreatment on serum NSE and S100 β protein index in elderly patients undergoing laparoscopic surgery.

2. Materials and methods

2.1. General materials

A total of 60 elderly patients of laparoscopic gastrointestinal surgery were randomly divided into 3 groups with 20 cases each group: propofol pretreatment group (Group S1), propofol pretreatment group (Group S2) and observation group (Group C). Three groups were all excluded the diseases like heart and cerebral vessels, immune system, central nervous system, liver and kidney. Group S1 (n=20) includes 13 males and 7 females. Age range from 62–73 years, mean age was (67.5±3.8) years, mean weight was (62.5±6.9) kg, ASA I grade has 16 cases, II grade has 4 cases; Group S2 (n=20) includes 20 males and 6 females, age range from (63–71) years, mean age was (65.5±4.2) years, mean weight was (63.5±4.8) kg, ASA I grade 17 cases, II grade 3 cases; Group C (n=20) contains 15 males and 5 females, age range from (65–77) years, mean age was (68.4±3.4) years, mean weight was (63.4±2.0) kg, ASA I grade 16 cases, II grade 4 cases. The difference of general materials between two groups has no statistical significance (P<0.05).

2.2. Anaesthesia method

All patients were fasting for 8 h before operation, liquid fasting for 4 h. Anesthesia, sedative and analgesic drugs cannot use previously. After enter the operating room, vein tunnel was opened, regular monitoring of heart rate, electrocardiogram, blood pressure and oxyhemoglobin saturation were carried out. Then the mask was provided for oxygen–inhalation. Patients were slowly injected with midazolam 0.05 mg/kg, fentanyl 4 μ g/kg, etomidate 0.2 mg/kg and atracurium 0.6 mg/kg for anesthesia induction. The mechanical ventilation was conducted after trachea cannula. Observation group S1 and S2 were treated with 6 mg/kg per h, 10 mg/kg per h propofol intravenous and anesthesia was maintained. Control group C was maintained without any infusion of propofol, injection pump was stopped after 30 min and established pneumoperitoneum (intra–abdominal pressure = 14 mmHg). Three groups of patients were continuously treated with rocuronium bromide and remifentanil to maintain proper depth of anesthesia and keep muscle relaxation during the operation. Meanwhile, based on the change of life signs of patients, cardioactive drug was applied propriety to control the stabilization of haemodynamics.

2.3. Obvervational index

Venous bloods (3–5 mL) were respectively taken from internal jugular vein respectively before pneumoperitoneum (H1); pneumoperitoneum was established after 1 h (H2); pneumoperitoneum was terminated immediately (H3); pneumoperitoneum was terminated after 1 h (H4), and then were placed in anticoagulative tube for sufficient mixing. After centrifugation (2 500 r/min) for 10 min, the upper serum was taken and placed in refrigerator at −70 °C. Meanwhile, blood samples (0.5 mL) (heparin anticoagulant and cut off the air) were immediately taken from transradial artery and jugular veins bulb at 4 time-point, venous blood gas analysis, blood glucose, blood lactic acid, Serum NSE and S100 β protein concentration were detected.

2.4. Statistic analysis

Data were analyzed using SPSS vesion 12.0 software. Measurement data were expressed with mean±SD. t-test was used for comparison among groups, and ANOVA was conducted with intra-group comparison, P-value<0.05 was considered statistically significant.

3. Results

3.1. Statistical difference in three groups

There was no statistical difference in gender, age, weight, pneumoperitoneum pressure, time of Pneumoperitoneum and operation in three groups (Table 1).

Table 1.
Comparison of general materials in three groups of patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age(years)</th>
<th>Weight(kg)</th>
<th>PP(mmHg)</th>
<th>TP(min)</th>
<th>TS(min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>20</td>
<td>67.5±3.8</td>
<td>62.5±6.9</td>
<td>12.8±0.6</td>
<td>151.2±12.7</td>
<td>189.1±28.9</td>
</tr>
<tr>
<td>S2</td>
<td>20</td>
<td>65.5±4.2</td>
<td>63.5±4.8</td>
<td>12.5±0.4</td>
<td>148.9±11.5</td>
<td>186.8±29.1</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>68.4±3.4</td>
<td>63.4±2.0</td>
<td>12.7±0.8</td>
<td>156.3±13.5</td>
<td>192.3±23.7</td>
</tr>
</tbody>
</table>

3.2. Serum NSE and S100β protein concentration in three groups of patients

Serum NSE and S100β protein concentration in three groups of patients at H1–H4 were detected respectively. The results showed that the serum NSE and S100β protein concentration at H2–H4 were significantly higher than H1 (P<0.05); the serum NSE and S100β protein concentration at H3 and H4 were significantly higher than H2 in three groups of patients (P<0.05); The serum NSE and S100β protein concentration at H4 were lower than H3 in three groups of patients (P<0.05). The concentration of serum NSE and S100β protein have no statistical significance at difference time-point between 2 groups (Table 2).

