

# Spinal Analgesia with Intrathecal Morphine versus Conventional Analgesia after Laparoscopic Colectomy: A Retrospective Cohort Study

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Abstract

Objective: Postoperative pain (POP) following abdominal surgery can vary from a few hours to several days. This acute, unrelieved pain can become chronic, requiring patients to take analgesics on an almost daily basis for comfort. Analgesia using general opioids has many side effects and intrathecal morphine is a good alternative. This study was conducted to evaluate the efficacy of intrathecal morphine (ITM) versus conventional analgesia in the management of postoperative pain in colectomy performed by laparoscopic surgery. Methods: Cohort study conducted at the Hôpital Nord in Marseille, from 01 January to 31 July 2021 in patients aged at least 18 years undergoing anaesthesia for scheduled colectomy by laparoscopic surgery. The primary endpoint was postoperative pain intensity and the secondary endpoints were morphine consumption, treatment side effects and length of hospital stay. Statistical analysis was performed using XLSTAT software. Results: We included 193 patients: 131 in the control group (conventional analgesia) and 62 in the ITM group. We observed: a significant decrease in pain (assessed by numerical scale) in favour of the ITM group in the post-anaesthetic care room, *i.e.* 3 (±4) vs 1 (±2), p < 0.0001 at H<sub>0</sub> and H<sub>2</sub>: 2 (±2) vs. 1 (±2); p < 0.0001 0.0001; and in the first 24 postoperative hours 5 (±3) vs. 2 (±3); p < 0.0001, a significant decrease in total morphine consumption at day zero in the ITM vs. control group (23 mg (±15) % vs. 2 mg (±5); p < 0.001), significantly greater morphine side effects in the control group (51% vs. 15%, p < 0.0001), a non-significant reduction in hospital length of stay in favour of the ITM group (8d (±6) vs. 6d (±4) days, p = 0.054). **Conclusion:** These results suggest that intrathecal morphine (ITM) in laparoscopic colectomy provides effective postoperative analgesia with low morphine consumption, and a reduction in morphine side-effects compared with conventional analgesia.

#### **Keywords**

Intrathecal Morphine, Colectomy, Laparoscopy, Conventional Analgesia

# **1. Introduction**

Postoperative pain (POP) following abdominal surgery can vary from a few hours to several days. This acute unrelieved pain can become chronic, requiring patients to take analgesics on an almost daily basis for comfort [1]. Postoperatively, more than two-thirds of patients report moderate to severe pain, but less than half of them report adequate pain relief. Many patients are even very dissatisfied with their pain management. This pain is correlated with increased morbidity and mortality, longer length of stay, delayed ambulation and regaining of autonomy, and a risk of pain becoming chronic [2].

The French Society of Anaesthesia and Critical Care (SFAR) recommends prescribing a strong opioid (morphine or oxycodone) systemically for severe postoperative pain, or if weaker analgesics are not strong enough to relieve patients [3]. However, the use of systemic morphine has many disadvantages (respiratory distress, paralytic ileus, pruritus, etc.) but also carries the risk of developing hyperalgesia and chronic post-surgical pain [3] [4].

Enhanced recovery after surgery (ERAS) programs have made morphine sparing one of their keystones, with the aim of limiting the use of systemic opioids. The aim is to limit the use of systemic opioids, through the use of co-analgesics and/or regional analgesia techniques (multimodal analgesia) [5] [6]. Morphine sparing reduces the length of hospital stay and helps prevent serious complications, particularly respiratory and digestive, such as paralytic ileus [7], as well as urinary retention, somnolence and postoperative delirium in the elderly [8].

Pain after major laparoscopic abdominal surgery is intense, but relatively short-lived compared with open surgery. It is a major component of the stress response, and if not adequately treated, can have adverse consequences, hence the importance of appropriate analgesia.

Numerous multimodal analgesia techniques have been developed, such as intravenous lidocaine [9] [10], abdominal trunk blocks [11] (ultrasound-guided or under direct laparoscopic guidance) or intraperitoneal injection of local

anesthetic [12]. These methods provide adequate postoperative analgesia, but often require systemic administration of morphine.

