ORIGINAL ARTICLE

# Duration of intrathecal morphine effect in children with idiopathic scoliosis undergoing posterior spinal fusion

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ABSTRACT

***Objective:*** *Intrathecal (IT) morphine improves pain control and decreases opioid requirements in children following thoracic and abdominal surgery. However, studies in children report variable durations of analgesia following IT morphine. The purpose of this study is to describe the duration of analgesia in children undergoing surgical correction of idiopathic scoliosis.*

***Design:*** *Retrospective chart review.*

***Setting:*** *Pediatric hospital within a tertiary care academic medical center.*

***Participants:*** *Forty-four pediatric patients with idiopathic scoliosis who received IT morphine following posterior spinal fusion (PSF).*

***Main outcome measure(s):*** *Mean opioid exposure 0-12 hours and 13-24 hours post-IT morphine.*

***Results:*** *Mean opioid exposure was significantly increased during the 13-24-hour compared to the 0-12-hour time period (23.0 ± 12.5 mg parenteral morphine vs 15.9 ± 1.7 mg; p = 0.0006). The only factors significantly associated with morphine exposure during the 0-12-hour period included the median pain score (0-12 hours) (odds ratio [OR], 1.92; 95% confidence interval [CI], 0.033-3.80; p = 0.046) and total acetaminophen dose (OR, 0.003; 95% CI, 0.0008-0.005; p = 0.011).*

***Conclusions:*** *These data indicate that patients experienced improved analgesia for at least 12 hours following IT morphine. Increased use of adjuvant analgesics such as acetaminophen may reduce opioid requirements following PSF procedures. More studies are needed to investigate the combination of adjuvants and IT morphine to reduce postoperative pain in this population.*

## INTRODUCTION

Idiopathic scoliosis is a condition characterized by abnormal curvature of the spine in the absence of underlying congenital or neuromuscular causes. It is defined as a lateral curvature of the spine greater than 10° in the coronal plane. The prevalence of idiopathic scoliosis in the pediatric population is estimated to be 0.5-3 percent, with the majority of cases diagnosed in adolescents and children greater than 10 years of age (late-onset or adolescent idiopathic scoliosis).[1]

Currently, posterior spinal fusion (PSF) with segmental spinal instrumentation is the preferred surgical procedure used for the treatment of idiopathic scoliosis.[1] The goals of this procedure include arrested curve progression, increased mobility, and improved coronal alignment and sagittal balance.[1,2] Complications associated with PSF include infection, significant intraoperative blood loss, and severe postoperative pain and muscle spasms.[1,2] Appropriate pain management includes opioid analgesia and benzodiazepines as an adjunct for muscle spasms. Opioids can be administered via several methods including intrathecal (IT) injection with patient controlled analgesia (PCA), PCA alone, or epidural catheter infusion.

IT morphine has been evaluated in children undergoing PSF and has been associated with significantly decreased intraoperative blood loss, reduced postoperative opioid requirements, increased time to first PCA demand, and improved pain control.[3-10] IT morphine is hydrophilic and does not readily cross the blood brain barrier, so relatively high concentrations are maintained in the cerebrospinal fluid for several hours. As a result, it has an extended duration of analgesia at a fraction of the intravenous morphine dose required to maintain equivalent analgesia.[11,12] The expected duration of effective analgesia with IT morphine is 18-24 hours in adults; however, pediatric studies have reported widely variable durations of analgesia.[9] Gall et al.[3] evaluated the effect of IT morphine doses of 2 and 5 μg/kg and found a median duration of 4 ± 1.3 hours and 9 ± 4.6 hours, respectively. However, Dalens and Tanguy[6] found that 19 of 20 patients remained pain free 48 hours following a dose of 25 μg/kg without the need for additional opioids. There are also conflicting reports concerning the correlation of IT morphine dose and duration of analgesia. Krechel et al.[4] retrospectively evaluated pain control in children undergoing upper abdominal or thoracic procedures who received IT morphine doses ranging from 3.75 to 10 μg/kg but were unable to establish a dose-response relationship. Because of the lack of reliable published data, the objective of this observational study was to identify the mean opioid exposure within 24 hours following administration of IT morphine to pediatric patients undergoing PSF procedures and to describe the duration of analgesia associated with IT morphine in children.

