Preoperative administration of intravenous flurbiprofen axetil reduces postoperative pain for spinal fusion surgery

KAZUNORI YAMASHITA1, MAKOTO FUKUSAKI1, YUKO ANDO1, ARIHIRO FUJINAGA1, TAKAHIRO TANABE1, YOSHIKI TERAO1, and KOJI SUMIKAWA2

1Department of Anesthesia, Nagasaki Rosai Hospital, 2-12-5 Sctogoshi, Sasebo 857-0134, Japan
2Division of Anesthesiology, Department of Translational Medical Science, Nagasaki University School of Medicine, Nagasaki, Japan

Abstract

Purpose. The aim of the study was to investigate postoperative analgesia and the opioid-sparing effect of the preoperative administration of intravenous flurbiprofen axetil in patients undergoing spinal fusion surgery.

Methods. Thirty-six patients were randomly allocated into one of three groups. Group A received preoperative flurbiprofen axetil, 1 mg·kg⁻¹. Group B received postoperative flurbiprofen axetil, 1 mg·kg⁻¹. Group C received a placebo. All groups were given a standardized anesthesia and intravenous morphine via a patient-controlled analgesia device for postoperative analgesia. The pain score was evaluated by a visual analog scale (VAS) at 0 (T₀), 1 (T₁), 2 (T₂), 6 (T₆), 12 (T₁₂), and 24 (T₂₄) h after surgery, and the morphine requirement was recorded during the study period.

Results. VAS in group A was significantly lower than that in group B at T₀ and T₁. VAS in group A was significantly lower than that in group C throughout the time course after surgery. Postoperative morphine consumption in group A was significantly lower than that in groups B and C at T₀ to T₃.

Conclusion. As compared with postoperative administration, preoperative administration of intravenous flurbiprofen axetil provides better postoperative analgesia and an opioid-sparing effect in patients undergoing spinal fusion surgery under general anesthesia.

Key words Flurbiprofen axetil · Postoperative pain · Opioid-sparing effect

Introduction

It is known that spinal fusion surgery is often associated with severe postoperative pain. Postoperative pain after spinal posterior fusion surgery is usually controlled by systemic opioids or nonsteroidal anti-inflammatory drugs (NSAIDs) because epidural analgesia is not indicated.

Although NSAIDs show an opioid-sparing effect [1–4], whether NSAIDs have a preemptive analgesic effect is controversial [5–7]. Reuben and Connelly [1] reported that the preoperative administration of celecoxib or rofecoxib, cyclooxygenase (COX)-2 selective inhibitors, showed a postoperative analgesic effect and an opioid-sparing effect after spinal stabilization surgery.

Flurbiprofen axetil (FA) is an injectable nonselective COX inhibitor. It has been reported that preoperative administration of FA reduces postoperative pain after hysterectomy [8], pulpectomy [9], laparoscopic cholecystectomy [10], and pediatric strabismus surgery [11]. However, there are few reports on whether preoperative FA can reduce postoperative pain and the postoperative opioid requirement after major spinal surgery.

This study was carried out to evaluate whether preoperative administration of intravenous FA can provide postoperative analgesia and reduce postoperative opioid consumption in patients undergoing spinal posterior fusion surgery under general anesthesia.

Materials and methods

With the approval of the Institutional Human Ethics Committee and written informed consent from each patient, we studied 36 patients with American Society of Anesthesiologists physical status I–II who were scheduled for spinal fusion surgery, that is, posterolateral fusion–pedicle screw fixation (PLF-PSF) of one vertebral space between L₅/L₆ or L₅/S₁. Excluded were patients aged less than 30 or more than 75 years and those with a history of allergy to any NSAIDs or opioids, coagulopathy, renal dysfunction, or peptic ulcer disease. NSAIDs and steroids were discontinued 24 h and 1 week prior to surgery, respectively.

