Effect of cefazolin sodium and amoxicillin sodium/clavulanate potassium on postoperative infection, pain and expression of inflammatory factors in patients undergoing orthopedic surgery

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Sent for review: 12 August 2023 Revised accepted: 4 November 2023

Abstract

Purpose: To investigate the comparative effect of two antibacterial treatments in orthopedic surgery.

Methods: A total of 96 patients who had undergone orthopedic surgery in Department of Nosocomial Infection Management, Suzhou Hospital of Integrated Traditional Chinese and Western Medicine, Suzhou, China from January 2021 to December 2022 were retrospectively analyzed and equally divided into two groups based on the postoperative medications administered to prevent infection. The control group was treated with amoxicillin sodium/clavulanate potassium while the study group was treated with cefazolin sodium. The incidence of postoperative infection, pain score, inflammatory factors and quality of life were determined and compared between both groups.

Results: The incidence of postoperative infection in the study group was lower than in the control group (p < 0.05). Prior to intervention, the visual analogue scale (VAS) scores of the two groups were similar (p > 0.05), but decreased significantly after intervention (p < 0.05), with the score of the former after intervention lower than that of the latter (p < 0.05). Prior to intervention, the inflammatory factor levels in both groups were identical (p > 0.05); however, the levels fell significantly in both groups after intervention (p < 0.05), but the levels in the study group were lower than in the control group (p < 0.05). The quality of life scores were also higher for both groups after intervention (p < 0.05), but higher for the study group than for the control group (p < 0.05).

Conclusion: Cefazolin sodium is more effective than amoxicillin sodium/clavulanate potassium in preventing infection in orthopedic patients after orthopedic surgery. However, there is a need to extend this treatment strategy to other clinical sites in order to validate these findings.

Keywords: Antibacterial infection, Cefazolin sodium, Amoxicillin sodium/clavulanate potassium, Orthopedic surgery, Quality of life, Inflammatory factors

INTRODUCTION

As a result of economic and social advances, the number of patients with orthopedic diseases has been rising in recent years [1]. Compared with other types of operations, orthopedic surgery is more complicated and are of longer duration. Patients are prone to incision infection after...
surgery due to extensive intraoperative bleeding and decreased body immunity [2]. Postoperative infection in orthopedic patients may cause bone defects or non-union, affecting treatment efficacy as well as prognosis of patients. Hence, it is necessary to actively prevent postoperative infection in orthopedic surgery [3]. Currently, antibacterial drug prophylaxis is mainly given half an hour before or after orthopedic surgery in clinical practice [4]. Cefazolin sodium has a wide antibacterial spectrum, and effectively inhibits staphylococci, Streptococcus pneumoniae, Klebsiella, Enterobacter aerogenes as well as Escherichia coli. Moreover, the drug has a long half-life [5]. Amoxicillin sodium/clavulinate potassium, also a common antibacterial drug, is a compound preparation composed of clavulanic acid and amoxicillin, and is effective against infections caused by enzyme-producing resistant bacteria [6]. The aim of this study was to determine the comparative prophylactic effect of two antibacterial therapies in orthopedic surgery.

METHODS

General patient profile

A total of 96 patients with orthopedic surgery admitted to Suzhou Hospital of Integrated Traditional Chinese and Western Medicine before surgery from January 2021 to December 2022 were retrospectively analyzed and divided into two groups based on their postoperative medication to prevent infection. Control group (n = 48) received amoxicillin sodium/clavulinate potassium, while the study group (n = 48) administered cefazolin sodium for postoperative infection prevention. Patient profile (including gender, age, fracture location, cause of fracture, etc) of both groups are shown in Table 1, and it indicates that there was no statistical difference between the profiles of the two groups (p < 0.05).

Ethical approval

All procedures involving human participants were approved by the Ethics Committee of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine (approval no. 2021-004) and followed the guidelines of the 1964 Helsinki Declaration and its later amendments for ethical research involving human subjects [7].

Inclusion criteria

(1) Met the criteria for orthopedic surgery; (2) patients aged 18 years or older; (3) patients were fully informed and agreed and signed to participate in the study.

Exclusion criteria

(1) A previous history of allergy to the study drug; (2) Have related lesions affecting heart, liver, lung and kidney function; (3) Shows ectopic function in coagulation mechanism; (4) Pregnant and lactating women; (5) Presence of tumors; (6) deficiency in mental and communication functions.

