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ORIGINAL ARTICLE

Cost comparison of intrathecal morphine to intravenous patient-controlled analgesia for the first 24 h post cesarean delivery: a retrospective cohort study

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Abstract
Purpose Intrathecal morphine provides superior pain control for patients undergoing cesarean delivery when compared to intravenous opioid patient-controlled analgesia. However, no study has assessed the overall cost associated with each modality as a primary outcome. The aim of this study is to determine the overall cost of each modality for the first 24 h post cesarean delivery.
Methods Charts of patients undergoing cesarean delivery at our institution from January 1, 2014 to December 31, 2014 were reviewed. Patients receiving intrathecal morphine were compared to patients undergoing general anesthesia and receiving intravenous opioid patient-controlled analgesia for post-procedure analgesia. The primary outcome measured was total cost of each modality for the first 24 h after delivery. Secondary outcomes included post-procedure pain scores, time to removal of the Foley catheter, need for rescue medications, and adverse events.
Results There was a significant difference in total cost of intrathecal morphine when compared to intravenous opioid patient-controlled analgesia ($51.14 vs. $80.16, $p < 0.001$). Average pain scores between 0–1 h (0 vs. 5, $p < 0.001$) and 1–6 h (2.5 vs. 3.25, $p < 0.001$) were less in the intrathecal morphine group. The intrathecal morphine group received more ketorolac ($p < 0.001$) and required more rescue opioids ($p = 0.042$). There were no significant differences in documented adverse events.
Conclusions The use of intrathecal morphine for post-cesarean pain control leads to a significant cost savings for the first 24 h when compared to intravenous opioid patient-controlled analgesia. Patients also experienced less pain and were not at increased risk for adverse events.

Keywords Intrathecal morphine · Cost analysis · Post-cesarean pain control

Introduction

Intrathecal (IT) morphine has been shown to be safe and effective in controlling post-cesarean delivery pain [1, 2]. When compared to patients receiving intravenous (IV) opioid patient-controlled analgesia (PCA), neuraxial morphine has been shown to be more effective in controlling pain for the first 24 h after cesarean delivery [3–5]. These studies also assessed common side effects of opioid medications and did find that patients receiving neuraxial morphine often reported a higher degree of pruritus compared to IV PCA administration; however, findings were more equivocal for nausea and vomiting [3–5]. Although the common opioid side effect of pruritus has been documented in patients receiving neuraxial morphine, studies have demonstrated that the most feared—and most closely monitored—consequence of neuraxial morphine, delayed respiratory depression, is a very rare occurrence. In one report assessing small but clinically relevant doses of IT morphine (25–100 μg), patients demonstrated no change in their carbon dioxide response curves and showed no evidence of respiratory depression [6]. Interestingly, suprathrapeutic doses of IT morphine (1–2 mg) also resulted in

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no incidence of respiratory depression [7]. Because of its effectiveness and overall safe profile, the American Society of Anesthesiologists (ASA) Task Force on Obstetric Anesthesia recommends the use of neuraxial over parenteral opioids for post-cesarean delivery analgesia [8].

Multiple studies have assessed different doses of IT morphine both with and without the use of scheduled non-opioid analgesics to determine the optimal combination for adequate pain control with minimal side effects [1, 2, 9–11]. Evidence supports the administration of 100 μg IT morphine in combination with scheduled non-opioid analgesics for post-cesarean pain control [11, 12]. In 2013, using an evidence-based approach, our institution developed a protocol using 100 μg IT morphine in combination with scheduled 30 mg IV ketorolac every 6 h for post-cesarean delivery analgesia. This protocol replaced our old policy of patients receiving an IV opioid PCA for the first 24 h after cesarean delivery. After this successful change in practice, we were interested in determining if this change also provided a cost savings to the hospital. A literature search produced one article that reported a cost analysis comparing IT morphine to opioid PCA as a secondary endpoint [10]. The aim of this study is to determine the overall cost associated with care of the patient as it relates to pain control and associated side effects for each modality for the first 24 h after cesarean delivery. Secondary aims include comparing pain scores, time to removal of the Foley catheter, and any adverse events between each group for the first 24 h. We hypothesize that when accounting for all aspects of pain control including medications, equipment, nursing care, and treatment of side effects, the overall cost associated with IT morphine will be significantly less than the cost associated with IV opioid PCA.

