Intrathecal Morphine and Oral Analgesics Provide Safe and Effective Pain Control after Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis

Ying Li, MD, Rebecca A. Hong, MD, Christopher B. Robbins, PhD, Kathleen M. Gibbons, MD, Ashlee E. Holman, MD, Michelle S. Caird, MD, Frances A. Farley, MD, Matthew D. Abbott, MD, Michelle C. Burke, MS

1Department of Orthopaedic Surgery, C.S. Mott Children’s Hospital, University of Michigan, Ann Arbor, MI
2Division of Pediatric Anesthesiology, C.S. Mott Children’s Hospital, University of Michigan, Ann Arbor, MI

Corresponding author:
Ying Li, MD
Department of Orthopaedic Surgery
C.S. Mott Children’s Hospital
1540 E. Hospital Drive, SPC 4241, Ann Arbor, MI 48109-4241
Phone: (734)936-5715
Fax: (734)647-3291
E-mail: yingyuli@med.umich.edu

The device(s)/drug(s) is/are FDA-approved or approved by corresponding national agency for this indication.
No funds were received in support of this work.
Relevant financial activities outside the submitted work: grants, travel/accommodations/meeting expenses.
Study Design: Retrospective comparative study.

Objective: To demonstrate that intrathecal morphine (ITM) and oral analgesics provide effective pain control after posterior spinal fusion (PSF) for adolescent idiopathic scoliosis (AIS), and this protocol has a low complication rate so patients can be admitted to a general care floor.

Summary of Background Data: Previous studies have shown that ITM combined with intravenous patient-controlled analgesia or epidural infusion (EPI) provides effective pain control after PSF for AIS. Due to concerns for respiratory depression, ITM patients were routinely admitted to the intensive care unit (ICU) postoperatively. There is little data on ITM combined with oral analgesics.

Methods: We identified AIS patients aged 10 to 17 years who had undergone PSF. Twenty-eight patients who received ITM were matched to 28 patients who received a hydromorphone EPI. The ITM group received oral oxycodone starting at 16 hours post-injection. The EPI group received oxycodone after the epidural catheter was removed on postoperative day 2. Pain scores, adverse events, and length of stay were recorded.

Results: A higher number of EPI patients received fentanyl (11 vs 3, \( P = 0.014 \)) in the post-anesthesia care unit (PACU). The ITM group had lower pain scores between PACU discharge and midnight (mean 2.9 vs 4.2, \( P = 0.034 \)). Pain scores were similar during the remaining postoperative periods. All ITM patients transitioned to oxycodone without intravenous opioids. Time to ambulation (19.9 vs 26.5 hours, \( P = 0.010 \)) and Foley catheter removal (21.3 vs 41.9
hours, $P < 0.001$) were earlier in the ITM patients. Length of hospital stay was shorter in the ITM group (3.1 vs 3.5 days, $P = 0.043$). Adverse events occurred at similar rates in both groups.

**Conclusions:** ITM and oral analgesics provide safe and effective pain control after PSF for AIS. Routine postoperative admission to the ICU is not necessary.

**Key Words:** intrathecal morphine; posterior spinal fusion; adolescent idiopathic scoliosis; pain management; epidural infusion

**Level of Evidence:** 3
Introduction

Posterior spinal fusion (PSF) for adolescent idiopathic scoliosis (AIS) can result in moderate to severe postoperative pain. Intravenous patient-controlled anesthesia (PCA),\textsuperscript{1,2} intrathecal morphine (ITM),\textsuperscript{3-8} and epidural analgesia (EPI)\textsuperscript{1,2,5,6,9-13} have all been shown to provide adequate pain control after PSF for AIS. Several studies have demonstrated superior pain control with EPI compared to PCA after spinal fusion for AIS.\textsuperscript{5,9,12} However, EPI is associated with a high rate of adverse events that lead to temporary or premature discontinuation of the catheter. Reported complications include respiratory depression, neurologic changes, oversedation, and uncontrollable pain secondary to catheter malfunction.\textsuperscript{5,9,12}