## METHODS

This was a retrospective, cross-sectional, observational study conducted in a tertiary care academic hospital licensed for 230 beds, including 25 pediatric intensive care unit (PICU) beds. Patients were included if they underwent posterior spinal fusion secondary to idiopathic scoliosis between January 1, 2011 and December 31, 2012, received IT morphine, and were ≤18 years of age at the time of procedure. Patients were identified through the institution's electronic database, Meditech (Medical Information Technology, Inc., Westwood, MA) and through the pain management team's patient database. Patients were excluded if they had scoliosis secondary to another identifiable cause, underwent anterior or anterior/posterior spinal fusion, did not receive IT morphine during surgery, or had incomplete medical records.

The primary objective was to compare mean opioid exposure between 0-12 hours and 13-24 hours post-IT morphine. Secondary objectives included identifying incidence of common adverse events associated with opioid exposure. An attempt was also made to determine potential risk factors (eg, IT morphine dose, patient demographic information, and adjunct agents administered) associated with increased opioid exposure within the 24-hour period following administration of IT morphine.

Data were collected using a standardized data collection form and were recorded by a single investigator. Data were accessed through Meditech and anesthesiology records. Demographic data were collected for each patient, including sex, age at admission, weight, height, length of stay in the postanesthesia care unit (PACU) and PICU, and total hospital length of stay. Additionally, patient race was collected, as a higher intravenous (IV) morphine clearance has been described among African American versus Caucasian children in pharmacokinetics and pharmacogenomics studies.[13]

Intraoperative medications including opioids and sedative agents were collected. Additional data gathered for the primary analysis included IT morphine dose and time administered and postoperative PCA regimen. For patients receiving a hydromorphone or fentanyl PCA, the cumulative dose was converted to morphine using an established equianalgesic conversion table.[14] To quantify changes made to PCA regimen, dose decreases were defined as a reduction in the hourly maximum dose (eg, bolus dose decrease, increase in lockout time, and decrease in basal rate) and dose increases were defined as an increase in the hourly maximum dose (eg, bolus dose increase, decrease in lockout time, or increase in basal rate). All nonopioid analgesic or adjuvant agents administered were collected.

To assess the effect of the analgesic agents, pain scores were collected using the Numeric Rating Scale (NRS) for the 24-hour period following IT morphine administration. Symptoms of opioid-associated adverse effects were also collected, including nausea/vomiting, pruritus, respiratory depression, sedation, and urinary retention. An adverse event was defined as documentation of any one of these events in the medical record or the administration of agent(s) to alleviate the adverse event (eg, naloxone for respiratory depression and diphenhydramine for pruritus).

Descriptive and inferential statistics were performed. All variables collected were profiled using descriptive, univariate statistics. Factors potentially associated with the outcome measures (total opioid dose 0-12 hours and 13-24 hours post-IT morphine and occurrence of an adverse effect) were analyzed via bivariable and multivariable analyses. Bivariable analyses included chi-square tests of association and independent/dependent measures *t* tests for means and median tests via Wilcoxon rank sum tests (depending on outcome variable measurement) for all variables considered in this research. The primary objective of comparing total opioid dose received between time periods (0-12 hours and 13-24 hours) was assessed via dependent measures *t* test. Two multivariate, conditional logistical regression analyses were conducted in an effort to assess the dependent variables (milligrams of morphine equivalents in the 0-12-hour period and milligrams of morphine equivalents in the 13-24-hour period), with several independent risk factors (ie, median pain scores, total acetaminophen dose in mg, and IV opioids in mg received in the operating room and PACU). Factors included in the multivariable analysis were selected based on the results of bivariable analyses, using $p < 0.2$ as a guide for inclusion in the multivariable analysis. Data management and analyses were conducted using Stata v13.1, with the a priori alpha set at $p < 0.05$.[15]

## RESULTS

Over the study period, 141 patients aged 0-18 years underwent a spinal fusion surgery. Of these, 44 patients met the inclusion criteria. Ninety-three patients were excluded from analysis. The most common reason for exclusion was scoliosis secondary to another underlying condition (n = 77). Additionally, 20 patients with idiopathic scoliosis were excluded who underwent anterior spinal fusion (ASF) or combined ASF/PSF procedure (n = 4), did not receive IT morphine (n = 10), or had insufficient documentation of IT morphine dose or administration (n = 6). The demographic data for the study group are given in Table 1.