3.3. Blood gas analysis and metabolic change of glucose

Blood gas analysis and metabolic change of glucose at H1–H4 time-point in three groups of patients were detected respectively. Compared to H1, oxyhemoglobin saturation was increased at H2 and H3 (P<0.05), while decreased in the difference of oxygen content in brain arteriovenous (P<0.05); but the blood glucose and blood lactate concentration had no significant difference (P>0.05) (Table 3).

Table 2.

<table>
<thead>
<tr>
<th>Index</th>
<th>Group</th>
<th>n</th>
<th>H1</th>
<th>H2</th>
<th>H3</th>
<th>H4</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSE</td>
<td>S1</td>
<td>20</td>
<td>4.11±1.81</td>
<td>6.75±1.45</td>
<td>14.89±2.31</td>
<td>13.12±1.56</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>3.98±1.56</td>
<td>6.56±1.39</td>
<td>13.97±2.45</td>
<td>13.56±1.38</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>3.89±0.76</td>
<td>6.89±1.35</td>
<td>14.38±2.38</td>
<td>12.37±1.37</td>
</tr>
<tr>
<td>S100β protein</td>
<td>S1</td>
<td>20</td>
<td>0.04±0.02</td>
<td>0.36±0.07</td>
<td>0.67±0.13</td>
<td>0.47±0.23</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>0.04±0.01</td>
<td>0.38±0.07</td>
<td>0.71±0.15</td>
<td>0.49±0.15</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>0.04±0.02</td>
<td>0.39±0.08</td>
<td>0.63±0.12</td>
<td>0.49±0.32</td>
</tr>
</tbody>
</table>

Table 3.

<table>
<thead>
<tr>
<th>Index</th>
<th>Group</th>
<th>n</th>
<th>H1</th>
<th>H2</th>
<th>H3</th>
<th>H4</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS (%)</td>
<td>S1</td>
<td>20</td>
<td>64±6</td>
<td>81±5</td>
<td>82±6</td>
<td>63±6</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>59±5</td>
<td>81±6</td>
<td>82±5</td>
<td>58±6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>59±6</td>
<td>79±7</td>
<td>80±4</td>
<td>58±3</td>
</tr>
<tr>
<td>DOCBA (mL/L)</td>
<td>S1</td>
<td>20</td>
<td>58±9</td>
<td>35±7</td>
<td>33±9</td>
<td>59±10</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>54±4</td>
<td>29±3</td>
<td>26±4</td>
<td>51±7</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>56±5</td>
<td>34±6</td>
<td>32±5</td>
<td>58±8</td>
</tr>
<tr>
<td>BG (mmol/L)</td>
<td>S1</td>
<td>20</td>
<td>0.28±0.12</td>
<td>0.28±0.13</td>
<td>0.32±0.19</td>
<td>0.27±0.19</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>0.37±0.11</td>
<td>0.39±0.11</td>
<td>0.31±0.12</td>
<td>0.31±0.15</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>0.31±0.15</td>
<td>0.37±0.15</td>
<td>0.45±0.19</td>
<td>0.39±0.18</td>
</tr>
<tr>
<td>LA (mmol/L)</td>
<td>S1</td>
<td>20</td>
<td>0.8±0.6</td>
<td>0.8±0.5</td>
<td>1.0±0.4</td>
<td>1.0±0.4</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>20</td>
<td>0.8±0.5</td>
<td>1.0±0.4</td>
<td>1.2±0.3</td>
<td>1.2±0.3</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>20</td>
<td>1.1±0.4</td>
<td>1.1±0.5</td>
<td>1.3±0.5</td>
<td>1.3±0.5</td>
</tr>
</tbody>
</table>

The difference of oxygen content in brain arteriovenous = arterial oxygen content - oxygen content of bulbus venae jugularis. OS: Oxyhemoglobin saturation; DOCBA: The difference of oxygen content in brain arteriovenous; BG: blood glucose; LA: lactic acid.

