Effect of parecoxib sodium on propofol combined with fentanyl anesthesia effect and postoperative recovery in elderly patients with laparoscopic surgery

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ABSTRACT

Objective: To study the effect of parecoxib sodium on propofol combined with fentanyl anesthesia effect and postoperative recovery in elderly patients with laparoscopic surgery.

Methods: A total of 80 cases of elderly patients who received laparoscopic surgery in our hospital from May 2013 to December 2015 were selected for study and randomly divided into observation group who received parecoxib sodium + propofol combined with fentanyl anesthesia and control group who received propofol combined with fentanyl anesthesia, and then pain threshold and serum indicators of two groups were compared.

Results: 2 h, 4 h, 6 h, 8 h, 10 h and 12 h after surgery, pain threshold EL50 of observation group was significantly higher than that of control group; serum Glu, PS, histamine, 5-HT, MCP-1, CCR2, JAK2, STAT3, p38MAPK, PX1, Orexin, IRAK1, TRAF6 and Fc γ R1 contents of observation group were significantly lower than those of control group; serum GABA and β-EP contents of observation group were significantly higher than those of control group.

Conclusion: Parecoxib sodium has inhibiting effect on the pain perception of propofol combined with fentanyl anesthesia for elderly patients with laparoscopic surgery and can reduce the synthesis of pain neurotransmitters, inflammatory factors and related molecules.

1. Introduction

Laparoscopic surgery is the clinically widely used method of minimally invasive surgery in recent years with the advantages of small surgical trauma and quick postoperative recovery. Nonetheless, the establishment of pneumoperitoneum during surgery will affect anesthesia effect to varying degrees, which will not only affect the stability of the vital signs, but also cause postoperative pain and delay the body function recovery. Clinical researches have reported that the proportion of moderate to severe pain 24 h after laparoscopic surgery is more than 30%, and the conventional treatment methods are the intramuscular injection or intravenous injection of analgesic drugs. Parecoxib sodium is the newly developed analgesic drug that can selectively inhibit the activity of cyclooxygenase 2 (COX2) and alleviate the pain caused by surgical trauma by the central and peripheral mechanisms[1-2]. In the following research, the effect of parecoxib sodium on propofol combined with fentanyl anesthesia effect and postoperative recovery in elderly patients with laparoscopic surgery was analyzed.

2. Case information and research methods

2.1 Case information

A total of 80 cases of elderly patients who received laparoscopic surgery in our hospital from May 2013 to December 2015 were selected for study, all of whom were 70-80 years old, met the indications of laparoscopic surgery, were informed of research matters, then received laparoscopic surgery and divided into two groups according to different intraoperative anesthesia methods, 40 cases in each group. Observation group received parecoxib sodium...
propofol combined with fentanyl anesthesia, including 25 male cases and 15 female cases who were (74±8) years old; control group received propofol combined with fentanyl anesthesia, including 27 male cases and 13 female cases who were (76±7) years old.

2.2 Anesthesia methods

After two groups entered into the operating room, ECG monitoring was connected and venous access was established, observation group of patients received intravenous injection of parecoxib sodium 1.5 mg/kg before anesthesia induction, control group received intravenous injection of equivalent dose of normal saline, and then midazolam 0.02 mg/kg, propofol 1.5 mg/kg, remifentanil 2.00 g/kg and CIS 0.25 mg/kg were given for anesthesia induction; after the completion of the induction, propofol 2.5 μg/kg and remifentanil 2.5 ng/kg were used for maintenance.

2.3 Anesthesia effect evaluation

Von Frey was used to assess the preoperative and postoperative mechanical pain threshold values of patients, the tip of the cellosilk vertically contacted with the skin around the incision, cellosilk was moderately bent for 1.5 s, the chosen cellosilk size increased gradually from 0.4 g until a pricking occurred, and the pain perception threshold was calculated according to the formula El50=Xf×kd, (Xf was the intensity value of the final measurement, k was the maximum likelihood estimator and d was log value of intensity spacing).

2.4 Serum indicator detection

High-performance liquid chromatography fluorescence method was used to detect glutamic acid (Glu), γ-aminobutyric acid (GABA) and 5-hydroxytryptamine (5-HT); enzyme-linked immunosorbent assay was used to substance P (PS), histamine, β-endorphin, MCP-1, CCR2, JAK2, STAT3, p38MAPK, PX1, Orexin, IRAK1, TRAF6 and Fc γ RI contents.

2.5 Statistical methods

SPSS 20.0 statistical software was used to input and analyze data, differences in data between two groups was analyzed by t test and differences were considered to be statistically significant at a level of P<0.05.

3. Results

3.1 Pain threshold El50 before and after surgery

Comparison before and after surgery was as follows: 2 h, 4 h, 6 h, 8 h, 10 h and 12 h after surgery, pain threshold El50 of two groups was lower than that before surgery; comparison between two groups was as follows: before surgery, pain threshold El50 was not different between two groups; 2 h, 4 h, 6 h, 8 h, 10 h and 12 h after surgery, pain threshold El50 of observation group was significantly higher than that of control group.