A single preoperative injection of ITM has been found to be a safe and effective method of pain control after PSF for AIS.\textsuperscript{3-8} ITM’s hydrophilic properties allow relatively high concentrations of the drug to be maintained in the cerebrospinal fluid for several hours.\textsuperscript{14} ITM can be administered at a fraction of the dose of intravenous morphine and result in an extended duration of analgesia ranging from 12 to 22.9 hours depending on the dose injected.\textsuperscript{4,7} AIS patients who receive ITM prior to PSF are usually given a PCA,\textsuperscript{3,5,7} continuous intravenous morphine infusion,\textsuperscript{4,15} or EPI\textsuperscript{8} for pain control postoperatively. Although adequate pain control has been reported with ITM combined with these other methods of pain management, an increase in pain scores has been observed at 24 hours postoperatively as the analgesic effects of ITM diminish.\textsuperscript{5,6,8} In addition, patients are routinely admitted to the intensive care unit (ICU) or close observation unit due to concerns for respiratory depression.\textsuperscript{3,5,8}
In June 2014, we implemented a protocol at our institution where AIS patients who receive ITM prior to PSF are transitioned directly to oral opioids postoperatively and are admitted to a general care floor. ITM was administered at a dose of 12 µg/kg (maximum 1000 µg) and patients were scheduled to receive oxycodone 18 hours after the injection of ITM. This was based on data from Tripi et al., where patients who were administered a moderate dose of ITM (mean 14 µg/kg, range 9-19 µg/kg) received their first rescue dose of narcotic at a mean of 16.7 hours after ITM injection. We previously demonstrated that this protocol is safe and effective. However, similar to other reports, we found significantly higher pain scores during the 24 to 48 hour postoperative period in our ITM patients compared to our EPI patients. We also found a high rate of minor adverse events, including nausea/vomiting, pruritus, and respiratory depression requiring the use of nasal cannula oxygen. As a result, we have modified our protocol so that oral opioids are administered earlier during the postoperative period, and adjuvant pain medications are ordered at an optimal dose and on a more consistent schedule. We have also decreased the dose of ITM that is administered to try to reduce adverse events.

The purpose of this study was to evaluate whether our new protocol provides more effective pain control after PSF for AIS, and if this protocol has a lower complication rate so patients can be admitted to a general care floor.

Materials and Methods

Approval from our Institutional Review Board was obtained. We identified patients aged 10 to 17 years who had undergone PSF for AIS and received ITM between May 2015 and April 2016.
These ITM patients were not included in our previous study as we implemented our updated ITM protocol in May 2015. The ITM patients were then matched by age ± 2 years and sex to patients who had undergone PSF for AIS and received a hydromorphone EPI between June 2014 and April 2015. Most of the EPI patients were included in our previous study as the control group. Inclusion criteria were patients with AIS who had undergone primary PSF and received either ITM or EPI for postoperative pain control. Exclusion criteria were patients with an underlying diagnosis, American Society of Anesthesiologists (ASA) physical status 4, and previous spinal fusion.

For the ITM group, an average dose of 9 µg/kg of ITM (range 5-10 µg/kg, maximum 800 µg) was injected by the anesthesiologist after induction of anesthesia and prior to incision. Postoperatively, patients were scheduled to receive 0.1 mg/kg of oral oxycodone (maximum 5 mg) 16 hours after the injection of ITM. No intravenous narcotics were ordered. Adjuvant pain medications and medications for adverse events were ordered. The detailed protocol is shown in Table 1.

For the EPI group, the catheter was placed by the surgeon under direct visualization prior to wound closure. A bolus of 5 µg/kg of hydromorphone (maximum 200 µg) and 1 µg/kg of fentanyl (maximum 50 µg) was administered, followed by a continuous infusion of 40-60 µg/h of hydromorphone and patient-controlled bolus doses of 5 µg with a lockout interval of 30 minutes. We did not routinely include a local anesthetic in the epidural infusion secondary to concern for masking a neurologic deficit. We have previously demonstrated the safety and efficacy of a narcotic-only epidural infusion after PSF for AIS. Adjuvant medications were
ordered. Patients were transitioned to oral oxycodone on postoperative day (POD) 2 after removal of the epidural catheter.

