The Safety And Efficacy of Intrathecal Opioid Analgesia for Acute Postoperative Pain: Seven Years' Experience with 5969 Surgical Patients at Indiana University Hospital

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To assess the efficacy of the analgesic technique and the incidence of complications, we prospectively evaluated patients who received intrathecal opioid analgesia (ITOA) to manage postsurgical pain. Daily quality assurance data were collected on the first postoperative day and tabulated for 5969 adult patients who had received ITOA for major urologic, orthopedic, general/vascular, thoracic, and nonobstetrical gynecologic surgery. A scale of 1–10 was used to quantify each patient's satisfaction with analgesia. The incidence of side effects, complications, and naloxone usage was also recorded and tabulated. The mean satisfaction score using a 10-point numeric rating scale was 8.51, with a score of 1 connoting "complete dissatisfaction" and 10 connoting "complete satisfaction." Side effects were minor and easily managed. Pruritus was the most common (37%). Respiratory depression was the least common (3%), easily detected by nursing observation, never life-threatening, and always responsive to treatment with naloxone. There were no deaths, nerve injuries, central nervous system infections, or naloxone-related complications. Postdural puncture headaches were rare (0.54%), as was the need for epidural blood patch (0.37%). **Implications:** Over a 7-yr period, intrathecal opioid analgesia was used to control acute postoperative pain on nearly 6000 patients, resulting in a high degree of patient satisfaction and a low incidence of side effects and complications.

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In 1979, Behar et al. (1) and Wang et al. (2) reported the first human use of epidural and intrathecal opioids to manage acute postoperative pain. Whereas epidural opioid analgesia has enjoyed widespread popularity, the intrathecal route is associated with inferior efficacy and safety, primarily because of a higher reported incidence of respiratory depression and somnolence (3). For example, Cousins (4), writing for the 1987 ASA refresher course manual regarding the topic of acute postoperative pain management, stated, "It would seem that the application of intrathecal opioids to routine clinical practice is at present strictly limited and possibly only justified when given concurrently with a local subarachnoid spinal anesthetics," and described epidural morphine as "most appropriate for acute pain." However, over the past decade, we have used intrathecal opioids extensively to provide postsurgical analgesia in nearly 6000 patients. This report summarizes our 7-yr experience with respect to efficacy and side effects.

Methods

For 7 yr (1990–1996), daily quality assurance data were collected and tabulated on the first postoperative day for 5969 adult (>18 yr old) male and female patients who, after giving written, informed consent, had received intrathecal opioid analgesia (ITOA) for major urologic (26%), orthopedic (17%), general/vascular (23%), thoracic (11%), and nonobstetrical gynecologic (23%) surgery (Table 1). Exclusion criteria for receiving ITOA were local infection (administration site), systemic infection, coagulopathy, excessive intraoperative bleeding, hypovolemia, metastatic disease of the vertebral column, allergy to any of the intrathecal medications, a history of continuing drug-seeking behavior, sleep apnea syndrome, or a history of postdural puncture headache (PDPH) or frequent headaches of any type.

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Table 1. Distribution of Patients Receiving ITOA

Urologic surgery (26% of patients)
Nephrectomy
Retroperitoneal lymph node dissection
Cystectomy with urinary reservoir
Cystectomy with ileal loop
Helmstein procedures
Radical prostatectomy
Transurethral resection of the prostate
Orthopedic surgery (17% of patients)
Total hip arthroplasty
Total knee arthroplasty
Major lower extremity resection for tumor
Repair of hip fracture
General and vascular surgery (23% of patients)
Pancreatic resection
Colectomy
Hiatal hernia repair
Cholecystectomy
Abdominal aortic aneurysms
Aortobifemoral bypass grafting
Redo herniorrhaphy
Adrenalectomy
Tumor debulking
Thoracic surgery (11% of patients)
Thoracotomy
Pneumonectomy
Lobectomy
Wedge resection
Pleurodesis
Gynecologic surgery (23% of patients)
Radical hysterectomy
Total abdominal hysterectomy
Vaginal hysterectomy
Pelvic exploratory laparotomy
Pelvic exenteration
Radical vulvectomy
Pelvic tumor debulking

ITOA = intrathecal opioid analgesia.

Table 2. Intrathecal Morphine: Typical Dosing Guidelines[a]

TURP, vaginal hysterectomy: 0.2–0.3 mg
Hip and knee surgery: 0.4–0.5 mg
Lower abdominal surgery (e.g., hysterectomy): 0.4–0.5 mg
Upper abdominal surgery (e.g., Whipple): 0.5–0.6 mg
Nephrectomy: 0.6–0.65 mg
Retroperitoneal lymph node dissection: 0.65–0.75 mg
Abdominal aortic aneurysm, thoracotomy: 0.65–0.8 mg

The 1% of patients receiving >25 μg of fentanyl underwent upper abdominal or thoracic procedures.