Methods

This study was approved by the University of Alabama at Birmingham (UAB) Institutional Review Board, and waiver of consent was obtained before the collection of data. This was a retrospective cohort study consisting of a consecutive series of patients who underwent a cesarean delivery at UAB's Women and Infants Center from January 1, 2014 to December 31, 2014. Patients were identified by searching for "cesarean delivery" and similar terms under the procedure tab of our electronic anesthesia database. We also limited the search to patients who received "spinal" or "general" anesthesia under the anesthesia type; therefore, any patient who had epidural anesthesia for her cesarean delivery was excluded from the initial search. Once the initial patient list was compiled, we initiated a search of the patients' electronic medical records through our hospital's electronic database to obtain demographics, postoperative outcomes data, and financial data. Patients who were <19 years old, had a history of chronic pain with documented outpatient opioid use, or received an amount of IT morphine greater than our standard 100-μg dose were excluded from the analysis. Patients who received IT morphine were compared to patients who received an IV PCA containing either morphine or hydromorphone for the first 24 h after the procedure. Because the expected duration of action of the IT morphine is approximately 24 h and most patients are tolerating oral intake and oral pain medication by post-procedure day 1, we routinely transfer pain management to our obstetrical colleagues after the first 24 h. Therefore, this study only includes the first 24 h that the patients are under our direct care.

Anesthetic method for cesarean delivery

At our institution, a routine protocol is followed for both spinal as well as general anesthesia for cesarean delivery. Unless contraindicated or the urgency of the procedure precludes it, cesarean delivery is performed under spinal anesthesia: 1.6 ml 0.75 % hyperbaric bupivacaine is administered with 15 μg fentanyl and 100 μg preservative-free morphine via a 25-gauge pencil-point spinal needle into the IT space. All patients receive a crystalloid bolus between 500 and 1000 ml at the time of spinal placement, and a phenylephrine infusion of 0.5 μg/kg/min is started immediately after IT injection. The phenylephrine infusion is titrated to maintain a systolic blood pressure within 20 % of the patient's baseline blood pressure. The patient is then placed in a left tilt position. The cesarean delivery begins when an anesthetic level to the T6 dermatome is confirmed.

For patients undergoing cesarean delivery under general anesthesia, induction does not occur until the surgical team is prepared to start the procedure. Rapid sequence induction of anesthesia is achieved with propofol 2–3 mg/kg and succinylcholine 1.5 mg/kg. Once endotracheal intubation occurs, general anesthesia is maintained with sevoflurane. After delivery of the newborn, the sevoflurane concentration is reduced, nitrous oxide is initiated to maintain a 50 % concentration with oxygen, and IV midazolam and opioids are given as appropriate.

Cost data calculation/definitions

The total cost incurred by each patient as it relates to her pain management for the first 24 h after cesarean delivery was calculated using the cost of each medication used to treat either pain or potential side effects of the opioid medication such as pruritus, nausea, and sedation; the cost of the equipment needed to administer the medication; the nursing cost for administration of any required medications; and the cost to monitor patients for the first 24 h.