All patients were recovered in the post-anesthesia care unit (PACU) and were then transferred to the general care floor. The ITM group was monitored with continuous pulse oximetry for 24 hours postoperatively and the EPI group was monitored with continuous pulse oximetry until the epidural catheter was removed. Oral opioids, adjuvant medications, and epidural infusions were managed by the pediatric anesthesia pain service. Pain was measured using a self-reported 0-10 numeric rating scale. Sedation was assessed using the University of Michigan Sedation Scale (range 0-4, where 4 is unarousable).

A trained research assistant reviewed the medical records to collect patient demographics; surgical data; pain and sedation scores; any adverse event; administration of analgesics, antiemetics and antipruritics; time to ambulation and Foley catheter removal; and length of hospital stay. For the purposes of this study, pain scores were recorded for the following time periods: PACU, PACU discharge to midnight, POD 1 midnight to 08:00, POD 1 08:00 to 16:00, POD 1 16:00 to midnight, POD 2, and POD 3.

Data was analyzed using SPSS v.22.0 (IBM Corp; Armonk, NY). Primary outcomes of pain and opioid dosage were treated as continuous variables, while adverse events were treated as dichotomous variables. Primary analyses that were conducted were unpaired t-tests between the ITM and EPI groups. Chi-square analysis was used for categorical data. Statistical significance was set at $P < 0.05$. 

Copyright © 2017 Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.
Results

We identified 37 ITM and 30 EPI patients. Nine ITM and 2 EPI patients could not be matched due to age and sex. Our final study group consisted of 28 ITM patients matched to 28 EPI patients. Demographic and surgical data were similar between the groups (Table 2).

Nine patients in each group received oral acetaminophen prophylactically in the preoperative area. The intravenous analgesics that were administered intraoperatively and in the PACU are presented in Table 3. Sufentanil infusions are contraindicated in patients who have received ITM so there was a significant difference in the number of ITM and EPI patients who received sufentanil versus remifentanil infusions intraoperatively. Fourteen (50%) EPI patients received diazepam intraoperatively compared to 5 (18%) ITM patients ($P = 0.011$). A significantly larger number of EPI patients required fentanyl in the PACU (11 vs 3 patients, $P = 0.014$). Although significantly more EPI patients received intravenous acetaminophen in the PACU, 3 ITM patients received oral acetaminophen in the PACU so there was no difference in acetaminophen administration between the groups (6 vs 3 patients, $P = 0.592$).

Total postoperative intravenous and oral analgesic doses administered after PACU discharge are shown in Table 4. All opioids administered by any route that were given in addition to the ITM or continuous epidural infusion were converted to an equianalgesic dose of oral morphine to calculate the oral morphine equivalents. All of the ITM patients were transitioned to oxycodone without the need for intravenous opioids. EPI patients underwent catheter removal and received
their first dose of oxycodone at a mean of 43.5 hours postoperatively (range 23.9-48.7 hours). 
As such, oral morphine equivalents were significantly higher in the ITM group on POD 1. 
However, on POD 3, oral morphine equivalents were significantly higher in the EPI group. 
Total oral acetaminophen administration was also significantly higher in the EPI group on POD 3. Total intravenous diazepam administration was higher in the EPI group on all postoperative days but was only significantly higher on POD 1 and 3.

The highest, lowest, and mean pain scores are presented in Table 5. The ITM patients had lower pain scores in the PACU and during the period between PACU discharge and midnight, but only the latter was significant. The pain scores for the ITM group then began to increase starting between midnight and 08:00 on POD 1 as the analgesic effects of the ITM started to diminish. However, there was no significant difference in pain scores between the ITM and EPI groups during the remaining time periods.