### Intraoperative and PACU opioids

All patients received remifentanil intraoperatively for anesthesia. A description of opioids each patient received is given in Table 2. The mean IT morphine dose was 369 ± 69 µg, corresponding to a weight-based dose of 6.75 ± 0.92 µg/kg (Table 3). Thirty-nine patients (88.6 percent) received additional opioid doses in the operating room following administration of IT morphine. Opioids were administered in the operating room for assumed pain based on changes in patients' vital signs in the interim between IT morphine injection and onset of analgesia. The mean opioid exposure in operating room was 6.4 ± 5.0 mg. Additionally, 35 patients (79.5 percent) received opioid doses in the PACU. The mean opioid exposure in PACU was 5.2 ± 5.0 mg.

**Table 1. Demographics (n = 44)**

| Variable | Number (percent) | |
|---|---|---|
| *Sex* | | |
| Female | 34 (77.3) | |
| Male | 10 (22.7) | |
| *Race* | | |
| White | 33 (75.0) | |
| Black/African American | 3 (6.8) | |
| Native American | 3 (6.8) | |
| Asian | 1 (2.3) | |
| Other | 4 (9.1) | |
| | **Mean ± SD** | **Median (range)** |
| *Patient characteristics* | | |
| Age, y | 14.1 ± 1.8 | 14 (11-18) |
| Weight, kg | 55.4 ± 12.1 | 54.4 (36.1-95.4) |
| Height, cm | 161.1 ± 8.4 | 160.0 (143-181.5) |
| *Length of stay* | | |
| PACU, h | 2 ± 0.6 | 1.9 (0.9-3.3) |
| PICU, d* | 1.2 ± 0.4 | 1 (1-2) |
| Hospital, d | 5 ± 1.4 | 5 (3-10) |

*32 patients (73 percent) were admitted to the PICU following surgery.

### PCA regimens

An overview of the initial PCA regimen is provided in Table 4. All patients received a demand-only PCA pump with either morphine (n = 31) or hydromorphone (n = 13) initiated in PACU (Table 2). There was a significant difference noted in the median number of PCA attempts between the 0-12-hour and

