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Original article

Intrathecal morphine injections in lumbar fusion surgery: case-control study

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Abstract

Introduction: Intrathecal morphine (ITM) is a well-known and extensively used method for analgesia in various surgical fields; however, its relevance in spine surgery is debated given the conflicting results in the literature. The aim of this study was to investigate the opioid-sparing effect of ITM after lumbar fusion.

Methods: This retrospective study involves two consecutive series of patients undergoing posterior lumbar fusion. The first cohort (Control group, n = 30) received the standard analgesia protocol while the second cohort (ITM Group, n = 30) had the standard protocol supplemented with ITM (100 µg of morphine hydrochloride). Morphine consumption, pain assessment (VAS), specific complications and postoperative recovery data were collected.

Results: Consumption of morphine at 24 hours and 48 hours postoperatively was lower in the ITM group than the control group ($p < 0.001$ and $p = 0.004$). The pattern was similar for pain on VAS at H6, H24 and H36 ($p = 0.001$; $p = 0.003$ and $p = 0.01$). The patients in the ITM group were able to get out of bed faster than the controls (1.13 days vs 1.83 days, $p = 0.002$) and the discharge was earlier in the ITM group (5.1 days vs. 6.2 days, $p = 0.002$). There was no difference in morphine-specific complications between the two groups.

Conclusion: Adding ITM to the analgesia protocol for lumbar fusion provides better management of postoperative pain, without increasing early complications, and it accelerates the recovery process after surgery.

Level of evidence: IV

Keywords: intrathecal morphine; spine; lumbar fusion; pain

Introduction

Lumbar fusion is reputed to cause significant postoperative pain, which impacts how quickly patients recover after the surgery. Morphine and its derivative are often used to prevent and treat pain, although these products have side effects that can negatively impact recovery after surgery (1).

Postoperative analgesia appears to be one of the key modifiable factors that can reduce the morbidity associated with these complex spine surgeries and accelerate the recovery after surgery (2). One widely used method is local infiltration analgesia (3,4).

Intrathecal morphine (ITM) injections were first described in 1979 (5). Since this first use, several studies have documented and popularized the use of ITM, especially in the context of gastrointestinal and gynecological surgical procedures (6). But various questions remain about ITM, in part because of the complications that have been reported (respiratory depression, pruritis, nausea/vomiting) and because of questions about the optimal dose and duration of analgesia.

The efficacy of ITM in the orthopedic and spine surgery context has been controversial (7–9). ITM for spine surgery is an attractive method because of the easy access to the thecal sac and its reliability (10–12). It is now thought that multimodal postoperative analgesia is one of the keys for enhanced recovery after surgery (ERAS) (13). It is especially widespread and featured in the media for knee, hip and shoulder surgery.

It is in this context that we carried out a study in our surgery unit to shed light on the analgesic role of ITM within the multimodal analgesia protocol for spine surgery. We hypothesized that adding ITM to a multimodal analgesia protocol for spine surgery will improve the management of postoperative pain and help patients recover faster after surgery.

Methods

Study overview

We carried out a retrospective study in our surgery unit of 60 consecutive patients operated between January 2018 and May 2019. There were two consecutive cohorts of patients. The first set of 30 patients received our facility's current anesthesia protocol, without ITM (control group). The second set of 30 patients received the same anesthesia protocol supplemented with ITM (ITM group). All patients were operated by the same surgeon.

Inclusion criteria

The patients included in the study underwent primary lumbar spine surgery, with or without laminectomy; posterolateral fusion involved an anterior interbody cage at L4L5, L5S1 or L4S1. All the intervertebral cages were inserted through the transforaminal route (TLIF). These surgical procedures were done through a posterior approach. Any dural breaches were sutured directly using a running Prolene 5.0 © suture and glued fascia patch. The patient was required to remain in dorsal decubitus for 24 hours.