Morphine doses were established for our adult patients primarily on the basis of patient stature (average, above average, below average) and the level of surgery. Doses were routinely reduced by 0.1 mg for elderly (>65 yr old) or debilitated patients and routinely increased by 0.1 mg for extremely tall patients.

TURP = transurethral resection of prostate.

[a] Doses previously established and published by our institution (38).

Preservative-free morphine (0.2–0.8 mg) was administered by the intrathecal route to all patients using dosing variables established at and published by our institution (Table 2). Of the patients, 74% received a combination of morphine plus fentanyl (99% received 25 μg; only 1% received either 37.5 or 50 μg) and bupivacaine (3.75 mg). The remainder received morphine plus fentanyl (23%), morphine alone (1.5%), or morphine as part of a standard spinal anesthetic (1.5%).

Most patients (98%) received ITOA at the end of surgery while still anesthetized and just before awakening. With the assistance of operating room personnel, the patient was carefully placed in a lateral decubitus and knee-chest position. After sterile preparation and draping, intrathecal medications were administered using the midline approach at the L3-4 or L4-5 lumbar interspace with a 22- or 25-gauge Quincke type needle. Positive aspiration of clear cerebrospinal fluid before and after injection was used to confirm correct needle placement. Patients were then returned to the supine position to awaken from anesthesia.

After discharge from the postanesthesia care unit, reduced-dose morphine (1–2 mg every 20 min to a total of 10 mg/4 h) or meperidine (10 mg every 20 min to a total of 100 mg/4 h) patient-controlled analgesia (PCA) was made available for the first 15 h after surgery in the event of any breakthrough pain. Nurses were instructed to contact a member of the acute pain service team if analgesia was felt to be inadequate. The following day, the PCA dosage was increased to a standard dose by halving the dosing interval and doubling the total dose.

Patients were cared for in all hospital locations (wards and intensive care units [ICUs]). Most patients were transferred to regular ward beds after surgery. Only those believed to be at an overall higher risk of developing respiratory depression or other complications (e.g., advanced age [>70 yr old], chronically debilitated, poor preoperative pulmonary function, major thoracic or aortic surgery) were routinely sent to the ICU, which provided an added measure of vigilance. Patients were not assigned to ward versus ICU beds after surgery based on the use of intrathecal analgesia. Nursing personnel followed standardized acute pain service orders that mandated hourly ventilatory evaluation for a full 24 h after surgery and that allowed them to intervene with treatment for any side effects. Full-time, in-house anesthesia coverage was available to manage problems related to spinal opioid use, and the nursing staff was encouraged to notify the acute pain service when necessary.

On the day after surgery, a physician member of the acute pain service evaluated patients to assess analgesia and to record side effects and complications. Data were recorded on preprinted 5 × 7-in. cards used for the service's daily quality assurance program. Patients were asked to quantify their satisfaction with their analgesia using a numeric rating scale (NRS) (5) ranging from 1 to

Table 3. Results: Satisfaction Scores and Incidence of Side Effects[a]

Scores	
Data collection rate	95.6%
NRS scores (scale of 1–10)	8.51
Side effects/complications	
Pruritus	37%
Nausea/vomiting	25%
Respiratory depression[b]	3.0%
Postdural puncture headache	0.54%
Epidural blood patch for postdural puncture headache	0.37%
Patient-controlled analgesia usage complications	0
Cerebrospinal fluid infections	0
Respiratory failure requiring intubation	0
Life-threatening respiratory failure	0
Nerve injury	0
Mortality	0
Naloxone usage complications	0

NRS = numeric rating scale.
[a] Incidence of urinary retention was excluded because it was artifactually low.
[b] Criteria defined in text.

10, with 1 connoting "complete dissatisfaction" and 10 connoting "complete satisfaction."

The incidence of specific spinal opioid side effects (e.g., pruritus, nausea/vomiting, respiratory depression, urinary retention) was also assessed by a resident or staff member of the acute pain service team. Pruritus, regardless of severity, was recorded whenever it was either clinically noticeable or when the patient complained. Nausea/vomiting was recorded whenever symptoms required treatment. Respiratory depression was defined as an increasing $Paco_2$ >50 mm Hg and/or a respiratory rate <8 breaths/min. Recording of urinary retention was unreliable, as many patients routinely received indwelling Foley catheters at the time of surgery. Also recorded were any complications related to the subarachnoid administration of drugs (e.g., nerve injury, infection, PDPH, and the need for epidural blood patch).