| Table 2. Summary of opioid received | | | | | | |
|---|---|---|---|---|---|---|
| **Patient** | **Age, y** | **Weight, kg** | **Additional opioids received in operating room and PACU** | **PCA** | **Oral opioids*** | **Total 24-h opioid dose in mg, mg/kg** |
| 1 | 14 | 48.2 | Hydromorphone × 3 doses | Hydromorphone | None | 38.4 (0.8) |
| 2 | 12 | 45.6 | Fentanyl × 2 doses, hydromorphone × 1 dose | Hydromorphone | None | 17.3 (0.38) |
| 3 | 15 | 71.8 | Hydromorphone × 2 doses | Hydromorphone | Oxycodone/ acetaminophen | 21.0 (0.29) |
| 4 | 17 | 58 | Fentanyl × 4 doses, hydromorphone × 1 dose, morphine × 4 doses | Morphine | Oxycodone | 15.0 (0.26) |
| 5 | 13 | 43.5 | Morphine × 2 doses | Morphine | None | 15.0 (0.34) |
| 6 | 13 | 48.8 | Morphine × 3 doses, fentanyl × 1 dose | Morphine | Hydrocodone/ acetaminophen | 26.7 (0.55) |
| 7 | 17 | 95.4 | Hydromorphone × 3 doses, fentanyl × 4 doses | Morphine | None | 49.5 (0.52) |
| 8 | 16 | 44.2 | Morphine × 4 doses | Morphine | Hydrocodone/ acetaminophen | 39.3 (0.89) |
| 9 | 12 | 54.1 | Morphine × 3 doses | Morphine | Hydrocodone/ acetaminophen | 31.2 (0.58) |
| 10 | 17 | 56.2 | Morphine × 1 dose | Morphine | Hydrocodone/ acetaminophen | 30.2 (0.54) |
| 11 | 16 | 54.6 | Morphine × 1 dose, fentanyl × 1 dose | Morphine | Hydrocodone/ acetaminophen | 22.4 (0.41) |
| 12 | 12 | 46.5 | Fentanyl × 1 dose, morphine × 2 doses | Morphine | Hydrocodone/ acetaminophen | 32.5 (0.7) |
| 13 | 12 | 36.1 | Fentanyl × 2 does | Hydromorphone | Hydrocodone/ acetaminophen | 15.3 (0.42) |
| 14 | 11 | 53.0 | None | Hydromorphone | Oxycodone/ acetaminophen | 60.1 (1.13) |
| 15 | 12 | 47.2 | Morphine × 6 doses, fentanyl × 5 doses, hydromorphone × 3 doses | Morphine | Hydrocodone/ acetaminophen | 48.3 (1.02) |
| 16 | 15 | 94.3 | Fentanyl × 2 doses | Hydromorphone | Oxycodone/ acetaminophen | 95.8 (1.02) |
| 17 | 13 | 56.6 | Fentanyl × 5 doses, morphine × 4 doses | Morphine | None | 25.0 (0.44) |
| 18 | 13 | 61 | Morphine × 1 dose, hydromorphone × 1 dose | Hydromorphone | Hydrocodone/ acetaminophen | 67.6 (1.11) |
| 19 | 16 | 69.3 | Morphine × 10 doses, fentanyl × 6 doses | Morphine | Hydrocodone/ acetaminophen | 17.7 (0.25) |
| 20 | 15 | 56.9 | Hydromorphone × 5 doses, morphine × 2 doses | Hydromorphone | None | 34.7 (0.61) |
| 21 | 16 | 55.9 | Hydromorphone × 4 doses, fentanyl × 1 dose | Morphine, hydro-morphone | None | 8.3 (0.15) |
| 22 | 16 | 45.2 | Fentanyl × 7 doses, hydromorphone × 4 doses | Morphine | None | 36.0 (0.8) |
| 23 | 13 | 46.7 | Morphine × 3 doses | Morphine | None | 30.0 (0.64) |
| 24 | 14 | 47.5 | Morphine × 8 doses | Morphine | Hydrocodone/ acetaminophen | 43.2 (0.91) |