Epidural analgesia is recommended for laparotomy colonic surgery [5]. However, its use in laparoscopic surgery is associated with prolonged hospital stay due to delayed mobilization [13] [14].

Intrathecal morphine injection (ITM) appears to have a significant analgesic effect [15] and could be an interesting method in this type of surgery. Indeed, intrathecal morphine has limited systemic absorption due to its hydrophilic properties, and therefore a minor effect on intestinal motility, unlike intravenous morphine. In addition, the doses of morphine required for analgesia are lower with this technique.

Reported disadvantages of this technique include the risks associated with intrathecal injection, pruritus and delayed respiratory depression [16] [17]. However, when a low dose of morphine is used, there does not appear to be any more respiratory depression than with systemic opioids [18].

ITM therefore appears to be an attractive strategy for patients undergoing laparoscopic colonic resection. There are currently few studies evaluating ITM in major laparoscopic surgery. The aim of this study was to compare the efficacy of intrathecal morphine on postoperative pain after laparoscopic colectomy versus conventional analgesia at the Hôpital Nord in Marseille.

## 2. Methods

#### 2.1. Type, Scope and Period of Study

This is a historical, monocentric, observational cohort study conducted in the anaesthesia-intensive care and digestive surgery sector of Marseille's Hôpital Nord during the period from January 1<sup>er</sup> 2018 to August 30<sup>st</sup> 2021.

#### 2.2. Population, Sampling and Patients Selection

The population consisted of all adult patients who had undergone anaesthesia for laparoscopic colectomy in closed surgery. Sampling was based on an exhaustive registry with consecutive patient recruitment.

All patients aged 18 or over who underwent anaesthesia for laparoscopic colectomy in scheduled surgery during the study period were included in the study. Excluded were patients on long-term morphine or morphine derivatives therapy, patients with allergy to the products used, patients who required conversion to laparotomy, and patients whose records were missing important study variables.

#### 2.3. Data Collection

The data was collected from digitised patient records, and a data collection form was drafted for those listed. The cohort was made up of two groups: patients receiving intrathecal morphine preoperatively, *i.e.* intrathecal morphine injection for postoperative pain relief (ITM group), and patients receiving conventional

analgesia, *i.e.* all methods other than spinal analgesia for postoperative pain relief (control group).

Intrathecal morphine was performed with a morphine dose of 100-300  $\mu$ g preoperatively, just prior to anaesthetic induction. As the onset of action of intrathecal morphine is 2 - 4 hours, we added a faster-acting liposoluble opioid (Sufentanil) and an alpha-2 agonist (Clonidine) were added to the morphine dose to potentiate the analgesic effect and prolong the block duration. Dosages varied between 2.5 and 5  $\mu$ g for Sufentanil and 50 - 75  $\mu$ g for Clonidine.

Both groups followed the same anaesthetic protocol: anaesthetic induction with propofol, intraoperative analgesia with Sufentanil, prevention of hyperalgesia with Ketamine, curarization with Rocuronim or Cisatracurium, prevention of postoperative nausea and vomiting (PONV) with Dexamethasone and Droperidol, orotracheal intubation and maintenance of anaesthesia with propofol in intravenous anaesthesia with target concentration (IVAC).

Postoperative analgesia was administered thirty minutes before the end of surgery. The ITM group received Paracetamol and Nefopam for analgesia, while the control group received non-steroidal anti-inflammatory drugs (NSAIDs) and morphine (morphine, tramadol) in addition to the above-mentioned analgesics. The control group received a wall block, surgical infiltration of local anaesthetics or intravenous Xylocaine by electric syringe for postoperative analgesia.

Side effects were managed with Naloxone for respiratory distress, Ondasetron for PONV, antihistamines and Naloxone for pruritus, and urinary catheterization for urinary retention.

#### 2.4. Study Variables

Preoperative data collected were: age, sex, weight, height, body mass index, ASA class (American Society of Anaesthesiologists), indication for colectomy (underlying pathology) and comorbidities.

Intraoperative data included: performance of intrathecal morphine, analgesic wall block, infiltration of local anaesthetic into trocar holes by the surgeon, the use of intravenous lidocaine, management of general anaesthesia (strategy and drugs used, prevention of postoperative nausea vomiting (PONV), analgesia at the end of the procedure, intraoperative complications and type of colectomy.