Medications included in the analysis were: preservative-free morphine for spinal use, IV morphine and hydromorphone cartridges for PCA use, rescue bolus medication of morphine and hydromorphone, ketorolac (routine administration every 6 h unless contraindicated), ondansetron, promethazine, diphenhydramine, and naloxone. The cost for each medication was provided by the hospital pharmacy. Our standard rescue medications doses are morphine 2 mg, hydromorphone 0.2 mg, ketorolac 30 mg, ondansetron 4 mg, promethazine 25 mg, diphenhydramine 25 mg, and naloxone 0.2 mg. The PCA cost was determined by averaging the cost it takes to perform annual preventative maintenance, clean, and deliver the PCA to each patient: this included the average labor expense for the UAB biomedical technician and the recorded average time it takes to perform each task. Because all patients who receive a PCA at our institution require continuous end-tidal carbon dioxide ($ETCO_2$) monitoring, the cost of the disposable sampling line ($11.50) was added to the overall cost associated with the PCA. From this, we determined the average total cost for each PCA per patient to be $31.26. For the nursing cost, we accounted for both nursing care in the post-anesthesia care unit (PACU) and post-partum floor. We received our data from the nurse managers of both the PACU and post-partum floor. With their input, we determined the average time it took to initiate a patient's PCA was 11 min at a total nursing cost of $4.55 and to administer any rescue medications was 8 min at a total nursing cost of $3.31 per event. Routine vital sign monitoring for each group includes (1) every hour for the first 4 h, then once every 4 h in the PCA group, and (2) strict adherence to the ASA guidelines in the IT morphine group [13]. Vital signs are routinely obtained by patient care technicians. It was determined that the average time it took gather routine vital signs was 5 min for a total cost of $1.04 per event.

Therefore, we used these equations for each group: (1) IV PCA cost = cost of opioid cartridge for PCA + cost of rescue drugs required + nursing cost + PCA cost; (2) IT morphine cost = cost of preservative-free morphine + cost of rescue drugs required + nursing cost. Two patients in the IT morphine group eventually had to receive an IV PCA for postoperative pain control, so the IV PCA cost was added to the overall cost of these two patients.

Secondary outcomes

Postoperative pain scores were recorded. Pain scores were assessed using a numerical pain scale (0 = no pain to 10 = severe pain). Pain scores were averaged for each patient during the following time intervals: 0–1, 1–6, 6–12, and 12–24 h post procedure. The time for removal of the Foley catheter was recorded. Adverse events such as respiratory depression (defined as a documented respiratory rate of less than 10 respirations per minute), surgical site infection, deep venous thrombosis, dropped babies, and PCA administration errors were also recorded from the electronic medical record.

Statistical analysis

Data were entered into an Excel (Microsoft, Seattle, WA, USA) database and then exported to SPSS (IBM, Chicago, IL, USA) for analyses. Descriptive statistics are presented as frequency and percent for categorical variables and as medians with standard deviation (SD) for continuous study variables. For continuous variables, including comparison of cost data between the groups, comparisons were performed with a paired, two-tailed *t* test for normally distributed (parametric) continuous variables and the Wilcoxon rank-sum test for nonparametric analysis. Either the chi-square test or the Fisher exact test was used to compare categorical data. A p value <0.05 was considered to represent a statistically significant difference between the two groups.

Results

Between January 1, 2014 and December 31, 2014, a total of 679 patients met the initial criteria of "cesarean delivery" and "spinal" or "general" anesthesia for inclusion in the study. After the exclusion criteria were applied, a total of 612 patients were analyzed; 494 (80.7 %) received IT morphine and 118 (19.3 % received) an IV PCA. Of the patients who received a PCA, 60 (50.8 %) received a morphine PCA and 58 (49.2 %) received a hydromorphone PCA. All patients in the IT morphine group underwent spinal anesthesia, and all patients in the IV PCA group underwent general anesthesia for the cesarean delivery. Patient characteristics are listed in Table 1.

Cost analysis

The median total cost per patient was $51.14 in the IT morphine group versus $80.16 in the IV PCA group ($p < 0.001$) (as shown in Fig. 1). Neither the median nursing cost per patient ($36.50 vs. $25.91, $p = 0.580$) nor the median rescue drug cost ($4.24 vs. $3.04, $p = 0.422$) were significant when comparing the IT morphine group to the IV PCA group. The itemized cost data are presented in Table 2.