4. Discussion

Recently, with the phenomenon of aging population in our country, surgical patients in elderly people become more and more apparent. Laparoscopic surgery was widely applied in elderly patients due to the advantages of minimal trauma and resume fast after the operation. CO₂ as a laparoscopic pneumoperitoneum gas was verified to obviously increase the level of CO₂ in vivo. According to the difference of compensation ability in patients, the reducing of pH value was different. Thus it performs as hypercapnia, respiratory acidosis and hepatorenal function, coagulation function, endocrine function, immunologic function and so on. Besides, CO₂ pneumoperitoneum can induce or aggravate the brain damage in elderly patients. On the other hand, CO₂ pneumoperitoneum can increase the intra-abdominal pressure and act on postcava that leads to the increase in central vein. Meanwhile, intra-abdominal pressure hypertension limits the movement of diaphragm and increases the pleural space pressure, thus to block the cerebral venous reflux and enhance the flow resistance of vertebral venous plexus and cerebrospinal fluid. And this is thought to be the main reason for the rise of intracranial pressure. On the other hand, CO₂ pneumoperitoneum can also act on diaphragm muscle and lead to the change in pleural cavity pressure and thoracic compliance, result to insufficient of alveolar ventilation. Then it causes the accumulation of CO₂. Besides, due to the increased of abdominal pressure caused by pneumoperitoneum and CO₂ absorbed into plasma through peritoneum that result in the rise of carbon dioxide partial pressure of arterial blood. Coupled with the decrease of breathing reserve and gas exchange function in elderly patients, and compensatory in cerebrospinal fluid amount raised, the cerebral blood flow increased eventually. These several factors lead to the increase of ICP and the occurrence of cerebral hyperperfusion, and then further enhance the potential risks of encephaldeema in elderly patients. Therefore, in the process of laparoscopic surgery, cerebral prevention and protection in elderly patients should arouse the attention by us clinical anesthesia. S-100β protein and NSE are two effectively and strong specificity biochemical index of cerebral injury. The specificity of S-100β protein existed in gliocyte, gitter and macroglial cell of nervous centralis. This kind of protein release increased when brain tissue damage caused by various reasons, such as central lesion and blood-brain barrier is destroyed. However, the specificity of NSE existed in neuron and neurogenic cell which is the specific proteins to reflect the damage of neuron and neuroendocrine cellular. The NSE released when brain tissue occurs ischemia, intoxication or damage, and then leads to nerve demyelination, neuron disintegration and blood brain barrier damage. Lots of human studies showed that serum NSE content positively associated with severity of cerebral injury and clinical prognosis[11,12]. This indicated that S-100β
Propofol is an intravenous anesthetics commonly used in clinic. Lots of studies showed that it has the protective effect on many vital organs and receives attention especially for its cerebral protection[13,14]. Guo et al[15] concluded that propofol has the protective effect on cerebral ischemia-reperfusion injury which may relate with the release of excitatory amino acid, ease the toxic effect of neurons excitation, decrease the exhaustion of inhibitory amino acid, enhance the protective inhibition of neuron, thus to reduce the neuron apoptosis, then increase the number of neuronal survival. The application of propofol pretreatment in SD rats of focal traumatic brain injury model confirmed that propofol can lower the content of NSE in cerebral trauma of rat brain tissues and relieve nervous lesion. Propofol pretreatment can improve the neurologic deficit score of post-traumatic rats in 2 h before trauma and significantly effect on brain protection. Similarly, Gan et al. proved that propofol can lower the content of S100 β and NSE in cerebral trauma of rat brain tissues and relieve nervous lesion. Propofol pretreatment can improve the neurologic deficit score of post-traumatic rats in 2 h before ischemia and significantly effect on brain protection[16].

This study showed that serum NSE and S100 β protein concentration in three groups of patients at H1 all within normal limits. After the pneumoperitoneum was established, serum NSE and S100 β protein concentration all occur increased at first and then decreased. Peak value all occur when pneumoperitoneum was removed immediately. Patients of observation groups (S1 and S2) were treated with propofol of 6 and 10 mg/kg per h. Compared to control group, the difference of serum NSE concentration among groups at different time-point had no statistical significance, which indicated that pump advance and the concentration of propofol have insufficient protection effect to demonstrate on laparoscopic surgery in elderly patients.

In summary, the establishment of pneumoperitoneum in laparoscopic surgery has certain influence on cerebral injury in elderly patients. The application of propofol pumping cannot improve injury degree of patients. So, whether the long-term propofol pumping can have improvement effect on cerebral function still needs to do further observation and research.

Reference