Effect of parecoxib sodium intervention before induction on incision pain and inflammatory stress response after orthopedic surgery

Fu-Sheng Wei, Xiu-Ze Li, Peng Xu

1. Introduction

The incision pain after orthopedic surgery is the most common postoperative complication, and persistent pain perception will activate the systemic inflammatory and stress response, cause the internal environment disorder and increase the risk of cardiovascular system complications. In clinical practice, the necessary analgesia after orthopedic surgery can create favorable conditions for postoperative recovery. Preemptive analgesia is a concept of analgesia developed in recent years, which provides analgesics in advance to reduce the afference of the noxious stimuli and thereby reduce the postoperative pain caused by noxious stimuli[1,2]. Traditional preemptive analgesia drugs opioids can easily induce nausea, vomiting as well as circulatory and respiratory depression, which is not conducive to postoperative recovery and increases the risk of cardiovascular complications. Parecoxib sodium is a kind of highly selective COX-2 inhibitor, which produces Valdecoxib through metabolism in the body to inhibit the activity of COX-2 and reduce the production of prostaglandins to exert anti-inflammatory and analgesic effect[3,4]. In the following studies, we specifically analyzed the effect of parecoxib sodium intervention before induction on incision pain and inflammatory stress response after orthopedic surgery.
all patients were in line with the orthopedic surgery indications, and the patients with lumbar anesthesia or epidural block anesthesia contraindications, those allergic to parecoxib sodium and those with history of chronic painful disease or chronic infectious disease were eliminated. A total of 114 patients were enrolled in the study and divided into Par group and control group by random number table method, with 57 cases in each group. There were 32 males and 25 females in the Par group, and they were 41-62 years old; there were 34 males and 23 females in the control group, and they were 41-64 years old. There was no significant difference in the general data between the two groups (P>0.05).

2.2. Analgesia and parecoxib sodium intervention methods

Both groups of patients accepted lumbar anesthesia combined with epidural block anesthesia, piercing, L2-3 space was chosen for puncture, 1.2-1.5 mL of 0.75% bupivacaine was provided via subarachnoid space, epidural cathetering was done towards the head, and 1% lidocaine + 0.375% ropivacaine 4 mL was provided during operation for maintenance. Par group were given intramuscular injection of 40 mg of parecoxib sodium 30 min before anesthesia, and control group were given intramuscular injection of same dosage of saline 30 min before anesthesia. After the operation, all patients were connected to patient-controlled intravenous analgesia pump. The analgesia program was sufentanil 100 µg+ normal saline 100 mL, the load dose was 0.5 mL, and the locking time was 15 min.

2.3. Laboratory detection methods

Before surgery as well as 1 d and 3 d after surgery, peripheral blood was collected for laboratory detection, a total of about 10 mL of peripheral blood was collected, 6-8 mL of peripheral blood was taken and centrifuged to separate serum, and then ELISA kit instructions were followed to determine PGE2, 5-HT, SP, NPY, COR and GH levels; the remaining peripheral blood was taken to extract RNA, and then the instructions of the PCR kit were referred to determine the mRNA expression levels of JAK2, STAT3, IL-1, IL-6, IFIT1, Nrf2 and HO-1.

2.4. Statistical methods

Software SPSS 20.0 was used to input data, the measurement data between two groups were analyzed by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1. Changes in pain neurotransmitters before and after surgery

Serum PGE2, 5-HT, SP and NPY levels were not significantly different between the two groups of patients before surgery (P>0.05) whereas serum PGE2, 5-HT, SP and NPY levels were significantly different after surgery (P<0.05), and serum PGE2, 5-HT, SP and NPY levels of Par group after surgery were lower than those of control group; compared with pain neurotransmitters of same group before surgery, serum PGE2, 5-HT, SP and NPY levels of both groups were significantly lower after surgery (P<0.05) (Table 1).

3.2. Changes in inflammatory molecules before and after surgery

Peripheral blood JAK2, STAT3, IL-1 and IL-6 mRNA expression were not significantly different between the two groups of patients before surgery (P>0.05) whereas peripheral blood JAK2, STAT3, IL-1 and IL-6 mRNA expression were significantly different after surgery (P<0.05), and peripheral blood JAK2, STAT3, IL-1 and IL-6 mRNA expression of Par group after surgery were lower than those of control group; compared with inflammatory molecules of same group before surgery, peripheral blood JAK2, STAT3, IL-1 and IL-6 mRNA expression of both groups were significantly higher after surgery (P<0.05) (Table 2).

Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>PGE2 (ng/mL)</th>
<th>5-HT (ng/mL)</th>
<th>SP (ng/mL)</th>
<th>NPY (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Par</td>
<td>57</td>
<td>Before surgery</td>
<td>236.2±29.4</td>
<td>1.62±0.22</td>
<td>145.2±17.8</td>
<td>281.3±33.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after surgery</td>
<td>167.5±22.1*</td>
<td>1.14±0.16*</td>
<td>103.5±12.7*</td>
<td>213.4±27.6*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after surgery</td>
<td>130.4±15.6*</td>
<td>0.89±0.10*</td>
<td>83.4±10.3*</td>
<td>184.5±20.3*</td>
</tr>
<tr>
<td>Control</td>
<td>57</td>
<td>Before surgery</td>
<td>241.2±29.5</td>
<td>1.66±0.19</td>
<td>147.1±17.2</td>
<td>283.1±32.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after surgery</td>
<td>221.5±26.7</td>
<td>1.33±0.17</td>
<td>129.4±15.2*</td>
<td>242.9±29.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after surgery</td>
<td>194.6±20.3</td>
<td>1.09±0.14</td>
<td>114.6±13.7*</td>
<td>227.5±27.2*</td>
</tr>
</tbody>
</table>

*: comparison between before and after surgery within group, P<0.05; *: comparison between the two groups after surgery, P<0.05.

Table 2

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>JAK2</th>
<th>STAT3</th>
<th>IL-1</th>
<th>IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Par</td>
<td>57</td>
<td>Before surgery</td>
<td>1.03±0.13</td>
<td>0.98±0.13</td>
<td>1.04±0.17</td>
<td>1.01±0.15</td>
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<tr>
<td></td>
<td></td>
<td>1 d after surgery</td>
<td>1.35±0.17*</td>
<td>1.29±0.15*</td>
<td>1.38±0.18*</td>
<td>1.28±0.14*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after surgery</td>
<td>1.61±0.22*</td>
<td>1.54±0.20*</td>
<td>1.64±0.25*</td>
<td>1.52±0.18*</td>
</tr>
<tr>
<td>Control</td>
<td>57</td>
<td>Before surgery</td>
<td>1.01±0.12</td>
<td>1.01±0.14</td>
<td>1.02±0.14</td>
<td>0.99±0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after surgery</td>
<td>1.86±0.22*</td>
<td>1.64±0.22*</td>
<td>1.77±0.23*</td>
<td>1.65±0.22*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after surgery</td>
<td>2.21±0.35*</td>
<td>2.09±0.34*</td>
<td>2.32±0.34*</td>
<td>2.18±0.34*</td>
</tr>
</tbody>
</table>

*: comparison between before and after surgery within group, P<0.05; *: comparison between the two groups after surgery, P<0.05.
of same group before surgery, serum PGE2, 5-HT, SP and NPY and after surgery showed that compared with pain neurotransmitters the changes of the corresponding neurotransmitters in serum before conducive to the production of pain [10,11].

Polypeptide neurotransmitters, which can mediate the conduction analgesic action arachidonic acid metabolism and generate the anti-inflammatory and which can inhibit the formation of prostaglandin in the process of transformed into the Valdecoxib with COX2-inhibitory activity, injection or intravenous injection and then is hydrolyzed by the liver COX2 inhibitor, and it enters the body through intramuscular.

Intraoperative noxious afference so as to reduce the degree of postoperative pain. Parecoxib sodium is a kind of highly selective intravenous analgesia could effectively inhibit postoperative pain and reduce the postoperative secretion of pain neurotransmitters, and the parecoxib sodium preemptive analgesia on the basis of routine patient-controlled intravenous analgesia can more effectively inhibit postoperative pain.

The direct damage caused during orthopedic operation and the persistent incision pain after operation can cause internal environment disturbance, and the excessive activation of inflammatory response is one of the characteristics of the internal environment disturbance [12,13]. Survivor activating factor enhancement (SAFE) pathway is the important mechanism for the body to start inflammatory response when subjected to external stimuli, JAK2/STAT3 signaling pathway is one of the many SAFE pathways, and it can be activated through cascade activation to start the expression of IL-1, IL-6 and other cytokines and participate in the activation of the inflammatory response [14]. IL-1 has pro-inflammatory activity, which can stimulate the activation of various inflammatory cells and increase the secretion of various inflammatory factors; IL-6 has multiple biological activities, plays an important role in both inflammatory response and immune response, and can mediate the amplification of inflammatory response [15]. In the study, in order to further clarify the influence of parecoxib sodium intervention before induction on postoperative pain, the changes in inflammatory response activation caused by pain before and after operation were analyzed, and the results showed that compared with inflammatory molecules of same group before surgery, peripheral blood PGE2, 5-HT, SP and NPY levels of Par group after surgery were lower than those of control group. It means that both parecoxib sodium preemptive analgesia and routine patient-controlled intravenous analgesia could effectively inhibit postoperative pain and reduce the postoperative secretion of pain neurotransmitters, and the parecoxib sodium preemptive analgesia on the basis of routine patient-controlled intravenous analgesia can more effectively inhibit postoperative pain.

Peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels were not significantly different between the two groups of patients before surgery (P>0.05) whereas peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels were significantly different after surgery (P<0.05), and peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels of Par group after surgery were lower than those of control group; compared with stress molecules of same group before surgery, peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels of both groups were significantly higher after surgery (P<0.05) (Table 3).

### 4. Discussion

Preemptive analgesia has been increasingly used for orthopedic surgery analgesia in recent years, which provides analgesics before anesthesia to reduce the pain hypersensitivity state caused by intraoperative noxious stimuli afference so as to reduce the degree of postoperative pain. Parecoxib sodium is a kind of highly selective COX2 inhibitor, and it enters the body through intramuscular injection or intravenous injection and then is hydrolyzed by the liver and transformed into the Valdecoxib with COX2-inhibitory activity, which can inhibit the formation of prostaglandin in the process of arachidonic acid metabolism and generate the anti-inflammatory and analgesic action [5-7]; PGE2 is an important product generated in the process of arachidonic acid metabolism, is also considered as the pain mediator that plays an important role in peripheral tissue, and can reduce the pain threshold of peripheral tissue and promote the inflammatory activity, which can stimulate the activation of various inflammatory cells and increase the secretion of various inflammatory factors; IL-6 has multiple biological activities, plays an important role in both inflammatory response and immune response, and can mediate the amplification of inflammatory response [15]. In the study, in order to further clarify the influence of parecoxib sodium intervention before induction on postoperative pain, the changes in inflammatory response activation caused by pain before and after operation were analyzed, and the results showed that compared with inflammatory molecules of same group before surgery, peripheral blood JAK2, STAT3, IL-1 and IL-6 mRNA expression of both groups were significantly higher after surgery, serum PGE2, 5-HT, SP and NPY levels of both groups were significantly lower after surgery, and serum PGE2, 5-HT, SP and NPY levels of Par group after surgery were lower than those of control group. It means that both parecoxib sodium preemptive analgesia and routine patient-controlled intravenous analgesia could effectively inhibit postoperative pain and reduce the postoperative secretion of pain neurotransmitters, and the parecoxib sodium preemptive analgesia on the basis of routine patient-controlled intravenous analgesia can more effectively inhibit postoperative pain.

Another characteristic of postoperative internal environmental disturbance is the excessive activation of the stress response. IFIT1...
is the molecule closely related to the abnormal synthesis and secretion of various endocrine hormones during stress response activation; on the one hand, IFIT1 can hinder the glucocorticoid receptor and suppress glucocorticoid activity to weaken the inhibitory effect of glucocorticoid on HPA axis and increase Cor secretion by adrenal cortex; on the other hand, the HPA axis dysfunction caused by IFIT1 can also cause the abnormal secretion of a variety of pituitary hormones, and the mass secretion of GH is closely related to the changes of energy metabolism and glucolipid metabolism in the process of stress[16,17]. In addition to the changes of endocrine hormones, the generation of oxygen free radicals will also increase during the stress reaction, which can activate the antioxidation pathway mediated by Nrf2 and increase the expression of antioxidant enzyme HO-1. In order to further clarify the influence of parecoxib sodium intervention before induction on postoperative pain, the changes of stress reaction activation caused by pain before and after operation were analyzed in the study, and the result showed that compared with stress molecules of same group before surgery, peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels of both groups were significantly higher after surgery, and peripheral blood IFIT1, Nrf2 and HO-1 mRNA expression as well as serum COR and GH levels of Par group after surgery were lower than those of control group. This means that the orthopedic operation and postoperative incision pain can cause the postoperative activation of stress response together, and the parecoxib sodium preemptive analgesia on the basis of routine patient-controlled intravenous analgesia can reduce the stress reaction activation degree and inhibit the postoperative stress reaction.

Based on the above discussion about pain mediators and inflammatory stress response, it can be concluded that the parecoxib sodium intervention before induction on the basis of routine patient-controlled intravenous analgesia can alleviate the incision pain after orthopedic surgery, and also restrain the activation of inflammatory stress response.

References