Postoperative outcomes and postoperative medication use

Postoperative outcomes and medications used are shown in Table 3. Significantly more patients in the IT morphine

Table 1 Patient characteristics

	Intrathecal (IT) morphine ($n = 494$)	IV opioid PCA ($n = 118$)	p value
Maternal age (years)	29.0 ± 5.6	27.0 ± 5.7	0.29
Body mass index (kg/m^2)	33.2 ± 8.0	31.1 ± 18.2	0.94
Surgery length (min)	53.0 ± 16.0	50.0 ± 24.9	0.22

Values are presented as median ± standard deviation

IV intravenous, *n* number of patients, *PCA* patient-controlled anesthesia

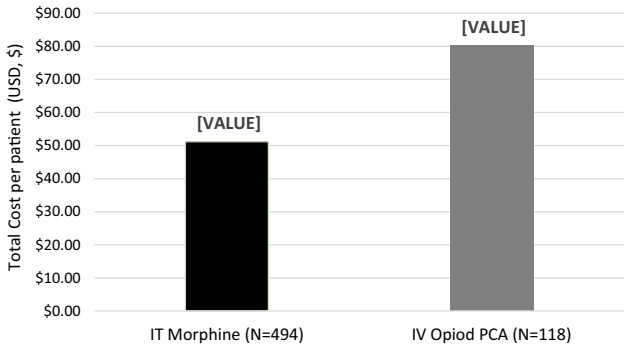

Fig. 1 Total cost per patient by type of analgesia. The IT morphine group had a significantly lower total cost per patient than the IV opioid PCA group ($p < 0.001$). *IT* intrathecal, *IV* intravenous, *PCA* patient-controlled analgesia

Table 2 Itemized cost data comparison between the IT morphine group versus the IV opioid PCA group

	Intrathecal (IT) morphine ($n = 494$)	IV opioid PCA ($n = 118$)	p value
Nursing cost median $	$36.50	$25.91	0.580
Total rescue drug cost, median $	$4.24	$3.04	0.422
Total PCA drug cost, median $	N/A	$15.88	N/A
Grand total cost, median $	$51.14	$80.16	<0.001

All costs are per patient ($ USD)

IT intrathecal, *IV* intravenous, *n* number of patients, *N/A* not applicable, *PCA* patient-controlled analgesia

group received ketorolac ($p < 0.001$). Patients in the IT morphine group also required significantly more rescue morphine ($p < 0.001$), whereas a significantly higher percentage of patients in the IV PCA group required rescue hydromorphone ($p < 0.001$). When the opioid bolus groups are combined, the IT morphine group received more total bolus opioids ($p = 0.042$). Almost all patients required at least one rescue bolus in both the IT morphine and the IV PCA groups (98 % vs. 97.4 %, $p = 0.497$). The median number of rescue bolus medications each patient required in the IT morphine and IV PCA groups was also not significant (6 vs. 5, $p = 0.887$). There were no significant differences observed with regard to the incidence of decreased respirations ($p = 0.134$), surgical site infections ($p = 0.386$), or time to removal of the Foley catheter ($p = 0.940$). No patients had a deep venous thrombosis or pulmonary thromboembolism (DVT/PTE) or babies dropped.

Postoperative pain scores

Figure 2 depicts the median pain scores for each group at the specified time intervals. The IT morphine group had significantly lower pain scores at 0–1 h ($p < 0.001$) and 1–6 h ($p < 0.001$) post procedure when compared to the IV PCA group.

Discussion

IT morphine is an effective means of providing postoperative analgesia for patients undergoing cesarean delivery. Although it is widely accepted as standard practice in many institutions and its use is endorsed by the ASA Task Force on Obstetric Anesthesia, no study has been designed to compare the cost associated with IT morphine versus the traditional opioid IV PCA as a primary outcome. The aim of this study was to determine the overall cost associated with care of the patient as it relates to pain control and associated side effects for each modality for the first 24 h after cesarean delivery. Secondary aims included comparing pain scores, time to removal of the Foley catheter, and any adverse events between each group for the first 24 h.