The postoperative data were: postoperative pain (assessed by numerical scale: from zero to ten (with pain >3/10 requiring treatment) at  $H_0$  (30<sup>ième</sup>, and 60<sup>ième</sup>, 90<sup>ième</sup> minutes),  $H_2$ ,  $D_1$  to  $D_5$ , consumption of analgesics, particularly morphinics, side effects of analgesics, postoperative complications and length of stay in the post-anaesthetics care unit (PACU) and hospital.

## 2.5. Judging Criteria

The primary endpoint was the intensity (assessed by numerical scale) of postoperative pain at 0minutes, 30 minutes, 60 minutes, 90 minutes and 120 minutes from awakening, the numerical scale of maximum pain from  $D_0$  to  $D_5$ . Secondary endpoints were:

- Morphine consumption before PACU discharge and from D<sub>1</sub> to D<sub>5</sub>;
- Morphine side effects (understood as adverse reactions that may occur after intrathecal morphine: respiratory depression, PONV, acute urine retention, pruritus, complications of spinal analgesia and failure to perform the spinal analgesia technique);
- Length of hospital stay.

#### 2.6. Statistical Analysis

Statistical analysis were performed using XLSTAT software (V 2021.3.1, Addinsoft, Paris France). Results are expressed in terms of mean  $\pm$  standard deviation (SD) for quantitative variables, or frequency (percentage) for qualitative variables. Associations between variables were assessed by the  $\chi^2$  test or Fisher exact test for qualitative variables, and by a Mann Whitney test for quantitative variables. A signifiance level of 5% was used.

#### 2.7. Ethical and Regulatory Aspects

The agreement of the head of department was obtained. Patient data were collected and processed in accordance with the General Data Protection Regulation (GDPR). Data collected as part of this study are registered in the GDPR/APHM register under number 2021-103. An advisory opinion from the Comité d'Éthique pour la Recherche en Réanimation (CERAR) indicated that the study did not raise any ethical issues and did not fall within the scope of the regulations governing research involving the human person (IRB 0010254-2021-119). We have no conflict of interest in this study.

## 3. Results

#### 3.1. Patient Flow Diagram

Figure 1 shows the patient flow diagram.

During this period, 286 patients were registered. Ninety-three were excluded: 14 for cancellation of surgery, 42 for conversion to laparotomy, 7 for long-term opioid treatment, 16 for missing data, 2 for extended resection to other organs and 2 for failure of spinal analgesia. The study thus included 193 patients: 131 in the control group and 62 in the intrathecal morphine group.

## **3.2. General Patient Characteristics**

**Table 1** shows the general characteristics of the patients.

The two groups were comparable in terms of socio-demographic characteristics. There was a higher proportion of ASA III patients in the control group (22% vs. 10%;  $p = 0.045^*$ ). Chronic inflammatory bowel disease and neoplastic pathologies accounted for the largest proportion of the cohort (90%). Right colectomy and coloproctectomy accounted for the major proportion of operative procedures.



Figure 1. Patient flow diagram.

#### 3.3. Anaesthetic Characteristics

 Table 2 shows anaesthetic characteristics.

Patients in the ITM group received ketamine more often intraoperatively (53% vs. 79%; p = 0.001\*) and tramadol more often postoperatively (29% vs. 50%; p = 0.006\*) than patients in the control group. Patients in the ITM group received significantly less morphine than patients in the control group (94% vs. 15%, p < 0.0001\*) and also less Paracetamol than patients in the control group (99% vs. 92%; p = 0.014\*). Consumption of Nefopam and non-steroidal anti-inflammatory drugs (NSAIDs) was comparable between the two groups. Patients in the ITM group received significantly fewer wall blocks (18% vs. 5%; p = 0.022\*) and intravenous Xylocaine (51% vs. 13%; p < 0.0001\*). Surgical infiltration rates were identical between the two groups. Patients in the ITM group received between 100 and 300 µg (mean 212.5 µg ± 73) of intrathecal morphine. Fifty or 80% had received Sufentanil [2.5 µg (n = 10), 5 µg (n = 40)] and 21 or 35% had received Clonidine [50 µg (n = 10), 75 µg (n = 11)].