After the induction of anesthesia with 5 mg·kg⁻¹ thiamylal and 2 μg·kg⁻¹ fentanyl, and tracheal intubation...
facilitated with 0.1 mg·kg⁻¹ vecuronium. Anesthesia was maintained with sevoflurane, 1.5%–2.5% end-tidal, and N₂O 60% in oxygen, and additional vecuronium was administered as needed. Percutaneous oxygen saturation was maintained at 98% or more, and end-tidal carbon dioxide tension was maintained at 35 mmHg during surgery. The depth of anesthesia was maintained with the bispectral index at a score of 40–50 to ensure similar anesthetic depth in all patients. Acetated Ringer’s solution was infused at a rate of 6 to 8 ml·kg⁻¹·h⁻¹ during surgery. The subjects were randomly assigned into one of three groups. Group A (n = 12) received intravenous FA, 1 mg·kg⁻¹ [9], before surgery. Group B (n = 12) received intravenous FA, 1 mg·kg⁻¹, after surgery. Group C (n = 12) received intravenous lipid emulsion (Intralipid, Terumo, Tokyo, Japan), 0.1 ml·kg⁻¹, as a placebo before surgery.

After spinal stabilization, morphine, 0.1 mg·kg⁻¹, was intravenously administered to all patients. Postoperative morphine was administered with a patient-controlled analgesia (PCA) pump (DIB PCA system Soft Shell Type OD-349; Hakko Medical, Tokyo, Japan; increment dose, 3 ml; lockout interval, 30 min).

The study was performed by three investigators in a double-blinded manner as follows: Each solution was prepared in a syringe by the first investigator, who was responsible for subject grouping. The second investigator, who did not know the type of test solution, performed the intravenous injection. The third investigator, who was blinded to the type of test solution, evaluated postoperative morphine consumption by measuring the weight of the pump using a precision electronic balance (model CB-X; Ishida, Kyoto, Japan).

Each patient was instructed to evaluate pain while at rest using a visual analog scale (VAS) ruler. A 100-mm horizontal VAS with end descriptors of “no pain” and “pain as bad as it could be” was used.

VAS was measured at 0 (T₀), 1 (T₁), 2 (T₂), 6 (T₃), 12 (T₄), and 24 (T₅) h after surgery by a trained nurse blinded to the study drug. Morphine consumption was recorded during the study period.

Data are expressed as means ± SD. Demographic data (age, height, and weight), operation time, and blood loss were analyzed with the Kruskal-Wallis test. Pain score, nausea score, and morphine doses were also analyzed with the Kruskal-Wallis test. If a significant result was obtained, a Mann-Whitney U test was performed. Significance was determined at P < 0.05.

**Results**

The demographic data of the three groups were similar (Table 1). VAS data are presented in Fig. 1. VAS in group A was significantly lower than that in group B at T₀ and T₁. VAS in group A was significantly lower than that in group C throughout the time course after surgery. Although VAS in group B was significantly lower than that in group C at T₂ and T₃, no significant difference of VAS was found between groups B and C from T₂ to T₅.

Postoperative morphine consumption in group A was significantly lower than that in groups B and C at T₃, while there were no significant differences among the three groups at T₄ to T₅ (Fig. 2).

No patient showed any adverse effect associated with FA.

**Discussion**

The present results show that preoperative FA provides better immediate postoperative analgesia and results in less morphine consumption during the early postopera-

---

**Table 1. Demographic data**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Operation time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (12)</td>
<td>60 ± 9</td>
<td>162 ± 10</td>
<td>63 ± 9</td>
<td>207 ± 53</td>
</tr>
<tr>
<td>B (12)</td>
<td>64 ± 13</td>
<td>154 ± 10</td>
<td>54 ± 10</td>
<td>168 ± 78</td>
</tr>
<tr>
<td>C (12)</td>
<td>61 ± 15</td>
<td>162 ± 10</td>
<td>64 ± 12</td>
<td>190 ± 40</td>
</tr>
</tbody>
</table>

Values are means ± SD
A, preoperative administration of flurbiprofen; B, postoperative administration of flurbiprofen; C, no administration of flurbiprofen.