We were able to demonstrate a significant overall cost savings in the IT morphine group when compared to the opioid IV PCA group. An important finding in the overall cost analysis is that there is no significant difference in cost of nursing care associated with each group. This finding should strengthen the support of IT morphine use as the concern for higher nursing costs—including the need for more frequent monitoring—associated with IT morphine patients was proven to be not significant. The major component to the monetary difference between the two groups is the overall PCA cost. After working with our Biomedical Department, we were able to determine the average cost to clean, maintain, and deliver a PCA unit was $19.76 per patient who used a PCA. Also, all patients using a PCA require continuous $ETCO_2$ monitoring. The additional cost

Table 3 Postoperative medications used and postoperative outcomes

	Intrathecal (IT) morphine ($n = 494$)	IV opioid PCA ($n = 118$)	p value
Medications administered			
Ketorolac	447 (90.3 %)	85 (72.0 %)	<0.001
Ondansetron	188 (38 %)	56 (47.5 %)	0.080
Promethazine	55 (11.1 %)	16 (13.6 %)	0.458
Diphenhydramine	146 (29.5 %)	39 (33 %)	0.459
Morphine bolus	319 (64.6 %)	34 (28.8 %)	<0.001
Hydromorphone bolus	99 (20.0 %)	56 (47.5 %)	<0.001
Total opioid bolus	418 (84.6 %)	90 (76.2 %)	0.042
Naloxone	0	0	–
Postoperative outcomes			
Rescue bolus (*n*)	486 (98 %)	115 (97.4 %)	0.497
Median number bolus/patient	6	5	0.887
Respirations <10 during first 24 h (*n*)	5 (1.0 %)	4 (3.9 %)	0.134
Surgical site infections	5 (1.0 %)	3 (2.5 %)	0.386
Deep venous thrombosis	0	0	–
Pulmonary thromboembolism	0	0	–
Babies dropped	0	0	–
PCA administration error	N/A	0	–
Patients requiring conversion to IV Morphine/hydromorphone PCA pump for adequate pain control	2	N/A	–
Time to removal of Foley catheter, median hours ± standard deviation	20.0 ± 5.8	21.0 ± 14.4	0.940

n number of patients, *N/A* not applicable

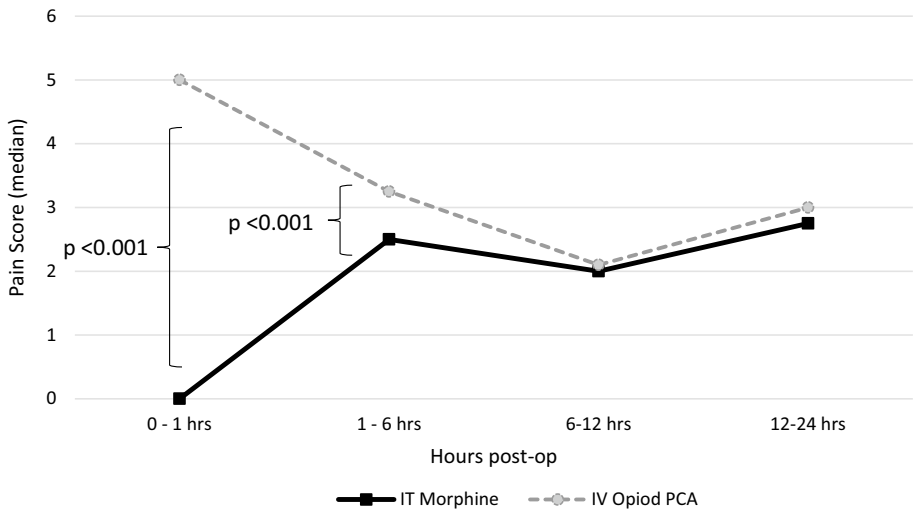

Fig. 2 Post-operative pain scores by type of analgesia. Pain scores between the IT morphine group compared to the IV opioid PCA group were significantly lower ($p < 0.001$) at the 0- to 1-h and 1- to 6-h intervals

of the $ETCO_2$ sampling line ($11.50) increases the overall PCA cost to $31.26. This item is an adjustable component in our equation, and its decreased use could lead to an overall savings to the hospital.