Anesthesia and analgesia protocol

All patients underwent the same anesthesia protocol consisting of general anesthesia and administration of the following agents: Propofol 2-3 mg/kg; Midazolam; ketamine; Sufentanil 1µg/kg; Cisatracurium 0.1–0.4 mg/kg; Sevoflurane 1 MAC=2.5%; Dexamethasone 8 mg IV (single dose); Paracetamol 1 g; Nefopam 20 mg; Profenid 100 mg (if not contraindicated); tranexamic acid (if not contraindicated).

All patients received a subfascial injection of 20 ml Ropivacaine 7.5% (or 150 mg) before the incision was closed. The patients were sent to the post-anesthesia care unit (PACU) immediately the surgery. The postoperative analgesic protocol was similar with step 1 analgesics (1 g paracetamol, 3–4 times per day, depending on age), step 2 (Nefopam, 20 mg, 6x per day) and step 3 (intravenous morphine by PCA pump if pain > 5 on VAS in PACU, otherwise per os) along with a 48-hour course of nonsteroidal anti-inflammatories (Profenid 50 mg, 3x per day, if not contraindicated).

Intrathecal injection procedure

Patients in the ITM group received a 100-µg injection of morphine hydrochloride diluted in 2 ml of injectable saline. This ITM was injected under the released level or in the L4L5 space when the canal was not released. The injection was done with an 18G needle.

Data collection

The following data were collected from medical and anesthesia records:

- Demographics: sex, height, weight, age at surgery
- Surgery-related: operative time, level operated and type of surgery, complications related to ITM (dural breach, unable to carry out)
- Postoperative: pain on VAS at H6, H24, H36 and H48, opioid analgesic consumption in IV morphine (mg) equivalents at H24 and H48, date of first standing, morphine-related complications (postoperative nausea and vomiting, pruritis, respiratory depression, urinary retention, confusion/disorientation), length of hospital stay, destination after PACU discharge.

Statistical analysis

The statistical analysis was done using Epi-Info software. Student's *t* test was done for variables that were normally distributed and a Mann-Whitney test with those that were not. Significance threshold was set at 5%. A repeated measures ANOVA was applied to the pain on VAS values and opioid consumption.

Results

The two groups were comparable in their demographics, operative time and laminectomy (Table 1). The breakdown of American Society of Anesthesiologists (ASA) grades was similar between the control and ITM groups: ASA 1 – 22 vs 23; ASA 2 – 7 vs 6; ASA 3 – 1 vs 1).

All the patients were transferred to the elective surgery ward after discharge from the PACU. None of the patients required intensive care during their hospital stay.

The pain on VAS was significantly lower at H6, H24 and H36 in the ITM group than the control group (H6: $F(1,59) = 7.19$; $p = 0.01$ / H24: $F(1,59) = 9.31$; $p = 0.003$ / H36: $F(1,59) = 6.19$; $p = 0.01$) although there were no differences at H48 ($F(1,59) = 0.5$; $p = 0.48$). Similarly, the opioid consumption in the ITM group was significantly lower than in the control group at H24 and H48 ($F(1,59) = 33.34$; $p < 0.0001$ and $F(1,59) = 9.1$; $p = 0.004$) (Table 2).

Upon exiting the PACU, 48% of patients in the control group used a morphine pump versus 47% in the ITM group ($p = 0.21$). There was a rebound effect in the ITM group; on the 2nd postoperative day, the patients consumed significantly more morphine than the patients in the control group (Δ morphine between H24 and H48 (mg): 8.3 ± 7.3 (0; 31) vs 11.8 ± 5.3 (3; 24); $p = 0.02$)

Patients in the ITM group were able to stand up on average on postoperative day 1.13 ± 1 versus 1.83 ± 0.9 days in the control group, which was statistically significant ($p = 0.002$). Discharge was also significantly earlier in the ITM group than the control group by about 1 day (5.1 ± 0.9 days vs 6.2 ± 1.8 days; $p = 0.002$).