Two patients (3.22%) failed spinal analgesia. We did not observe any other complications associated with the use of intrathecal morphine.

# 3.4. Postoperative Pain Assessment in the Post-Anaesthetic Care Unit (PACU)

 Table 3 shows the numerical scale of postoperative pain.

Postoperative pain assessed by numerical scale was significantly higher in the control group over the entire PACU stay ( $p < 0.0001^*$ ).

	Control group n = 131	ITM Group n = 62	Р
Male, n (%)	69 (53)	26 (42)	0.170
Female, n (%)	62 (47)	36 (58)	0.170
Age, year (±SD)	55 (±19)	52 (±17)	0.279
BMI, kg/m <sup>2</sup> (±SD)	25 (±5)	24 (±4)	0.362
ASA class, n (%)			
Ι	3 (2)	2 (3)	0.657
II	98 (75)	54 (87)	0.060
III	29 (22)	6 (10)	0.045*
IV	1 (1)	0 (0)	1
Underlying pathology, n (%)			
CIBD	57 (44)	32 (52)	0.345
Neoplasia	51 (39)	25 (40)	0.876
Diverticulosis	14 (11)	1 (2)	0.040*
Endometriosis	4 (3)	4 (6)	0.272
Polyposis	4 (3)	0 (0)	0.307
Cystic pneumatosis	1 (1)	0 (0)	1
Surgical procedures, n (%)			
Left angular colectomy	5 (4)	2 (3)	1
Right colectomy	35 (27)	10 (16)	0.144
Left colectomy	14 (11)	4 (6)	0.434
Subtotal colectomy	18 (14)	7 (11)	0.819
Total colectomy	5 (4)	0 (0)	0.178
Coloprotectomy	22 (17)	23 (37)	0.003*
Ileo-caecal resection	18 (14)	11 (18)	0.519
Sigmoidectomy	14 (11)	5 (8)	0.796

Table 1. General patient characteristics.

Legend: SD = standard deviation, ITM = Intrathecal Morphine, BMI = body mass index, ASA = American Society of Anesthesiologists, CIBD: chronic inflammatory bowel disease.

# 3.5. Morphine Consumption at Day Zero

Figure 2 shows morphine consumption on day zero.

There was a significant reduction in total morphine consumption at day zero in the ITM group compared with the control group (23 mg (±15) % *vs.* 2 mg (±5);  $p < 0.001^*$ ).

Table 2. Anaesthetic characteristics.

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	Control group n = 131	ITM Group n = 62	Р
Intra- and postoperative analgesia, n (%)			
Paracetamol	130 (99)	57 (92)	0.014*
NSAIDs	56 (43)	17 (27)	0.560
Nefopam	101 (77)	41 (66)	0.118
Tramadol	38 (29)	31 (50)	0.006*
Ketamine	70 (53)	49 (79)	0.001*
Systemic morphine	123 (94)	9 (15)	<0.0001*
RA, n (%)			
Wall block	23 (18)	3 (5)	0.022*
Surgical infiltration	24 (18)	5 (8)	0.084
Xylocaine IVES	67 (51)	10 (13)	<0.0001*
Dose: intrathecal products			
Morphine (average)		$212.5~\mu g\pm73$	
Sufentanil (2.5 µg)		10	
Sufentanil (5 µg)		40	
Clonidine (50 µg)		10	
Clonidine (75 µg)		11	

Legend: ITM = Intrathecal morphine, IVES = intravenous electric syringe, RA = regional anaesthesia, NSAID = non-steroidal anti-inflammatory drug.

## Table 3. Immediate postoperative pain in the PACU.

	Control group n = 131	ITM Group n = 62	Р
Numerical scale at 0 minutes (±SD)	3 (± 4)	1 (± 2)	<0.0001*
Numerical scale at 30 minutes (±SD)	4 (± 3)	1 (± 2)	<0.0001*
Numerical scale at 60 minutes (±SD)	4 (± 3)	1 (± 2)	<0.0001*
Numerical scale at 90 minutes (±SD)	3 (± 2)	1 (± 2)	<0.0001*
Numerical scale at 120 minutes (±SD)	2 (± 2)	1 (± 2)	<0.0001*

Legend: ITM = Intrathecal morphine, SD = standard deviation.