| Table 2. Summary of opioid received (continued) | | | | | | |
|---|---|---|---|---|---|---|
| **Patient** | **Age, y** | **Weight, kg** | **Additional opioids received in operating room and PACU** | **PCA** | **Oral opioids*** | **Total 24-h opioid dose in mg, mg/kg** |
| 25 | 13 | 45.9 | Morphine × 8 doses, fentanyl × 6 doses | Morphine | None | 18.0 (0.39) |
| 26 | 13 | 64.2 | Hydromorphone × 2 doses | Hydromorphone | Hydrocodone/ acetaminophen | 10.3 (0.16) |
| 27 | 16 | 60.7 | Morphine × 1 dose, fentanyl × 3 doses | Morphine | Oxycodone | 47.5 (0.78) |
| 28 | 15 | 49.3 | Fentanyl × 1 dose, morphine × 4 doses, hydromorphone × 1 dose | Morphine, hydro-morphone | None | 41.3 (0.84) |
| 29 | 14 | 42.8 | Hydromorphone × 2 doses, morphine × 2 doses, fentanyl × 1 dose | Hydromorphone | Hydrocodone/ acetaminophen | 42.8 (1.0) |
| 30 | 14 | 65.7 | Morphine × 8 doses, fentanyl × 2 doses | Morphine | Hydrocodone/ acetaminophen | 66.3 (1.0) |
| 31 | 18 | 59.7 | Hydromorphone × 1 dose, morphine × 3 doses | Hydromorphone | Hydrocodone/ acetaminophen | 27.3 (0.46) |
| 32 | 13 | 53.1 | Fentanyl × 1 dose | Morphine | Hydrocodone/ acetaminophen | 37.7 (0.71) |
| 33 | 17 | 62 | Fentanyl × 4 doses, morphine × 2 doses | Morphine | Hydrocodone/ acetaminophen | 61.0 (0.98) |
| 34 | 12 | 52.9 | Morphine × 2 doses | Morphine | Hydrocodone/ acetaminophen | 36.3 (0.69) |
| 35 | 15 | 57.2 | Morphine × 2 doses, fentanyl × 7 doses, hydromorphone × 5 doses | Morphine | None | 55.0 (0.96) |
| 36 | 15 | 54.9 | Morphine × 2 doses, fentanyl × 3 doses | Hydromorphone | Hydrocodone/ acetaminophen | 52.8 (0.96) |
| 37 | 13 | 40.6 | Fentanyl × 2 doses, morphine × 5 doses, hydromorphone × 1 dose | Morphine, hydro-morphone | Hydrocodone/ acetaminophen | 61.3 (1.51) |
| 38 | 11 | 51.7 | Morphine × 6 doses, fentanyl × 3 doses | Morphine | Hydrocodone/ acetaminophen | 56.7 (1.1) |
| 39 | 15 | 63.8 | Fentanyl × 2 doses, morphine × 1 dose | Morphine, hydro-morphone | Hydrocodone/ acetaminophen | 87.6 (1.37) |
| 40 | 13 | 41.1 | Morphine × 3 doses | Morphine | Hydrocodone/ acetaminophen | 56.1 (1.36) |
| 41 | 13 | 72.9 | Fentanyl × 2 doses | Morphine | Hydrocodone/ acetaminophen | 27.2 (0.37) |
| 42 | 13 | 47.6 | Fentanyl × 5 doses | Morphine | None | 35.5 (0.75) |
| 43 | 13 | 60.3 | Fentanyl × 3 doses, morphine × 3 doses | Morphine, hydro-morphone | None | 9.0 (0.15) |
| 44 | 14 | 55.6 | Morphine × 2 doses, fentanyl × 4 doses | Hydromorphone | Hydrocodone/ acetaminophen | 62.2 (1.12) |

*Oral opioids received after the patient's PCA therapy was discontinued.

13-24-hour time periods, 13 (range, 2-41) versus 20 (3-48), respectively, $p < 0.001$. Additionally, there was a significant difference in the median number of PCA boluses between the 0-12-hour and 13-24-hour time periods, 19 (range, 3-212) versus 27 (5-462), $p = 0.021$.

Twenty-four patients (54.5 percent) required at least one adjustment to their PCA regimen due to uncontrolled breakthrough pain or adverse effects. These PCA adjustments occurred across both time periods. During the 0-12-hour period, 15 changes were noted

| Table 3. IT morphine and PCA data (n = 44) | | |
|---|---|---|
| **Data** | **Mean ± SD** | **Median (range)** |
| *IT morphine* | | |
| Actual dose, µg | 369 ± 69 | 379 (250-525) |
| Weight-based dose, µg/kg | 6.75 ± 0.07 | 6.92 (3.9-9.11) |
| *PCA initial regimen** | | |
| Bolus dose, mg | 0.98 ± 0.33 | 1 (0.2-2) |
| Bolus dose, mg/kg | 0.019 ± 0.005 | 0.018 (0.004-0.033) |
| Lockout, min | 10 ± 1.3 | 10 (10-15) |
| Basal rate, mg/h | 0 ± 0 | 0 (0-0) |
| Hourly maximum, mg | 5.5 ± 1.6 | 6 (1.7-12) |
| Hourly maximum, mg/kg | 0.10 ± 0.03 | 0.10 (0.03-0.20) |
| *Data reflect PCA initial regimen in morphine equivalents. | | |