There were a few significant findings when we considered all medications involved in treating pain or potential side effects of opioid medications. We noted a significantly higher administration of ketorolac in the IT morphine group when compared to the IV PCA group. Again, our standard practice is to administer scheduled ketorolac every 6 h in combination with either the IT morphine or opioid IV PCA. The most likely explanation as to the significant difference between the groups is that there were a larger number of patients in the general anesthesia group (i.e., the IV PCA group) in which ketorolac was contraindicated. Patients in this group more than likely had significantly

higher incidence of coagulopathy precluding spinal anesthesia or were severely preeclamptic with hemolysis, elevated liver enzymes, and low platelets (HEELP) syndrome, or had renal dysfunction. Studies have shown excellent pain relief when IT morphine is combined with a non-opioid antiinflammatory medication [9, 11]. We acknowledge that the significant difference between the groups could affect postoperative pain scores. Another significant finding is the increased requirement of rescue opioid required in the IT morphine group. This was not unexpected as the requirement of rescue opioids in this group has been shown in the past [11]. One possible explanation in our study could be the different pain expectations in each group. As the anesthetic level recedes in the IT morphine group, the patients begin to experience this "unexpected pain" that was initially not present. This "new" pain could possibly explain the higher demand for bolus opioid medication. We also searched for medications used in the treatment of nausea, itching, and sedation. We found no significant difference in the use of these medications in either group.

Because pain scores were not documented at the same time postoperatively for each patient, we averaged all pain scores documented for each patient during each designated time period (0–1, 1–6, 6–12, and 12–24 h). We found significant differences between the IT morphine and the opioid IV PCA group at 0–1 and 1–6 h. The large difference in the IT morphine group compared to the other IV PCA group at 0–1 h postoperatively is likely the result of residual spinal block. However, the significant pain relief experienced from hours 1 to 6 postoperatively could be attributed to the effects of the IT morphine in combination with the ketorolac. The opposite trends in pain scores (Fig. 2) could be associated with a new "unexpected pain" that patients in the IT morphine group experience with the complete return of sensation after the spinal block recedes.

Other data such as respiratory depression and surgical site infections were not significant. Fortunately, there were no incidences of DVT/PTE or dropped babies in either group. Another outcome studied and found to be nonsignificant was the time to removal of the Foley catheter.

Limitations of our study include its retrospective study design; we can only assume data analyzed were appropriately documented at the time of the encounter. However, given our large sample size, we believe there is validity in reporting our significant results. We would also like to discuss our decision to compare the spinal group to the general anesthesia group. We could have chosen to compare the IT morphine group to patients receiving spinal anesthesia then given an opioid IV PCA for postoperative pain control from an earlier year. However, we chose to compare the IT morphine group with the general anesthesia group receiving an opioid IV PCA because we implemented a standard protocol for the treatment of post-cesarean delivery pain control in 2014. This protocol includes the use of scheduled ketorolac in patients in whom it is not contraindicated. By comparing patients receiving the same protocol, this more closely represents our standard practice. Again, we recognize that early postoperative pain scores are better in the IT morphine group likely because of the effects of the spinal anesthesia.

In conclusion, the use of IT morphine has been shown to be a safe and effective means to treat post-cesarean delivery pain in the first 24 h after surgery [1, 2, 8–11]. Our aim was to show that the use of IT morphine when compared to opioid IV PCA was also cost effective. We found, when considering all aspects of patient care as it relates to pain control for the first 24 h after cesarean delivery, that there is a significant cost savings with the use of IT morphine when compared to an opioid IV PCA. Therefore, IT morphine not only provides adequate postoperative analgesia for patients undergoing cesarean delivery, it is also significantly less expensive.

Compliance with ethical standards

Sole funding for this project was provided through departmental funds and had no involvement in the study design, data collection, and analysis.

Conflict of interest The authors report no conflicts of interest.

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