There were no differences in morphine-related complications between the two groups (Table 3). There were no occurrences of dural breach during the ITM injection or instances where the injection was not technically feasible.

Discussion

Our study confirms the effectiveness of low-dose ITM in the context of spine surgery. ITM improves the management of early postoperative pain, allowing patients to get up earlier and be discharged earlier. This procedure is clearly defined and its mechanism of action has been described in animal studies (14).

ERAS was initially developed in the 1990 by Professor Kehlet and his team. It is defined as a multidisciplinary approach to the patient's overall care during the peri-operative period aiming to quickly restore the patient's prior physical and mental capacities (2,15,16). Every surgery has this objective. According to the French National Authority for Health (HAS)(13), for orthopedic surgery procedures, ERAS is mainly recommended for total joint replacement of the knee and hip. By definition, its indications can be expanded, including to spine surgery. During the postoperative period, ERAS procedures are based on optimal multimodal analgesia, resuming eating quickly and early mobilization of patients.

In their 2019 report, the French Anesthesia and Intensive Care Society (SFAR) (17) and the French Society of Orthopedic and Traumatology Surgery (SOFECOT) gave a grade of 2+ (strong evidence) for its postoperative opioid-sparing effects (18). This opioid-sparing effect helps to reduce the length of hospital stay and to prevent serious complications, particularly gastrointestinal and respiratory ones. And according to SFAR recommendations, this opioid-sparing effect also helps to reduce opioid-induced hyperalgesia and to limit complications. Opioids are also said to modify immune function by interacting with natural killer cells (19).

One of the controversies surrounding ITM is the dose. The dose requires close postoperative monitoring. Complications vary depending on the dose. France *et al* (10) reported that ITM was effective in the context of lumbar spine surgery. Their protocol adjusted the dose to the patient's weight (mean dose of 900 µg) with Naloxone used in 7% of patients and a rebound effect after 24 hours. Ziegeler *et al* (20) established the efficacy of a 400 µg dose in a study of 46 patients, Technanivate *et al* (11) validated a dose of 300 µg, while Vaquerizo-Garcia *et al* (21) used a dose of 250 µg. Dhaliwal *et al* (22) recently validated a dose of 200 µg. Our study provides data on the effectiveness and safety of a 100 µg ITM dose. No opioid antagonists were required, and the complication rate was similar to the control group.

In a recent meta-analysis, Pendi *et al* (23) concluded that ITM was effective in the first 24 hours postoperative despite a higher complication rate in the ITM group, although our study's findings were different. Our study only looked at the postoperative opioid consumption, pain level and complications. We had no information on patient-specific data. In a different meta-analysis, Musa *et al* found that ITM was effective up to 48 hours postoperative without increasing the morphine-related complication rate (24).

Based on these studies, it appears that a low dose of ITM greatly reduces the morphine-related complication rate and thus limits the probability the patient will require intensive care or continuous postoperative care. With the development of minimally invasive surgery, it is essential that patient safety and ERAS be the main objectives of our surgical and anesthetic procedures. In another meta-analysis, Phan *et al* (25) described a higher satisfaction rate after minimally invasive surgery than standard surgery, in part because of less pain in the minimally invasive procedures. Conversely, multimodal analgesia procedures in each study of the above meta-analysis were different or not disclosed, making it difficult to draw conclusions.

The limits of ITM use are clearly outlined by several published studies (26–28) in so-called “fragile” patients, such as patients with respiratory, liver or kidney failure, obstructive sleep apnea (OSA), ASA score of 3 or more, patients who have never taken opioids, who are obese (BMI above 35 kg/m²) or more than 70 years of age. These at-risk patients are contraindicated to ITM or require special monitoring such as pulse oximetry or close clinical monitoring in the recovery room or continuous care unit (17), with no real consensus about true contraindications or simply precautions to take.