| Table 4. Opioid exposure* | | | |
|---|---|---|---|
| **Variable** | **Mean ± SD** | | **p-Value** |
| | **0-12 h** | **13-24 h** | |
| *Total morphine* | | | |
| mg | 15.9 ± 1.7 | 23 ± 12.5 | 0.0006 |
| mg/kg | 0.28 ± 0.03 | 0.43 ± 0.23 | 0.0005 |
| *PCA* | | | |
| mg | 15.8 ± 11.4 | 21.2 ± 12.2 | 0.0059 |
| mg/kg | 0.29 ± 0.18 | 0.39 ± 0.23 | 0.0045 |
| *Additional opioid* | | | |
| mg | 0.12 ± 0.58 | 1.88 ± 1.71 | <0.0001 |
| mg/kg | 0.003 ± 0.013 | 0.03 ± 0.03 | <0.0001 |
| *Opioids other than morphine were converted to morphine equivalents using equianalgesic conversions. | | | |

(five dose increases, seven dose decreases, and three changes from morphine to hydromorphone). During the 13-24-hour period, 20 changes were noted (12 demand dose increases, six dose decreases, and two changes from morphine to hydromorphone). Additionally, three patients (6.8 percent) required the addition of a basal infusion rate; two of these patients in the 0-12-hour period. Of the five patients who were switched from morphine to hydromorphone, two changes were due to adverse effects, one due to poor pain control, one due to an incorrect initial order, and one for an unknown reason (Table 2).

### Cumulative opioid exposure

Thirty patients received at least one non-PCA opioid dose during the study period. Additional IV opioid doses were administered to two patients in the 0-12-hour time period. During the 13-24-hour time period, 30 patients (68.2 percent) received additional opioids including oral hydrocodone/acetaminophen, oxycodone, or oxycodone/acetaminophen.

The mean total opioid exposure from all sources during the study period is given in Table 4. The patients received 38.9 ± 3.1 mg IV morphine equivalents or 0.71 ± 0.05 mg/kg. There were significant differences in the total morphine dose and PCA regimen dose in mg and mg/kg between the 0-12-hour and 13-24-hour periods.

### Pain scores

Pain scores on a scale of 0-10 were recorded for each patient. For the purpose of analysis, pain scores were grouped according to the highest score, lowest score, and median score for each patient. There was a significant difference in the overall median score between the 0-12-hour and 13-24-hour periods, 2 (0-6) versus 3 (0-8), respectively, $p < 0.001$. In addition, there was a significant difference in the median lowest score between the 0-12-hour and 13-24-hour periods, 0 (0-2) versus 0 (0-6), $p = 0.033$. There was no significant difference between the median highest pain scores between the two time periods, 5 (2-10) versus 6 (2-10), respectively, $p = 0.126$.

### Adjuvant agents

Adjuvant agents commonly administered included acetaminophen and diazepam. Thirty-eight patients (86.4 percent) received at least one dose of acetaminophen IV, and 30 patients (68.2 percent) received at least one dose of oral acetaminophen. Most commonly, oral acetaminophen exposure was due to administration of combination oral opioid products during the 13-24-hour time period. Additionally, 25 patients (56.8 percent) received diazepam IV and 15 patients (34.1 percent) received oral diazepam.

Four patients (9.1 percent) received additional potentially pain-modulating medications in the 24 hours following surgery. One patient restarted home medications that included citalopram and divalproex, and a second patient restarted citalopram alone. Additionally, one patient received gabapentin

for postoperative neuropathic pain and another was prescribed scheduled ketorolac.

### Adverse events

The incidence of opioid-associated adverse events during the study period is reported in Table 5. The most common adverse events were nausea and vomiting, occurring in 30 patients (68.2 percent). Patients were treated with ondansetron, promethazine, and, in refractory cases, prochlorperazine. Pruritus was reported in 22 patients (50 percent), 19 of which required treatment with diphenhydramine. Seven patients (15.9 percent) experienced oversedation and five patients (11.4 percent), respiratory depression. Only nine of these cases were considered clinically significant and required treatment. The most common interventions included withholding or decreasing the PCA dose, holding other medications, such as diazepam, or in the case of respiratory depression, providing oxygen. No patients required naloxone for opioid reversal, PICU admission, or intubation for opioid-associated adverse events within the study period. Five patients (11.4 percent) experienced urinary retention that improved upon administration of fluid boluses. Additional adverse events were reported in four patients (9.1 percent) and included hallucinations, muscle cramps or weakness, and hypotension.