Figure 2. Morphine consumption on the day of surgery.

# 3.6. Judging Criteria

# 3.6.1. Primary Endpoint

Table 4 shows the maximum intensity (assessed by numerical scale) of postoperative pain.

Pain assessment by numerical scale showed that pain was significantly less intense in the ITM group over the first 24 hours. This difference became less significant on Day 1, levelling off on subsequent days.

Table 4. Maximum intensity (as assessed by numerical scale) of postoperative pain.

	Control group n = 131	ITM Group n = 62	Р
Maximal numerical scale J0 (±SD)	5 (±3)	2 (±3)	<0.0001*
Maximal numerical scale J1 (±SD)	2 (±2)	3 (±2)	0.701
Maximal numerical scale J2 (±SD)	2 (±2)	2 (±2)	0.687
Maximal numerical scale J3 (±SD)	1 (±2)	2 (±3)	0.784
Maximal numerical scale J4 (±SD)	2 (±3)	1 (±2)	0.961
Maximal numerical scale J5 (±SD)	1 (±2)	2 (±2)	0.091

Legend: *ITM* = *Intrathecal morphine*, SD = standard deviation, D = day.

#### 3.6.2. Secondary Endpoints

# 1) Morphine consumption

 Table 5 shows the cumulative doses of morphine consumed postoperatively.

Morphine consumption was significantly lower in the PACU discharge in the ITM group (11 mg ( $\pm 8$ ) *vs.* 1 mg ( $\pm 2$ ) compared at the control group p < 0.0001<sup>\*</sup>.

Morphine consumption was significantly lower on D0 in the ITM group (11 mg ( $\pm 8$ ) vs. 1 mg ( $\pm 3$ ); p < 0.0001<sup>\*</sup>), but decreased over the days until reaching a statistically null difference on D5 (p > 0.05).

The cumulative total dose between D0 and D5 postoperatively was significantly reduced between the ITM group compared at the control group (31 mg ( $\pm$ 24) vs. 6 mg ( $\pm$ 12); p < 0.0001\*).

	Control group n = 131	ITM Group n = 62	Р
Day of intervention (mg ± SD)	23 (±15)	2 (±5)	<0.0001*
At PACU output (mg ± SD)	11 (±8)	1 (±2)	<0.0001*
D0 (mg ± SD)	11 (±8)	1 (±3)	<0.0001*
D1 (mg ± SD)	3 (±5)	1 (±2)	0.072
D2 (mg ± SD)	2 (±4)	1 (±3)	0.307
D3 (mg ± SD)	2 (±3)	1 (±3)	0.149
D4 (mg ± SD)	1 (±3)	0.6 (±2)	0.290
D5 (mg ± SD)	0.7 (±2)	0.3 (±1)	0.326
Total cumulative dose at D5 (mg ± SD)	31 (±24)	6 (±12)	<0.0001*

Table 5. Cumulative postoperative morphine doses (mg).

Legend: ITM = Intrathecal morphine, SD = standard deviation; D = day, PACU: post-anaesthetic care unit.

#### 2) Morphine-related post-operative side effects and length of stay

**Table 6** shows morphine-related post-operative side effects and length of stay. Morphine-related side effects were significantly more frequent in the control group vs ITM group (51% vs.15%, p <  $0.0001^*$ ). Respiratory distress (35% vs. 6%, p <  $0.0001^*$ ) and postoperative nausea and vomiting (18% vs. 3%, p =  $0.005^*$ ) were significantly more frequent in the control group than in the ITM group.

The length of hospital stay was shorter in the ITM group 6 ( $\pm$ 4) days vs. 8 ( $\pm$ 6) days in the control group, and the difference was not significant (p = 0.054). Two patients failed spinal analgesia (3.22%). No other complications related to spinal analgesia were observed.