Treatments

For the control group, 0.5 – 1.0 g of Amoxicillin sodium/clavulanate potassium (State medical permit no. H20056310; Harbin Pharmaceutical Group General Pharmaceutical Factory, Harbin, Heilongjiang, China) was mixed with 100 ml normal saline half an hour before surgery and administered intravenously. After surgery, the treatment was repeated, and subsequently, twice daily for 4 days.

For the study group, 0.5 – 1.0 g of cefazolin sodium (State medical permit no. H23020945), produced by Harbin Pharmaceutical Group General Pharmaceutical Factory (Harbin, Heilongjiang, China) was mixed with 100 ml normal saline half an hour before surgery and administered intravenously. The treatment was repeated after surgery, and then twice daily for 2 days.

Evaluation of parameters/indices

Postoperative infection

The incidence of postoperative infection was recorded and compared between both groups.

Pain

Visual analogue scale (VAS) was applied to evaluate the pain symptoms of the patients, and the score ranged from 0 to 10. A higher score indicated more severe pain in the patients.

Inflammatory factors

Fasting venous blood samples (10-mL) were collected from the patients before treatment and in the morning after treatment. The samples were centrifuged in a medical centrifuge (Changsha Weierkang Xiangying Centrifuge Co. Ltd, TDZ4-WS type) at a speed of 3000 r/min for 10 min at a radius of 10 cm. The serum (upper layer) was collected and divided into two tubes (tubes A and B) and stored in a −60 °C refrigerator.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Study group (n=48)</th>
<th>Control group (n=48)</th>
<th>Statistical value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>37.92±2.12</td>
<td>38.02±2.11</td>
<td>0.232</td>
<td>0.817</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>75.23±5.11</td>
<td>74.98±5.08</td>
<td>0.240</td>
<td>0.811</td>
</tr>
<tr>
<td>Education level (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junior high school and below</td>
<td>16, 33.33</td>
<td>17, 35.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>26, 54.17</td>
<td>25, 52.08</td>
<td>0.050</td>
<td>0.975</td>
</tr>
<tr>
<td>High school or above</td>
<td>6, 12.50</td>
<td>6, 12.50</td>
<td></td>
<td></td>
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<tr>
<td>Gender (n, %)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28, 58.33</td>
<td>27, 56.25</td>
<td>0.043</td>
<td>0.837</td>
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<tr>
<td>Female</td>
<td>20, 41.67</td>
<td>21, 43.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cause of injury (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traffic accident</td>
<td>24, 50.00</td>
<td>23, 47.92</td>
<td></td>
<td></td>
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<tr>
<td>High-altitude fall</td>
<td>12, 25.00</td>
<td>11, 22.92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture location (n, %)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper limb</td>
<td>22, 45.83</td>
<td>20, 41.67</td>
<td>0.169</td>
<td>0.681</td>
</tr>
<tr>
<td>Lower limb</td>
<td>26, 54.17</td>
<td>28, 58.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking history (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28, 58.33</td>
<td>29, 60.42</td>
<td>0.043</td>
<td>0.835</td>
</tr>
<tr>
<td>No</td>
<td>20, 41.67</td>
<td>19, 39.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol history (n, %)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>14, 29.17</td>
<td>15, 31.25</td>
<td>0.049</td>
<td>0.824</td>
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<td>No</td>
<td>34, 70.83</td>
<td>33, 68.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical History (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12, 25.00</td>
<td>13, 27.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>36, 75.00</td>
<td>35, 72.92</td>
<td>0.054</td>
<td>0.816</td>
</tr>
<tr>
<td>Census register (n, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-local</td>
<td>1, 2.08</td>
<td>2, 4.17</td>
<td>0.344</td>
<td>0.558</td>
</tr>
</tbody>
</table>
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Tube A was employed for the determination of inflammatory factors, while C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) were determined by enzyme-linked immunosorbent assay (ELISA).

Quality of life

Using Generic Quality of Life Inventory 74 (QOLI-74) [8], the quality of life of both groups was evaluated before and after treatment. The scale includes emotional function, psychological status, physical function and social function. Each item was scored from 0 to 100 points; the higher the score, the better the quality of life of the patients.

Statistical analysis

Data were statistically processed using SPSS 23.0. Enumeration data (postoperative infection) were expressed as n and %, while Chi square ($\chi^2$) test was applied for comparison between the groups. Measurement data (VAS score, inflammatory factors, quality of life score) were expressed as mean ± SD, whereas t-test was used for comparison of data. $P < 0.05$ was considered statistically significant.