### Regression analysis

Two multivariate, conditional logistic regressions were performed to evaluate the effect of various factors on milligrams of morphine in the 0-12-hour period and the 13-24-hour period. Factors associated with a significant association with the milligrams of morphine in the 0-12-hour period included median pain score (0-12 hours) (odds ratio [OR], 1.92; 95% confidence interval [CI], 0.033-3.80; p = 0.046) and total acetaminophen dose (mg) received (OR, 0.003; 95% CI, 0.0008-0.005; p = 0.011). The additional IV opioids received in the operating room and PACU (OR, 0.195; 95% CI, 0.584-0.194; p = 0.317) was not significantly associated with the total milligrams of morphine required during this time period. There were no significant predictors of the milligrams of morphine in the 13-24-hour period.

**Table 5. Adverse effects**

| Variable | Number (percent) | |
|---|---|---|
| | Incidence | Clinically significant |
| Nausea/vomiting | 30 (68.2) | 30 (68.2) |
| Pruritus | 22 (50.0) | 19 (43.2) |
| Sedation | 7 (15.9) | 4 (9.1) |
| Respiratory depression | 5 (11.4) | 5 (11.4) |
| Urinary retention | 5 (11.4) | 5 (11.4) |

## DISCUSSION

Previous studies have demonstrated that administration of IT morphine provides safe and effective pain relief in pediatric patients with scoliosis who have undergone spinal fusion surgery.[6] IT morphine has also been shown to provide a longer duration of pain relief compared to traditional methods of opioid administration.[4,7] However, the reported duration of pain relief in children has varied widely among studies, with no clear relationship to dose administered.[3-6] This study sought to evaluate the effective duration of pain relief achieved in this population and any factors associated with a shortened period of analgesia, which may result in additional opioid exposure and adverse effects.

Patients undergoing PSF procedures in our study were managed according to an IT morphine protocol which includes 7 µg/kg IT morphine approximately 1 hour before closure of the surgical incision, followed by a PCA started in PACU, IV acetaminophen every 6 hours for 24 hours, and diazepam every 6 hours as needed for muscle spasms. Pain scores are monitored at least hourly for the first 12 hours and every 2 hours for the next 12 hours. Each patient is followed by an interdisciplinary pediatric pain management team, which authorizes addition of any other pain medications and changes to the PCA regimen. Thirty-two patients (72.7 percent) underwent surgery prior to implementation of the current protocol. These patients were more likely to receive enteral acetaminophen as needed rather than scheduled and IV. The range of IT morphine doses was also greater in this group; however, the median dose was similar both before and after protocol implementation. None of the previous studies assessed the effect of adjuvant agents such as acetaminophen and diazepam on opioid requirements following IT morphine administration for PSF. Investigations into the effectiveness of a multimodal approach including nonopioid adjuvant agents on pain scores and mean opioid requirements in this

patient population would be beneficial to determine the utility and optimal use of these agents.

Two previous studies in children have used IT morphine doses similar to that used in our protocol. Tripi et al.[5] described a duration of analgesia of 16.7 hours following IT morphine doses of 9-19 μg/kg (mean 14 μg/kg) in children with scoliosis undergoing PSF. Krechel et al.[4] reported a similar duration of analgesia of 21.8 hours with doses of 3.75-10 μg/kg in children undergoing thoracic or abdominal surgeries. The authors also attempted to develop a dose-response curve but were unable to correlate IT morphine dose and duration of effect. Our study attempted to provide some clarity to the duration of IT morphine. Our data suggest that the duration of effect of IT morphine is at least 12 hours in most children undergoing PSF. However, our study suggests that the duration of activity did not last over the 24-hour period, as we noted that the total morphine dose and PCA regimen dose were significantly higher between the 13-24-hour and 0-12-hour periods.