Time to ambulation (19.9 ± 4.9 vs 26.5 ± 11.9 hours,  \( P = 0.010 \)) and Foley catheter removal (21.3 ± 5.8 vs 41.9 ± 6.8 hours,  \( P < 0.001 \)) were earlier in the ITM patients. In addition, length of hospital stay was shorter in the ITM group (3.1 ± 0.6 vs 3.5 ± 0.6 days,  \( P = 0.043 \)).

There was no difference in adverse events between the groups. There was a high rate of nausea/vomiting (25 [89%] ITM and 21 [75%] EPI patients) and moderate rate of pruritus (18 [64%] ITM and 12 [43%] EPI patients) in both groups. Respiratory depression that could be managed with nasal cannula oxygen was more common in the EPI patients (7 [25%] vs 2 [7%] patients) but this was not significant. Oversedation was noted in 5 (18%) ITM and 2 (7%) EPI patients.
patients. Two (7%) ITM patients had an unplanned admission to the ICU. One patient developed symptomatic bradycardia and hypotension in the PACU that was attributed to the ITM. He weighed 48 kg and received 480 µg of ITM (10 µg/kg). He received one dose of glycopyrrolate, and his bradycardia and hypotension resolved. He was admitted to the ICU for monitoring. No other interventions were necessary and he was transferred to the general care floor on POD 1. The remainder of his postoperative course was uneventful and he was discharged home on POD 3. He never experienced any respiratory depression nor did he require nasal cannula oxygen during his hospitalization. The second patient was unable to be extubated at the completion of surgery due to respiratory depression, likely secondary to the ITM. She was morbidly obese with a weight of 104 kg (body mass index of 40 kg/m²) and received 800 µg of ITM (7.7 µg/kg). She was admitted to the ICU. No naloxone was administered and she was extubated on the morning of POD 1. After extubation, she had several episodes of hypopnea while sleeping, likely related to her morbid obesity and indicative of a high likelihood of underlying obstructive sleep apnea. Thus, she was monitored in the ICU for one additional day. She was transferred to the general care floor on POD 2 and was discharged home on POD 4. No EPI patients had an unplanned admission to the ICU.

Discussion

ITM provides effective analgesia after PSF for AIS.\textsuperscript{3-8} We previously demonstrated that these patients can be successfully transitioned to oral opioids postoperatively and be admitted to a general care floor.\textsuperscript{6} However, although our patients had significantly better pain scores in the PACU, they experienced suboptimal pain control during the 24 to 48 hour postoperative period
when the analgesic effects of the ITM had disappeared. Other authors have demonstrated a similar increase in pain scores during this time period.\textsuperscript{5,8}

This study presents the results of our new protocol. We found significantly better pain scores in the ITM patients compared to the EPI patients during the time period between PACU discharge and midnight. In contrast to our previous study,\textsuperscript{6} there was no significant difference in pain scores in the PACU. However, the EPI group in our current study required significantly more fentanyl in the PACU. Our ITM patients were transitioned to oral oxycodone 16 hours after injection of ITM, which is at approximately midnight on the evening after surgery. Although our ITM group had an increase in pain scores starting between midnight and 08:00 on POD 1, pain scores were similar to the EPI group. We interpret this as a successful transition of our ITM patients to oral opioids, as the analgesic effects of the dose of ITM used in our protocol are expected to diminish at approximately 16 hours postoperatively. More consistent administration of adjuvant pain medications during wound closure and the postoperative period may have also helped with pain control as the effects of the ITM wore off. None of our ITM patients required any intravenous opioids after PACU discharge.

Pain scores were similar between the groups for all remaining postoperative time periods. However, significantly more EPI patients received diazepam on POD 1, ketorolac on POD 2, and oral morphine equivalents, acetaminophen, and diazepam on POD 3. The higher total administered doses of oral morphine equivalents and diazepam may represent worse pain and muscle spasms in the EPI group, as both our new ITM protocol and previous EPI protocol had additional oxycodone ordered as needed for breakthrough pain and diazepam ordered as needed.
for spasms. Since ketorolac and acetaminophen were ordered around the clock with both the ITM and EPI protocols, the difference in total doses administered on POD 2 and 3 may have been secondary to earlier hospital discharge in the ITM patients.