RESULTS

Postoperative infection

In the study group, 1 patient had postoperative infection, i.e., an infection rate of 2.08 % (1/48), while in the control group, 10 patients had postoperative infection, i.e., an infection rate of 12.50% (6/48). Thus, the incidence of postoperative infection in the study group was significantly lower than in control group ($\chi^2 = 3.8523, p = 0.0497$).

Pain

Before intervention, VAS scores were similar for the two groups ($p > 0.05$) but decreased significantly in both groups after intervention ($p < 0.05$); however, the score for the study group was lower than for the control group ($p < 0.05$, Table 2).

### Table 2: Comparison of pain symptoms between both groups (point, mean ± SD, n = 48)

<table>
<thead>
<tr>
<th>Group</th>
<th>1 h before surgery</th>
<th>3 h after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>5.40±0.49</td>
<td>2.19±0.49</td>
</tr>
<tr>
<td>Control</td>
<td>5.42±0.50</td>
<td>3.92±0.50</td>
</tr>
</tbody>
</table>

$\chi^2$-value 0.198, $P$-value 0.844, <0.001

*Statistically significant compared with value at 1 h before surgery ($p < 0.05$)

Inflammatory factors

Prior to intervention, the inflammatory factor levels in both groups were similar ($p > 0.05$), but the levels in both groups after intervention were lower ($p < 0.05$); the levels significantly lower in the study group than in the control group ($p < 0.05$, Table 3).

### Table 3: Comparison of inflammatory factors between both groups (mean ± SD, n = 48)

<table>
<thead>
<tr>
<th>Group</th>
<th>CRP (mg/L) 1 h before surgery</th>
<th>3 h after surgery</th>
<th>TNF-α (pg/mL) 1 h before surgery</th>
<th>3 h after surgery</th>
<th>IL-6 (pg/mL) 1 h before surgery</th>
<th>3 h after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>3.83±0.12</td>
<td>0.66±0.06</td>
<td>39.66±7.21</td>
<td>23.21±2.21</td>
<td>29.16±3.15</td>
<td>17.52±3.02</td>
</tr>
<tr>
<td>Control</td>
<td>3.84±0.10</td>
<td>1.92±0.21</td>
<td>38.70±7.14</td>
<td>31.23±2.34</td>
<td>29.20±3.17</td>
<td>23.04±3.13</td>
</tr>
</tbody>
</table>

$\chi^2$-value 0.444, $P$-value 0.658, <0.001

Quality of life

Prior to intervention, the quality of life scores for both groups ($p > 0.05$) were identical, but the scores for both groups increased significantly after intervention ($p < 0.05$); however, the score for the study group was significantly higher than for the control group ($p < 0.05$, Table 4).

DISCUSSION

Most orthopedic diseases are caused by accidents, and surgical therapy is mainly adopted in clinical practice [9]. However, orthopedic surgery has some levels of complexity and is longer in duration than most other surgical procedures. The application of various instruments during surgery also causes inevitable damage to local tissues; thus, incision infection is likely to occur after surgery [10]. Patients with mild incision infection after orthopedic surgery are relatively simple to treat, but the incision healing time and hospital stay will be prolonged, resulting in increased treatment costs for patients [11].
Patients with more severe infections may have fatal and disabling conditions, posing a threat to their lives and safety. Therefore, for patients undergoing orthopedic surgery, it is necessary to strengthen the prevention of postoperative infection in clinical practice [12].

Previous reports have confirmed that the bacteria causing postoperative incision infection are mainly Gram-positive bacteria, such as Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa. Therefore, the selection of antibacterial drugs warrants a wide antibacterial spectrum and high safety characteristics [13]. Amoxicillin sodium/clavulanate potassium is a compound preparation composed of clavulanic acid and amoxicillin, with the latter being a β-lactamase inhibitor that represses β-lactamase derived from resistant bacteria. In combination with amoxicillin, clavulanic acid ensures that amoxicillin does not lose its activity due to β-lactamase [14]. Amoxicillin sodium/clavulanate potassium is frequently used in clinical practice for lower respiratory tract infections, otitis media, sinusitis, skin tissue infections, and urinary tract infections, induced by sensitive bacteria. Furthermore, it is also used to treat urinary tract infections triggered by Enterobacter species [15]. Cefazolin sodium is a first-generation cephalosporin antibacterial drug in clinical practice, with a wide antibacterial spectrum, which greatly suppresses streptococci other than Gram-positive bacteria, staphylococci, and enterococci, especially against Gram-positive bacteria and has stronger antibacterial activity [16].