Results

Data for 5705 of 5969 patients receiving ITOA (95.6%) were tabulated and analyzed with respect to satisfaction, the incidence of side effects, and the occurrence of any other significant complications (Table 3). Although all patients were appropriately observed by the acute pain service staff, 264 had either incomplete data or lost data cards. The mean NRS score for analgesic satisfaction was 8.51.

The most frequent side effect was pruritus, which occurred in 37% of the patients and represented the entire range of severity (i.e., from mild to severe). Symptoms, however, were easily managed with conventional therapy using diphenhydramine. Rarely, when symptoms did not respond to this treatment, a naloxone infusion (1.6 mg in 250 mL of isotonic sodium chloride solution infused at 30–50 mL/h for 8 h) was uniformly effective without affecting the quality of analgesia. Nausea with or without emesis occurred in 25% of patients. Symptoms were easily managed with conventional antiemetic therapy (promethazine or droperidol).

The incidence of respiratory depression was 3%. All cases were easily detected by routine nursing observation, and patients readily responded to naloxone therapy. There were no instances of respiratory arrest, and none of the patients required emergent endotracheal intubation. Naloxone infusions, when used, were usually administered within the first 3 h after surgery. The reported frequency of urinary retention (1.8%) is undoubtedly invalid and artifactually low, because many patients routinely received indwelling urinary catheters and, as such, has been excluded from Table 3. All cases of urinary retention were managed exclusively by catheterization.

There were no cases of ITOA-related mortality, nerve injury (although most patients received ITOA while asleep), or central nervous system infection, and there were no complications related to naloxone use. There were no manifestations of parenteral opioid overdose in patients using a reduced dose morphine or meperidine PCA within 24 h of receiving intrathecal opioids. PDPHs were rare (31 of 5705; 0.54%), as was the need for epidural blood patch (21 of 5969; 0.37%). The acute pain service made no attempt to correlate needle size to the occurrence of headache because, early in our program, headache seemed most likely when needle placement was protracted and difficult or when performed by a junior resident.

Discussion

In contrast to epidural analgesia, the management of postsurgical pain by administering a single dose of intrathecal opioid has failed to gain widespread popularity. This largely results from the inherent inability to reinforce the dose and to extend the duration of analgesia, as well as a widespread perception that this route is potentially more hazardous.

Early reports of intrathecal opioid usage seemed both promising and discouraging. For example, Wang et al.'s (2) first administration of 0.5- and 1.0-mg doses of intrathecal morphine to postsurgical cancer patients resulted in 15–22 h of analgesia without respiratory depression or somnolence. However, others reported an unacceptably high frequency of delayed respiratory depression, although the morphine doses used were extremely large (2–15 mg) (6–13). Subsequently, small or "mini-dose" morphine (<1.0 mg) was reported to be effective for managing acute postoperative pain after a variety of surgeries and to do so

without any evidence of respiratory depression, thus implying that the earlier reported complications were more likely related to the use of large doses than to the route of administration (14–21).

In 1989, Stoelting (22) discussed some of the specific advantages of ITOA and encouraged the anesthesia community to consider this approach as the "preferable" route of neuroaxial opioid administration. These advantages included the technical ease of administration, the simplicity of postoperative management, and the rapid onset of action related to the immediate availability of opioid in the cerebrospinal fluid for binding to dorsal horn receptors.

In 1994, the *Anesthesia Patient Safety Foundation Newsletter* published new guidelines describing the components of a quality assurance model from Arizona. In this newsletter, Blitt et al. (23) listed the "avoidance of subarachnoid opiates" as a strategy to improve perioperative safety. Responding in a letter to the editor, Abouleish (24) challenged these guidelines as being unsubstantiated by the scientific evidence, and warned of the legal consequences of making avoidance the standard of care. Our data, which document experience with a large series of patients over an extended time, suggest that intrathecal opioids can be used safely in a setting similar to that of epidural opioids.

The most feared complication of spinal opioids is that of respiratory depression. We believe that our incidence of 3% is representative of potential rather than true respiratory depression because our treatment guidelines encourage early preemptive intervention. All patients responded to a naloxone infusion without reversing analgesia. There were no respiratory catastrophes, deaths, or patients who required emergent intubation.

The incidence of pruritus (37%) and nausea/vomiting (25%), representing the complete spectrum of symptoms with respect to severity, occurred at a frequency not unlike that reported for parenteral and epidural opioids (25–29). These side effects were managed using traditional interventions (i.e., diphenhydramine, promethazine, droperidol).