ITM is only one option for analgesia among a range of procedures that have been proven. Chen *et al* (29) showed that ultrasound-guided lateral muscular interfascial block was safe and effective, with significant reduction of pain on VAS up to H36. Ueshima *et al* (30) had similar findings up to H24. The meta-analysis done by Perera *et al* (31) concluded that local anesthetic infiltration was effective at controlling postoperative pain after lumbar fusion. The meta-analysis by Guay *et al* (32) on epidural analgesia found only a low to moderate level of evidence on its ability to reduce postoperative pain.

Limitations

Our study has its limitations, with the primary one being the retrospective design. Also, we focused on short constructs, thus a surgical procedure with lower complication risk than long constructs and more complex transpedicular osteotomy procedures. We did not have any complications related to the injection itself, although this possibility has been documented (20,22) and there are questions about how to best address it. Ziegeler *et al* (20) reported the post-injection effects and found no significant differences on any symptoms. Dhaliwal *et al* (22) found a non-significant difference in the dural breach rate between the two groups ($p = 0.67$) and did not attribute any to the injection itself. Thus, a dural breach caused by the injection itself appears to be very rare. It seems appropriate to treat these dural breaches in the same manner as any other breach, according to surgeon preferences.

Conclusion

Based on our study’s findings, ITM is an effective analgesia method for managing postoperative pain after spine surgery. In our study, this method and dose (100 ug) did not lead to more complications than in the control group. The novelty of this study is its dose of 0.1 mg morphine hydrochloride, which is lower than in other published studies. When there is no dural breach, we do not recommend strict dorsal decubitus postoperatively.

Conflict of interest: none

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Author contributions:

Anais De Bie: Data collection, writing of article

Renaud Siboni: Critical review of article

Mohammed Smati: Creation of anesthesia protocol, anesthesia of patients included in the study

Xavier Ohl: Study sponsor, review and correction of final version of article

Simon Bredin: Primary investigator, surgery on all patients, correction of article

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Table 1: Patient demographics and operative time

	Control group	ITM group	<i>p</i> value
Age (years)	62.3 ± 12 (42; 84)	63 ± 9.5 (45; 81)	0.4
Sex ratio (M/F)	1/1	2/3	0.22
BMI (kg/m²)	28.4 ± 6.8 (15.9; 40.1)	26.9 ± 6.7 (16.7; 38.5)	0.19
Operative time (min)	126.4 ± 37.5 (76; 191)	129.6 ± 29.2 (75; 184)	0.36
Laminectomy (%)	56.7%	52.9%	0.39

Values are mean ± standard deviation (min; max). BMI: Body mass index

Table 2: Pain on VAS and morphine consumption after surgery

	Control group	ITM group	<i>p</i> value
Pain on VAS H6 (cm)	6.3 ± 1.2 (5; 8)	5.8 ± 1.8 (3; 8)	0.01
Pain on VAS H24 (cm)	5.4 ± 1.8 (3; 8)	4.2 ± 1.7 (1; 6)	0.003
Pain on VAS H36 (cm)	4.6 ± 1.2 (2; 7)	3.6 ± 1.7 (1; 6)	0.01
Pain on VAS H48 (cm)	3.7 ± 1.4 (2; 6)	3.4 ± 1.9 (1; 6)	0.48
Morphine consumption H24 (mg)	28 ± 4.9 (19; 36)	20.4 ± 5.3 (12; 32)	<0.001
Morphine consumption H48 (mg)	35.4 ± 5 (28; 44)	30.8 ± 3.9 (21; 39)	0.004
Time to 1st morphine dose (min)	23.9 ± 11.4 (5; 44)	31.4 ± 10.5 (11; 45)	0.004

Values are mean ± standard deviation (min; max)

Table 3: Morphine-related complications

	Control group	ITM group	<i>p</i> value
Postop nausea or vomiting (n)	16	12	0.15
Respiratory depression (n)	0	0	
Urinary retention (n)	4	5	0.36
Pruritis (n)	9	9	0.28
Confusion/disorientation	5	4	0.32

Values given are the number of patients (30 patients per group)