In the present study, the two drug regimens were applied in preventing postoperative infection in patients undergoing orthopedic surgery. The results revealed that the incidence of postoperative infection in the study group was lower than in the control. This implied that cefazolin sodium had greater effect in infection prevention than amoxicillin sodium/clavulanate potassium combination. The findings suggest that cefazolin sodium has a broader antibacterial spectrum than amoxicillin sodium/clavulanate potassium, and also has a longer drug half-life in plasma. Therefore, it has a more sustained antibacterial effect than amoxicillin sodium/clavulanate potassium [17]. Moreover, cefazolin sodium is rapidly distributed in parts of the body, except the head, after entering the body, and the anti-infective effect is striking [18,19].

Due to soft tissue injury in orthopedic surgery patients, numerous related immune cells release inflammatory factors during the immune response, resulting in a significant increase in TNF-α, CRP, IL-6, and other inflammatory factors which interact with each other [19]. The massive production of inflammatory factors leads to the stimulation of synoviocytes, chondrocytes, etc, which produce prostaglandin E2, protein polysaccharide, and collagenase, thereby damaging the cartilage matrix of the patients and giving rise to increased risk of infection [20]. The findings of the present study indicate that the inflammatory factor levels in the two groups before the intervention were similar. However, cefazolin sodium was considerably more effective in reducing inflammatory factors than amoxicillin sodium/clavulanate potassium.

The results revealed that cefazolin sodium was superior to amoxicillin sodium/clavulanate potassium in relieving pain symptoms. Furthermore, it was considered that cefazolin sodium relieved the pain while reducing the risk of infection by repressing inflammatory response.

Based on the results, the improvement in patients’ quality of life correlates with the recovery of their physical and mental state. Thus, overall, cefazolin sodium was superior to amoxicillin sodium/clavulanate potassium in relieving pain, preventing infection, has better recovery prognosis, and substantially improves the quality of life of patients.

**CONCLUSION**

The findings of this study show that, compared with amoxicillin sodium/clavulanate potassium, cefazolin sodium is better at relieving postoperative pain, reducing inflammatory factors

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**Table 4: Comparison of quality of life between both groups (mean ± SD, n = 48)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Affective function</th>
<th>Psychological state</th>
<th>Physical function</th>
<th>Social function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 h before surgery</td>
<td>3 h after surgery</td>
<td>1 h before surgery</td>
<td>3 h after surgery</td>
</tr>
<tr>
<td>Study</td>
<td>47.12±8.10</td>
<td>59.55±6.02*</td>
<td>45.77±7.31</td>
<td>56.49±6.66*</td>
</tr>
<tr>
<td>Control</td>
<td>47.20±8.11</td>
<td>53.48±6.31*</td>
<td>44.30±7.11</td>
<td>50.27±6.41*</td>
</tr>
<tr>
<td><em>t</em> value</td>
<td>0.048</td>
<td>0.999</td>
<td>4.662</td>
<td>0.348</td>
</tr>
<tr>
<td><em>P</em> value</td>
<td>0.962</td>
<td>&lt;0.001</td>
<td>0.321</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Statistically significant compared with value at 1 h before surgery (p < 0.05)
and enhancing quality of life, as well as lowering the risk of infection in patients undergoing orthopedic surgery. Therefore, this single drug regimen should be preferred to the combination regimen in minimizing orthopedic surgery infections, but these findings need to be validated in further clinical trials.

DECLARATIONS

Acknowledgements

None provided.

Funding/Sponsorship

This work was supported by Science and Technology Project of Integrated Traditional Chinese and Western Medicine of Suzhou City, Jiangsu Province (Grant no. skjyd201214) and Youth Science and Technology Project of Suzhou City, Jiangsu Province (Grant no. kjxw2020079).

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Yan Wang and Yiqun Zhou designed the study and carried them out; Yan Wang, Fengzhu Xie, Fang Chen, Wenting Su supervised the data collection, analyzed and interpreted the data, and Yan Wang and Yiqun Zhou prepared the manuscript for publication and reviewed the draft of the manuscript. All authors read and approved the manuscript for publication.

Ethical Approval

The study was approved by the Ethics Committee of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine (approval no. 2021-004).

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Use of Artificial Intelligence/Large Language Models

None provided.

Use of Research Reporting Tools

None provided.

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