There is no clear evidence that intrathecal morphine confers any specific preventative protection against the development of PDPH (30), although the addition of intrathecal fentanyl to hyperbaric bupivacaine was reported to be associated with a lower incidence in a uncontrolled and retrospective study.[1] In our series, the incidence of PDPH and that of patients subsequently requiring an epidural blood patch was remarkably low and is consistent with data from another large series of consecutive spinal anesthetics (32). Selection criteria may have influenced our experience because ITOA was not offered to those with a history of frequent headaches. Additionally, most postoperative patients remain supine and well hydrated after major surgery. Our staff overwhelmingly use the midline approach and the Quincke needles (25-gauge for those <60 yr old and 22-gauge for those >60 yr old) that are included our spinal trays, and PDPH has not been a significant problem.

Table 4. Comparative Costs of ITOA Versus Continuous Epidural Analgesia[a]

	Spinal	Epidural
Tray	$44.83	$96.91
Infusion pump	None	$42.00/day
Intraspinal drug		
Morphine cost (ampule)	$5.21	$5.21
Fentanyl cost (ampule)	$4.25	$4.25
Morphine infusion cost	None	$23.50/day
Total costs[b]	$54.29	$171.87

ITOA = intrathecal opioid analgesia (requires a standard spinal tray).
[a] Excludes differences in professional fees for administration and follow-up.
[b] One-day management (based on 1996 pricing at our institution).

One benefit of the intrathecal route is a reduction in costs. Based on the prevailing charges during 1996 at our institution, intrathecal opioids cost less than one third as much as epidural opioids (Table 4). Epidural analgesia requires a more expensive administration tray and incurs the added expenses associated with infusion (drug costs, infusion pumps, delivery tubing, professional fees, follow-up care). Because the planned use of intrathecal analgesia did not determine where the patients were sent after surgery (ward versus ICU), costs related to the location of in-patient care should not have been affected. However, in practices in which the use of neuroaxial analgesia does affect the patient's postoperative site of hospitalization, the potential cost-savings from using the intrathecal route would not offset the added expenses associated with ICU observation. There is no single opioid available for intrathecal administration that can afford both immediate and prolonged analgesia. Combining fentanyl (lipid-soluble, quick onset) and preservative-free morphine (water-soluble, long duration) with small-dose bupivacaine synergistically confers the benefits of both rapid and sustained analgesia, and has become a common practice for our service (33–38).

The co-administration of parenteral opioids concomitantly with spinal opioids has long been regarded as a significant risk factor for the development of respiratory depression (39). However, we routinely made a reduced-dose PCA unit available to our patients during the first 24 h after surgery, and we have done so without incurring respiratory depression. Additionally, PCA therapy was continuous after the beneficial effects of intrathecal analgesia wore off. Judicious parenteral supplementation seems to be a safe

[1] Johnson MD, Hertwig L, Vehring PH, Datta S. Intrathecal fentanyl may reduce the incidence of spinal headache [abstract]. Anesthesiology 1989;71:A911.

and reasonable practice that can enhance overall patient acceptance of spinal opioid analgesia.

It is important to have an educated and dedicated nursing staff who are trained in the use of standardized acute pain service orders and can intervene with treatment (40). Monitoring all patients for potential side effects and establishing the availability of full-time physician coverage are crucial to ensuring patient safety. Anesthesia staff should respond to all nursing concerns in a rapid, reasonable, and credible manner so as not to discourage this necessary communication or alienate this essential link to the patient. Indeed, this requires a willingness to adopt appropriate intervention policies that are committed to the possibility of erring on the side of overtreatment.

In a large continuous series conducted over more than half a decade, intrathecal opioids provided highly satisfactory postoperative analgesia and were rated by patients as being >85% effective in controlling acute pain during the first 24 h after surgery. A single dose administered at the time of surgery was simple to perform and manage, rendered good neuroaxial analgesia during the first postoperative day, and served as an effective therapeutic bridge until the patient could use PCA or oral analgesia more effectively. The incidence and severity of side effects were acceptable and easily controlled, and there were no serious or life-threatening complications. When strict protocols for serial patient assessment are observed and response to side effects is timely, patients can be managed safely on regular hospital wards. Small-dose ITOA is a safe, effective, and relatively inexpensive modality for the routine management of acute postoperative pain after a variety of major surgical procedures.

KHG respectfully dedicates this article to former mentor, Dr. Nicholas M. Greene, whose professional preeminence as a teacher and scholar has benefited hundreds of residents, thousands of clinicians, and millions of patients. To all of his grateful students, he is and will remain an inspiration and visionary in the field of anesthesia.

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