EFFICACY OF INTRATHECAL MORPHINE AFTER LAPAROSCOPIC SURGERY FOR COLORECTAL CANCER AT CAN THO UNIVERSITY OF MEDICINE AND PHARMACY HOSPITAL

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ABSTRACT

Background: *There have been many studies in using intrathecal morphine order to reduce pain after obstetrics and gynecological surgeries, abdominal surgeries and orthopedic surgeries. These studies have shown that intrathecal morphine is very effective for pain relief after surgery. However, intrathecal morphine also has side effects especially in obstetric and gynecological surgeries such as pruritus, postoperative nausea and vomiting, and delayed respiratory depression. Although postoperative analgesia with intrathecal morphine has been widely used in obstetrics and gynecological surgeries, orthopedic surgeries, there have been very few studies on postoperative pain relief with intrathecal morphine for colorectal surgery. Laparoscopic colorectal surgery requires multimodal analgesia, so using intrathecal morphine to reduce postoperative pain in this surgery is essential in clinical practice. Therefore, studying the effectiveness of intrathecal morphine in this surgery is necessary, so we conducted this study.* ***Objectives:*** *To assess the effectiveness of analgesic and side effects of intrathecal morphine after laparoscopic colorectal surgery.* ***Materials and Methods:*** *This was a descriptive, cross-sectional study, including 63 patients undergoing laparoscopic colorectal cancer surgery with intrathecal morphine before general anesthesia. The degree of analgesia was assessed based on VAS. The postoperative side effects observed were postoperative nausea and vomiting, respiratory depression, and pruritus.* ***Results:*** *The analgesic effect at rest and on slight movement was 95.2%, and 88.9% respectively with VAS ≤ 3. The side effects were postoperative nausea and vomiting (6.3%), and pruritus (1.6%), both postoperative nausea and vomiting and pruritus (3.2%).* ***In conclusion****, 300µg intrathecal morphine showed a safe and positive analgesic effect for laparoscopic colorectal cancer surgery.*

Keywords: *intrathecal morphine, laparoscopic colorectal surgery, analgesia, pain relief, VAS.*

I. INTRODUCTION

Presently, pain management after surgery is absolutely necessary for clinical practice for patient satisfaction. Intrathecal morphine has demonstrated its role. There have been many studies in clinical practice on intrathecal morphine for laparotomy and laparoscopic surgery such as obstetric and gynecological, urological, hepatobiliary-pancreatic, orthopedic, and even thoracic surgery. The results showed that analgesia was effective in the first 24 hours post – operation and few patients required more medicines for pain relief [3], [10], [11], [12].

Globally, the recommended dose for intrathecal morphine ranges from 50 to 500µg. Many studies have also indicated that a dose of 300µg had positive effects with a long duration of pain relief and similar side effects to lower doses. However, the concerns about side effects of intrathecal morphine such as postoperative nausea and vomiting, pruritus, and delayed respiratory depression have prevented the majority of Vietnamese

anesthesiologists from using high doses (above 200µg) of intrathecal morphine. Furthermore, in most clinical studies, the dose of intrathecal morphine has not exceeded 200 µg. Such studies also focused on obstetric, gynecological, orthopedic surgeries rather than other surgeries, especially colorectal surgery.

In the Mekong Delta, there also have not been any studies of the benefits or side effects of intrathecal morphine for laparoscopic colorectal surgery. Therefore, we conducted the study in order to evaluate the effectiveness of intrathecal morphine and investigate the side effects after laparoscopic surgery for colorectal cancer.

II. MATERIALS AND METHODS

2.1. Materials

2.1.1. Study population

The study was conducted on the patients scheduled for elective who were indicated for laparoscopic surgery for colorectal cancer. They agreed to participate in the study at Can Tho University of Medicine and Pharmacy hospital. There are no contraindications of lumbar puncture.

2.1.2. Time and place of study

The study was conducted at Can Tho University of Medicine and Pharmacy Hospital from 2020-2021.

2.2. Methods

2.2.1. Study design

This was a prospective, descriptive cross-sectional study.

2.2.2. Sample size

The study utilized the sample calculation formula:

$$n = Z^2_{1-\alpha/2} \frac{p \times (1-p)}{d^2}$$

With: n: was sample size, p = 0.04.

According to a study by Wongyingsinn M., spinal anesthesia with a dose of 150-200 µg intrathecal morphine in laparoscopic colectomy on 24 patients, the rate of delayed respiratory depression was 4% [13].

d: is the allowable error, with d = 0.05.

α: is the design significance level (with α = 0.05).

The study was conducted on a total of 63 samples.

2.2.3. Study contents

The patient received spinal anesthesia with 300µg intrathecal morphine. Standardized general anesthesia was administered immediately after the lumbar puncture. After preoxygenation, 2 µg/kg fentanyl, 2 mg/kg propofol, and 0.6 mg/kg of rocuronium were administered, and the trachea was intubated. Standard IV medication of 1.000mg paracetamol and 8mg ondansetron were given before the end of surgery [8]. Sugammadex was used to reverse muscle relaxants for all patients. Extubation criteria were recovery from

anesthesia, spontaneous breathing, hemodynamic stability and normothermia, but the decision for extubation was at the discretion of the anesthesia and surgery providers [14].