	Control group n = 131	ITM Group n = 62	р
Overall rate, n (%)	67 (51)	9 (15)	<0.0001*
PONV, n (%)	23 (18)	2 (3)	0.005
Respiratory distress, n (%)	46 (35)	4 (6)	<0.0001*
Urinary retention, n (%)	1 (1)	3 (5)	0.098
Ileus, n (%)	6 (5)	2 (3)	1
LOS hospital, d (±SD)	8 (±6)	6 (±4)	0.054

Table 6. Morphine-related postoperative side effects and length of stay.

Legend: ITM = Intrathecal morphine, PONV = postoperative nausea and vomiting, LOS = length of stay, SD = standard deviation.

# 4. Discussion

This study was conducted to compare the analgesic efficacy of intrathecal morphine (ITM group) versus conventional analgesia using systemic morphine (control group). We observed a decrease in pain intensity in the ITM group compared with the control group ( $p < 0.0001^*$ ), a decrease in morphine consumption postoperatively for cumulative doses and on day zero ( $p < 0.0001^*$ ), more side effects in the control group than in the ITM group ( $p < 0.0001^*$ ) and a slight trend towards shorter length of stay in the ITM group than in the control group, with no significant difference (p = 0.054).

Our cohort size (193 patients) falls within the range of studies in Koning's meta-analysis [18], which was between 80 and 150 patients. Chronic inflammatory bowel disease (CIBD) and neoplastic pathologies were the predominant underlying conditions characterized by chronic pain and therefore at high risk of chronic postoperative pain [19], underlining the importance of better pain management, notably with intrathecal morphine. The dose of intrathecal morphine used (100 - 300  $\mu$ g, average 212.5  $\mu$ g ± 73) is recommended to avoid side effects [16] [20]. Ketamine for the prevention of postoperative hyperalgesia was predominantly administered in the ITM group, in accordance with the SFAR guidelines [21], but also represents a bias in this study. Postoperative pain management in this cohort complies with the SFAR and the French Society of Digestive Surgery recommendations, giving a Grade 1+ (Strong) to the prescription of a multimodal analgesia technique favouring non-morphine analgesic agents and/or a regional anaesthesia technique [5]. Studies on the intraoperative use of intravenous lidocaine by electric syringe [9] [10], and TAP block [11] [12] show that these techniques provide adequate postoperative analgesia, but often require systemic morphine administration.

On the primary endpoint of postoperative pain intensity (numerical scale) at 0, 30, 60, 90, and 120 minutes from awakening, and the maximum pain scale from  $D_0$  to  $D_5$ , the ITM protocol showed significant advantages (NS < 3, p < 0.001<sup>\*</sup>), as reported by other authors [22]. This effective analgesia over the first 24 hours was noted in Meylan's meta-analysis [17]. However, this analgesic effi-

cacy became less significant with each passing day, until it was almost non-existent at  $D_5$ . This is in line with the study by Wongyingsinn *et al.* [23] which, in addition to effective analgesia over the first 24 hours, also describes a low pain threshold up to 72 hours in the ITM group, albeit with an increased need for analgesics in the latter.

In the ITM group, there was a significant reduction in total morphine consumption at D0 compared with the control group. These results corroborate those of Wongyingsinn [23], who found lower morphine consumption in the ITM group, *i.e.* between 3 - 15 mg in the ITM group vs. 23 - 47 mg in the PCA group for laparoscopic colonic resection. Koning *et al.* [18], in their meta-analysis of 40 studies of ITM in abdominal surgery, found a low rate of morphine consumption in patients receiving ITM. In our cohort, there was no uniformity of intrathecal sufentanil and/or clonidine doses, due to the absence of a well-defined protocol, even though this practice is recommended [20].

The cumulative dose of morphine consumed from  $D_0-D_5$  was significantly lower in the ITM group, *i.e.* 6 mg (±12) vs. 31 mg (±24) in the control group, in favour of the improved rehabilitation after surgery program in abdominal surgery. Morphine sparing is the keystone of improved rehabilitation after surgery [5] [6] [24]. The length of hospital stay was not significantly different between the two groups, unlike in Koning's meta-analysis [18], due to the power of the study. Complications of ITM are dose-dependent [20].