Despite decreasing the ITM dose with our new protocol, we still saw a high rate of minor adverse events. However, there was no significant difference compared to our EPI group. Our complication rate for both groups is higher than the rates reported in other studies.\textsuperscript{4,5,7-9} In addition to documentation of an adverse event, we also considered administration of an antiemetic or antipruritic evidence of nausea/vomiting or pruritus. Since this was a retrospective study, it is difficult to know whether these medications were administered for prophylaxis or treatment, so there is a possibility that we over-reported the incidence of nausea/vomiting and pruritus. Nevertheless, we can certainly improve management of these minor adverse events in our ITM patients.

Respiratory depression and oversedation occurred at similar rates in both groups. Respiratory depression and oversedation secondary to ITM at the dose administered in this study have been reported previously, and can usually be treated with nasal cannula oxygen.\textsuperscript{4,7} Two ITM patients had unplanned admissions to the ICU, likely secondary to the ITM. While one morbidly obese patient with probable obstructive sleep apnea remained intubated until the respiratory depressant effects of the ITM had worn off, it is encouraging that no patients experienced respiratory depression requiring reintubation or other intervention beyond nasal cannula oxygen and that no patients required vasopressor medications. The remainder of the postoperative course was uneventful for these two patients, and they were discharged on POD 3 and 4, respectively.
In our previous study, 62 (10%) ITM patients had unplanned admissions to the ICU for closer neurological and blood pressure monitoring following transient loss of transcranial electric motor-evoked potentials during surgery. Both patients received norepinephrine and fluid boluses to maintain their mean arterial blood pressure above 70 mmHg per surgeon request. No patients in that study were admitted to the ICU for adverse events that were directly attributable to the ITM. We feel that a 4% rate of unplanned ICU admission for reasons related to ITM (2/48 patients from our previous and current studies) is acceptable and that it is safe to routinely admit these patients to the general care floor. However, it is important to recognize the potential adverse events associated with ITM. Our anesthesiologists now administer ITM at a dose of 8 µg/kg to most patients and at even lower doses to patients who are morbidly obese and/or report signs or symptoms concerning for obstructive sleep apnea. We also recommend that all patients who receive ITM are monitored with continuous pulse oximetry for 24 hours postoperatively to detect dangerous respiratory depression prior to the actual occurrence of an adverse event.

Similar to our previous study, we found a significant decrease in time to ambulation, time to Foley catheter removal, and decreased length of hospital stay in the ITM group. Superior postoperative pain control, and absence of an epidural catheter and pump likely facilitated earlier mobilization with physical therapy, resulting in earlier hospital discharge.

Limitations of this study are the small sample size. Our study may have been underpowered to detect differences in some of our outcomes, especially the rate of adverse events. In addition, this was a retrospective study so data collection was dependent on accurate documentation in the
medical record. Nine patients in each group received oral acetaminophen preoperatively and this may have influenced whether these patients received additional acetaminophen intraoperatively or in the PACU. Although we found that a significantly larger number of EPI patients received intravenous acetaminophen in the PACU, we were unable to determine retrospectively whether the acetaminophen was administered prophylactically or for treatment of pain. Similarly, we used administration of antiemetics and antipruritics as a proxy for adverse events, which may have led to over-reporting as these medications are often given prophylactically.

In conclusion, ITM and oral analgesics provide safe and effective pain control after PSF for AIS. Patients can be transitioned directly to oral opioids without the need for intravenous opioids. In our study, ITM patients had lower pain scores during the immediate postoperative period and similar pain scores during the remaining postoperative periods compared to EPI patients. Minor adverse events, such as nausea/vomiting and pruritus, are common. Respiratory depression can usually be treated with nasal cannula oxygen. Patients who receive ITM can be routinely admitted to a general care floor postoperatively.