Cumulative morphine exposure during this study was 38.9 ± 3.1 mg (0.71 ± 0.05 mg/kg) for the 24 hours following IT morphine administration. This total excludes opioids given intraoperatively after IT morphine or in PACU, as these doses were often given on the assumption that the onset of analgesia of IT morphine had not yet occurred. Two previous studies have reported cumulative opioid exposure following IT morphine in this patient population. Tripi et al.[5] reported mean opioid requirements of 1.4 ± 0.5 mg/kg and 1.5 ± 0.5 mg/kg in their high-dose (≥20 μg/kg) and moderate-dose (9-19 μg/kg) treatment groups over the first 48 hours following posterior spinal fusion. Gall et al.[3] reported mean 24-hour PCA morphine exposure of 12 ± 12 mg in patients receiving an IT morphine dose of 5 μg/kg. Mean opioid exposure in this study is difficult to compare to that found in Tripi et al.[5] due to differences in length of time studied following IT morphine. However, compared to the results reported by Gall et al.,[3] patients in this study required a higher mean opioid exposure over the 24 hours following surgery.

We noted several indicators that IT morphine did not provide analgesia for ≥12 hours in some patients. This was evidenced by the number of PCA dose increases in the 0-12-hour period, including addition of basal infusions. Additionally, in our regression analysis, increased acetaminophen exposure was significantly associated with decreased morphine requirements in the 0-12-hour postoperative period. Additional studies in pediatric and adult populations have reported improved postoperative pain with adjunct acetaminophen, with some studies reporting reduced opioid consumption; however, effects on opioid consumption are inconsistent between studies.[16-18] Diazepam use was not significantly associated with morphine exposure. However, because only 37 patients (84 percent) received diazepam and the median number of doses during the study period was 2 (range, 0-6), there may not have been enough use to detect a difference.

Nausea and vomiting were reported in a large number of patients. Because of the retrospective nature of this study, any documentation of nausea or vomiting or administration of an antiemetic medication in the first 24 hours after IT morphine was considered an occurrence of this event. Because of this, many patients may have experienced nausea and vomiting due to anesthesia medications or a combination of factors, rather than opioid exposure alone.

This study did have limitations. First, PCA usage for an entire nursing shift was often documented only at the end of each shift, at 0700 and 1900. The 0-12-hour time period was therefore approximated by IT morphine administration time to 0700 on postoperative day 1 and the 13-24-hour time period by 0700-1900 on postoperative day 1. On occasions where PCA usage was not recorded, usage was calculated from the PCA settings and recorded cassette volume changes over the time period. This also precluded us from evaluating time to first opioid dose as reported in previous studies.[3,5] Second, our current IT morphine protocol uses acetaminophen IV scheduled for the 24 hours following surgery. This agent received a Food and Drug Administration-approved indication in November 2010 and was not routinely administered to our PSF patients until May 2011. Third, although pain scores were routinely documented, precipitating factors for increased pain such as movement, coughing, or initiation of physical therapy, were not recorded. Additionally, we did not attempt to correlate administration of as-needed adjuvant medications or PCA injections to painful stimuli. Fourth, because of the high percentage of white patients in our study, we were unable to assess the potential role of race in the duration of analgesia of IT morphine. Finally, the total number of patients included in this study may not be enough to truly conclude no significant differences existed in those analyses where we were unable to detect significant differences and/or associations.

The inability to detect significant differences may have been the result of insufficient statistical power.

## CONCLUSION

This study noted increased opioid requirements and median pain scores in the 13-24-hour time period compared to the 0-12-hour time period following IT morphine administration, suggesting that children tended to experience improved pain control for at least 12 hours following IT morphine administration. Increased use of adjuvant analgesics such as acetaminophen may reduce opioid requirements following PSF procedures. Future studies should investigate the combination of these adjuvants in addition to IT morphine to reduce postoperative pain in this population.

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