3.2 Pain–related neurotransmitters

1 d after surgery, analysis of the contents of serum pain-promoting neurotransmitters of two groups was as follows: serum pain-promoting neurotransmitters Glu, PS, histamine and 5-HT contents of observation group were significantly lower than those of control group; analysis of the serum pain-inhibiting neurotransmitters of two groups was as follows: serum pain-inhibiting neurotransmitters GABA and β-EP contents of observation group were significantly higher than those of control group.

3.3 Inflammatory factors and related signaling pathway

1 d after surgery, analysis of the contents of serum inflammatory

Table 1
Comparison of pain threshold EI50 between two groups before and after surgery.

<table>
<thead>
<tr>
<th>Group</th>
<th>Before surgery</th>
<th>2 h</th>
<th>4 h</th>
<th>6 h</th>
<th>8 h</th>
<th>10 h</th>
<th>12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>14.9±1.8</td>
<td>13.1±1.5</td>
<td>11.5±1.5</td>
<td>10.3±1.2</td>
<td>12.9±1.3</td>
<td>13.5±1.4</td>
<td>13.7±1.2</td>
</tr>
<tr>
<td>Control</td>
<td>15.2±1.6</td>
<td>9.6±0.9</td>
<td>7.7±0.8</td>
<td>7.1±0.6</td>
<td>8.5±0.7</td>
<td>9.3±1.0</td>
<td>9.6±1.1</td>
</tr>
<tr>
<td>T</td>
<td>0.182</td>
<td>5.869</td>
<td>6.573</td>
<td>6.138</td>
<td>7.684</td>
<td>7.023</td>
<td>7.551</td>
</tr>
<tr>
<td>P</td>
<td>&gt;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 2
Serum pain-related neurotransmitter contents of two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Glu (nmol/L)</th>
<th>PS (pg/mL)</th>
<th>Histamine (pg/mL)</th>
<th>5-HT (nmol/L)</th>
<th>GABA (nmol/L)</th>
<th>β-EP (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>112.3±12.8</td>
<td>56.2±7.4</td>
<td>44.2±5.7</td>
<td>247.5±28.7</td>
<td>79.3±8.7</td>
<td>263.2±28.9</td>
</tr>
<tr>
<td>Control</td>
<td>176.5±20.4</td>
<td>92.4±10.3</td>
<td>89.5±10.2</td>
<td>372.6±41.3</td>
<td>34.2±4.1</td>
<td>177.5±20.2</td>
</tr>
<tr>
<td>T</td>
<td>6.923</td>
<td>8.784</td>
<td>10.582</td>
<td>7.113</td>
<td>12.582</td>
<td>7.894</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>
</tr>
</tbody>
</table>
factors of two groups was as follows: serum inflammatory factors MCP-1 and CCR2 contents of observation group were lower than those of control group; analysis of the contents of serum related signaling pathway molecules of two groups was as follows: serum signaling pathway molecules JAK2, STAT3 and p38MAPK contents of observation group were significantly lower than those of control group;

3.4 Pain-related molecules

1d after surgery, analysis of the contents of serum pain-related molecules of two groups was as follows: serum PX1, Orexin, IRAK1, TRAF6 and FcγRI contents of observation group were lower than those of control group.

4. Discussion

Laparoscopic surgery is the clinically widely used method of minimally invasive surgery that can significantly reduce the trauma caused by surgical operation. However, intraoperative establishment of pneumoperitoneum and CO₂ diffusion can cause abdominal acidification and reduced peritoneal tension, resulting in reduced peritoneal support ability for abdominal visceral tissue ability and the occurrence of significant pain[3]. Opioids are the most widely used clinical analgesic drugs, drug administration through intramuscular injection can effectively alleviate the degree of pain, but excessive use of opioids can suppress the immune function. Parecoxib sodium is a newly developed non-steroidal drug that can selectively inhibit COX-2 function and reduce the synthesis of prostaglandin in peripheral tissues, thus alleviating pain hypersensitivity phenomenon caused by parecoxib sodium[4,5].

In the study, parecoxib sodium was given on the basis of propofol combined with fentanyl anesthesia in order to exert the inhibiting effect of parecoxib sodium on pain. Pain threshold is the objective method for clinical assessment of anesthesia effect, and both repeatability and objectivity of it are stronger than the comparison of simple vital signs. Surgical trauma and incision stretch will cause the hyperalgesia of the skin surrounding the incision and the decrease of pain threshold. In the research, Von Frey was used to detect and analyze the pain threshold of the skin around the incision, and results showed that 2 h, 4 h, 6 h, 8 h, 10 h and 12 h after surgery, pain threshold E₁₀ of observation group was significantly higher than that of control group. It indicated the pain threshold of observation group was higher and had stronger tolerance to pain stimuli, thus reflecting that parecoxib sodium could obtain more accurate anesthetic effect and analgesic effect.