Table 1. Intrathecal morphine (ITM) protocol for posterior spinal fusion for adolescent idiopathic scoliosis.

- Administer ITM (8-10 µg/kg, maximum 800 µg) after induction and before incision
- Triple antiemetic therapy (dexamethasone 0.1 mg/kg, maximum 4 mg; diphenhydramine 12.5 mg; ondansetron 0.1 mg/kg, maximum 4 mg) to be given to all patients in operating room
- IV acetaminophen (15 mg/kg) to be given to all patients during wound closure, then ordered q6h ATC
  - Change from IV to PO on POD 1
- IV ketorolac (0.5 mg/kg, maximum 15 mg) to be given to all patients during wound closure, then ordered q6h ATC x 48h
  - Start PO ibuprofen after 48h
- IV diazepam (0.05 mg/kg) to be ordered q6h as needed for muscle spasms x 24h
  - Can be given in PACU if needed
  - Increase to 0.1 mg/kg and change to PO on POD 1
- 16 hours after injection of ITM: start oxycodone (0.1 mg/kg, maximum 5 mg) PO q4h ATC with additional 2.5 mg PO q2h as needed for breakthrough pain

For adverse events:
- IV ondansetron (0.1 mg/kg, maximum 4 mg) q6h ATC x 24h for nausea/vomiting and pruritus prophylaxis for all patients
- IV nalbuphine (0.03 mg/kg, maximum 2.5 mg) q6h ATC x 24h for nausea/vomiting and pruritus prophylaxis for all patients
- IV naloxone 0.1mg IV as needed for respiratory depression; standing order for all patients

IV, intravenous; ATC, around the clock; PO, per os (by mouth); PACU, post-anesthesia care unit
**Table 2.** Demographic and surgical data.

<table>
<thead>
<tr>
<th></th>
<th>Intrathecal morphine</th>
<th>Epidural</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group size (n)</td>
<td>28</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>14.8 ± 1.7 (range 11-17)</td>
<td>14.4 ± 1.7 (range 11-17)</td>
<td>0.414</td>
</tr>
<tr>
<td>Male</td>
<td>6 (21%)</td>
<td>6 (21%)</td>
<td>-</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.8 ± 12.5</td>
<td>58.9 ± 15.2</td>
<td>0.976</td>
</tr>
<tr>
<td>ASA 1/2/3</td>
<td>4 (14%)/22 (79%)/2 (7%)</td>
<td>9 (32%)/18 (64%)/1 (4%)</td>
<td>0.265</td>
</tr>
<tr>
<td>Median number of levels fused</td>
<td>11 (range 6-14)</td>
<td>11 (range 8-13)</td>
<td>0.621</td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>483 ± 351</td>
<td>405 ± 226</td>
<td>0.334</td>
</tr>
</tbody>
</table>

ASA, American Society of Anesthesiologists
Values are shown as the mean ± standard deviation and n (%).
Table 3. Patients in each group who received intravenous analgesics intraoperatively and in the post-anesthesia care unit (PACU).

<table>
<thead>
<tr>
<th></th>
<th>Intraoperatively</th>
<th>P-value</th>
<th>PACU</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ITM</td>
<td>EPI</td>
<td>ITM</td>
<td>EPI</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>0</td>
<td>21 (75%)</td>
<td>&lt;0.001</td>
<td>N/A</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>22 (79%)</td>
<td>6 (21%)</td>
<td><strong>0.001</strong></td>
<td>N/A</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>17 (61%)</td>
<td>19 (68%)</td>
<td>0.577</td>
<td>N/A</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>25 (89%)</td>
<td>17 (61%)</td>
<td>0.231</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Morphine</td>
<td>0</td>
<td>0</td>
<td>2 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>0</td>
<td>1 (4%)</td>
<td>0.313</td>
<td>0</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>13 (46%)</td>
<td>11 (39%)</td>
<td>0.701</td>
<td>0</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>22 (79%)</td>
<td>19 (68%)</td>
<td>0.365</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>5 (18%)</td>
<td>14 (50%)</td>
<td><strong>0.011</strong></td>
<td>11 (39%)</td>
</tr>
<tr>
<td>Ketamine</td>
<td>5 (18%)</td>
<td>2 (7%)</td>
<td>0.225</td>
<td>0</td>
</tr>
<tr>
<td>Midazolam</td>
<td>19 (68%)</td>
<td>24 (86%)</td>
<td>0.114</td>
<td>0</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>0</td>
<td>0</td>
<td>3 (11%)</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>