In our cohort, side effects were more frequent in the control group due to the high dose of morphine. Respiratory distress was more frequent in the control group (35%) than in the ITM group (6%). Controversy remains over the correlation between the dose of morphine administered intrathecally and the risk of occurrence of delayed respiratory distress. This distress is due to the cephalic migration of morphine, which occurs after 6<sup>ième</sup> hours and persists until 12<sup>ième</sup> hours on average [25]. The meta-analysis by Meylan et al. [17] demonstrated the efficacy of ITM in major and abdominal surgery within the first 24 hours postoperatively, despite a higher rate of respiratory complications in the ITM group, probably due to the wide variability in morphine doses used in the studies (100 -4000 µg). This was not the case in our cohort, due to the low dose of intrathecal morphine used (100 to 300 µg). In a recent study of over 600 patients, Merchea et al. [26] reported the efficacy and safety of ITM in colorectal surgery for low intrathecal morphine doses (mostly below 200 µg). Their rate of respiratory distress was only 0.2. In a meta-analysis published in 2020, Koning et al. [18] confirmed the efficacy of ITM in reducing intra- and postoperative morphine consumption, and that the risk of respiratory distress appeared at doses >1000 µg. Guidelines [20] recommends intrathecal morphine doses of between 100 and  $300 \ \mu g$  for effective analgesia, and not to exceed  $300 \ \mu g$  to prevent the risk of respiratory distress. This 300 µg threshold is corroborated by the work of Gehling et al. [16] and our own. The occurrence of PONV was 18% in the control group versus 3% in the ITM group, in contradiction with the meta-analysis by

Koning *et al.* [18] and the study by Wongyingsinn *et al.* [23], both of which found no significant difference. The explanation lies in the low doses of morphine used in our study, as recommended by experts [20]. There was no significant difference between the two groups for the occurrence of ileus and urinary retention as described in the literature [18] [23]. In our cohort, we recorded a spinal analgesia failure rate of 3.22%, in line with the 1% to 6% reported in the literature [26] [27].

# **5.** Conclusions

The results of our study suggest that intrathecal morphine in laparoscopic colectomy provides effective analgesia for acute postoperative pain, reduced postoperative morphine consumption and fewer morphine-related side effects than conventional analgesia.

In view of the above-mentioned advantages, it would be interesting to carry out additional prospective and more robust studies in resource-limited settings to confirm the benefits, and the impact on reducing the cost of analgesia, and to establish evidence-based protocols.

## **Study Strengths and Limitations**

The present study confirms the analgesic efficacy of morphine spinal analgesia in abdominal surgery as described in the literature [28]-[30], as well as its contribution to improved rehabilitation after surgery program in abdominal surgery, the key to which is to minimize systemic morphine consumption [5] [6]. It also confirms the absence of major side effects in this simple technique, which has a high success rate.

The monocentricity and retrospective nature of this study may have led to a selection bias, even though the basic characteristics of the patients were comparable. Patients in the ITM group were therefore operated on more recently than those in the control group. This confounding bias is limited by the fact that over the three years of data collection, anaesthetic management (in addition to ITM) and surgical management of these patients remained identical. As the practice of ITM in our team was not protocolized, morphine dosage and the addition of Sufentanil or Clonidine were left to the free will of the anaesthetist. We limited, but did not eliminate, the information bias associated with missing data by using precise markers to diagnose postoperative complications (prescription of an antiemetic or oxygen, evacuating bladder catheterization), but the retrospective nature of our study means that we cannot guarantee the completeness of the collection of these complications.

There was also a co-intervention bias due to the higher proportion of Ketamine use in the ITM group, linked to the retrospective nature of the study. However, this bias was negligible, insofar as the proportion of patients in the control group was not negligible, but this did not prevent the occurrence of postoperative pain.

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# **Authors' Contributions**

Lionel Diyamona: Study design, drafting of the manuscript and data collection;

John Nsiala, Bruno Pastene, Manon Colin, Marc Leone: study design and correction of the manuscript;

Wilfrid Mbombo: Study design and drafting of the manuscript;

All other authors: Reading and correction of the manuscript.

# **Conflicts of Interest**

The authors declare no conflicts of interest regarding the publication of this paper.

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