The generation of pain perception is associated with the synthesis and release of a variety of neurotransmitters in the body. Glutamic acid (Glu) and γ-aminobutyric acid (GABA) are the excitatory neurotransmitter and inhibitory neurotransmitter in the body respectively. Glu can increase the postsynaptic membrane NMDA expression and induce pain; GABA can be combined with the receptor GABA-AR on postsynaptic membrane and alleviate pain[6,7]. Substance P (PS) and β-endorphin (β-EP) are two kinds of neuropeptides that also have the neurotransmitter effect and can transmit pain signals, and SP can transmit pain signals into the center and increase the release of histamine and 5-hydroxytryptamine (5-HT), thus causing pain[8,9]; β-EP has inhibiting effect on the release of SP, and can alleviate pain response[10]. In the research, analysis of the contents of above serum pain-related neurotransmitters showed that serum Glu, PS, histamine and 5-HT contents of observation group were lower than those of control group while GABA and β-EP contents were higher than those of control group. It indicated that parecoxib sodium had inhibiting effect on the release of pain-related neurotransmitters, inhibited the synthesis of pain-promoting neurotransmitters and increased the synthesis of pain-inhibiting neurotransmitters.

Surgical trauma can cause the activation of inflammatory reaction and the release of inflammatory cytokines, thereby causing pain reaction of the body through a variety of downstream signaling molecules. Monocyte chemoattractant protein (MCP-1) can be combined with chemokine receptor 2 (CCR2) to activate the downstream JAK2/STAT3 signaling pathway and p38MAPK

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Inflammatory factors</th>
<th>Related signaling pathway molecules</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MCP-1 (ng/mL)</td>
<td>CCR2 (ng/mL)</td>
</tr>
<tr>
<td>Observation</td>
<td>103.5±12.5</td>
<td>136.4±16.5</td>
</tr>
<tr>
<td>Control</td>
<td>186.4±20.4</td>
<td>295.3±34.2</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Group</th>
<th>PX1 (ng/mL)</th>
<th>Orexin (ng/mL)</th>
<th>IRAK1 (ng/mL)</th>
<th>TRAF6 (ng/mL)</th>
<th>FcγRI (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>103.4±11.5</td>
<td>67.5±7.8</td>
<td>136.5±16.5</td>
<td>93.6±10.4</td>
<td>162.3±18.6</td>
</tr>
<tr>
<td>Control</td>
<td>179.5±20.4</td>
<td>104.3±12.5</td>
<td>244.2±27.6</td>
<td>168.7±18.5</td>
<td>302.2±33.6</td>
</tr>
<tr>
<td>T</td>
<td>8.282</td>
<td>7.684</td>
<td>7.194</td>
<td>9.039</td>
<td>9.682</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>
</tr>
</tbody>
</table>
signaling pathway, thus resulting in pain perception[11,12]. Studies have confirmed that CCR2 blockers can reverse the mechanical hyperalgesia of rats. The activation of JAK2/STAT3 pathway can cause the accumulation of Ca$^{2+}$ in cells and will act on the NMDARs to cause central facilitation, thus causing pain perception. P38MAPK can be activated to p-p38MAPK to cause hyperalgesia by regulating the expression of COX-2. In the research, analysis of the contents of above serum inflammatory factors and downstream signal molecules showed that serum MCP-1, CCR2, JAK2, STAT3 and p38MAPK contents of observation group were lower than those of control group. It indicated that parecoxib sodium had inhibiting effect on the release of inflammatory factors and the activation of downstream signal molecules.

In the occurrence process of incision pain, the expression of a variety of pain-related molecules is abnormal. Pannexin (PX) is a kind of connexin that includes three subtypes PX1-3, PX1 has the richest expression, and it can adjust the exchange of ATP and Ca$^{2+}$ inside and outside the astrocytes and cause pain[13]; Orexin can be combined with receptor OXR to activate the Gq coupling protein and lead to Ca$^{2+}$ influx as well as cause the postsynaptic membrane depolarization and cause pain[14]; IRAK1 and TRAF6 are important proteins in TLR4 downstream pathways that can increase the excitability of neurons and cause pain sensitization[15]; Fc$\gamma$ receptor I (Fc$\gamma$ RI) is the high-affinity receptor of IgG, the combination of the two can lead to Ca$^{2+}$ influx and action potential changes and cause pain[16]. In the research, analysis of the contents of serum pain-related molecules showed that serum PX1, Orexin, IRAK1, TRAF6 and Fc$\gamma$ RI contents of observation group were lower than those of control group. It indicated that parecoxib sodium had inhibiting effect on the expression of pain-related molecules.

Based on above discussion, it can be concluded that parecoxib sodium has inhibiting effect on the pain perception of propofol combined with fentanyl anesthesia for elderly patients with laparoscopic surgery and can reduce the synthesis of pain neurotransmitters, inflammatory factors and related molecules.

References