ITM, intrathecal morphine group; EPI, epidural group. Values are shown as n (%).
Table 4. Total postoperative intravenous and oral analgesic doses (mg/kg/day) administered in each group.

<table>
<thead>
<tr>
<th></th>
<th>POD 0</th>
<th>POD 1</th>
<th>POD 2</th>
<th>POD 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ITM</td>
<td>EPI</td>
<td>P-value</td>
<td>ITM</td>
</tr>
<tr>
<td>Oral morphine</td>
<td>0.003 ±</td>
<td>0.007</td>
<td>0.098</td>
<td>0.160 ±</td>
</tr>
<tr>
<td>equivalents</td>
<td>0.001</td>
<td></td>
<td></td>
<td>0.109 ±</td>
</tr>
<tr>
<td>Oral acetaminophen</td>
<td>11.35 ±</td>
<td>8.09</td>
<td></td>
<td>36.06 ±</td>
</tr>
<tr>
<td></td>
<td>0.001</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous ketorolac</td>
<td>0.282 ±</td>
<td>0.174</td>
<td>0.725</td>
<td>1.08 ±</td>
</tr>
<tr>
<td></td>
<td>0.005</td>
<td>0.023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous diazepam</td>
<td>0.026 ±</td>
<td>0.026</td>
<td>0.043 ±</td>
<td>0.085</td>
</tr>
<tr>
<td></td>
<td>0.003</td>
<td></td>
<td>0.042</td>
<td></td>
</tr>
</tbody>
</table>

POD, postoperative day; ITM, intrathecal morphine group; EPI, epidural group
Values are shown as the mean ± standard deviation.
Table 5. Highest, lowest, and mean reported numeric rating scale pain scores (0-10) for both groups for the first 3 postoperative days.

<table>
<thead>
<tr>
<th></th>
<th>Highest pain score</th>
<th>Lowest pain score</th>
<th>Mean pain score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ITM</td>
<td>EPI</td>
<td>ITM</td>
</tr>
<tr>
<td>PACU</td>
<td>3.9 ± 3.1</td>
<td>5.2 ± 3.6</td>
<td>2.5 ± 2.5</td>
</tr>
<tr>
<td>PACU discharge-23:59</td>
<td>3.9 ± 2.7</td>
<td>5.4 ± 2.2</td>
<td>1.9 ± 1.6</td>
</tr>
<tr>
<td>POD 1 00:00-08:00</td>
<td>5.0 ± 2.8</td>
<td>4.8 ± 1.9</td>
<td>3.2 ± 2.1</td>
</tr>
<tr>
<td>POD 1 08:01-16:00</td>
<td>5.9 ± 2.8</td>
<td>4.7 ± 1.8</td>
<td>3.3 ± 2.4</td>
</tr>
<tr>
<td>POD1 16:00-23:59</td>
<td>5.7 ± 2.5</td>
<td>4.8 ± 2.2</td>
<td>3.5 ± 2.0</td>
</tr>
<tr>
<td>POD 2</td>
<td>6.5 ± 2.2</td>
<td>6.0 ± 2.4</td>
<td>2.5 ± 1.9</td>
</tr>
<tr>
<td>POD 3</td>
<td>6.3 ± 2.4</td>
<td>5.5 ± 2.4</td>
<td>2.4 ± 1.5</td>
</tr>
</tbody>
</table>

ITM, intrathecal morphine group; EPI, epidural group; PACU, post-anesthesia care unit; POD, postoperative day.

Values are shown as the mean ± standard deviation and unadjusted P-values.