All patients were monitored according to institutional guidelines outlined in a standardized intrathecal for analgesia order set. This consists of continuous pulse oximetry and nursing assessments every hour for the first 12 hours, then every 2 hours for the next 12 hours, and then every four hours in a general care setting [2].

General characteristics such as age, gender, occupation, BMI, medical history, ASA classification, surgical type, time of surgery and anesthesia, and changes in vital signs during and post operation are included. For effective pain relief after surgery, the VAS score was evaluated in 2 cases: at rest and on slight movement [3]. Classification for pain relief effectiveness in the first 24 hours based on VAS as perfect (0-1), good (2-3), acceptable (4-6) and ineffective (>6). The duration of effective pain relief with a VAS score is ≤ 4. Side effects included postoperative nausea and vomiting (PONV), respiratory depression, and pruritus. The level of sedation is assessed based on the Ramsay scale [1]. Patient satisfaction in the first 24 hours after surgery was classified into three levels such as very satisfied (no pain, no complaints, no side effects, and feels comfortable), satisfied (mild pain at the surgical site, the side effects after surgery are mild and transient, and no other complaints), dissatisfied (a lot of pain after surgery, the side effects last long after surgery, many complaints after surgery due to pain)

2.2.3. Ethics approval

Our study was approved by the Medical Ethics Committee of the CTUMP on medical research with No. 421/QĐ-ĐHYDCT. The informed consent form (No.401/PCT/HĐĐĐ) was accepted on 4th May 2020.

All the study participants were clearly explained the purpose and the study methods. This study ensures the voluntary participation of research subjects. Study participants were allowed to refuse or not answer questions when they felt uncomfortable. The subject's personal information and research data will be encrypted after data collection to ensure privacy for study participants.

III. RESULTS

There were 63 patients with colorectal cancer selected for scheduled laparoscopic surgery. They were qualified for the study. The results were shown as follows.

In this study, the average age was 59.4; the male/female rate was 1.4; and ASA physical status II accounted for a high proportion, with 44.4% (Table 1). There were 7 different types of surgery (table 2). Among them, rectal resection had the highest rate (60.3%), total colectomy was 3.2% and other types of colectomy were 12.7%.

Table 1. Baseline Characteristics

Baseline characteristics	Results
Age: $\overline{X}$ ± SD (min-max)	59.4 ± 12.6 (24-87)
High (cm): $\overline{X}$ ± SD (min-max)	160 ± 0.6 (150-170)

Baseline characteristics	Results
Weigh (kg): $\overline{X}$ ± SD (min-max)	55.3 ± 7.6 (35-70)
Sex: (male, female) (n,%)	37(58.7)/26(41.3)
ASA physical status I, II, III	10, 28, 25 (15.9/44.4/39.7)

In this study, the average age was 59.4; the male/female rate was 1.4; and ASA physical status II accounted for a high proportion, with 44.4%.

Table 2. Type of surgery

Type of surgery	Number	Percentage (%)
Right hemicolectomy	6	9.5
Transverse colectomy	1	1.6
Left hemicolectomy	6	9.5
Sigmoid resection	2	3.2
Rectal resection	38	60.2
Total colectomy	2	3.2
Other types of colectomy	8	12.7
Total	63	100

For the type of surgery, rectal resection had the highest rate (60.3%). Total colectomy and other types of colectomy were 3.2% and 12.7% respectively.

Table 3. Duration of surgery and anesthesia

	$\overline{X}$ ± SD	Min	Max
Operating time (min)	234.6 ± 71	100	390
Anesthesia time (min)	262.1 ± 69.1	130	420

The average time of surgery was 234.6 minutes; the average time of anesthesia was 262.1 minutes.

Table 4. VAS score

Time	VAS at rest	VAS on slight movement
	$\overline{X}$ (min-max)	$\overline{X}$ (min-max)
1 h postoperatively	1.1 (0-3)	1.6 (0-4)
2 h postoperatively	0.92 (0-3)	1.3 (0-4)
4 h postoperatively	0.83 (0-3)	1.2 (0-3)
12 h postoperatively	1.02 (0-4)	1.3 (0-4)
24 h postoperatively	1.3 (0-4)	1.7 (0-4)

Effective pain relief after surgery was observed at the points of 1, 2, 4, 12 and 24 hours after surgery, both at rest and on slight movement (Table 4). The postoperative VAS

scores at rest were ≤ 3 in 4 hours and ≤ in 24 hours; meanwhile, all postoperative VAS scores on slight movement were ≤ 4 in 24 hours.

Table 5. Postoperative pain relief level

	Resting			**Moving**		
Level	Perfect	Good	Average	Perfect	Good	Average
N	39	21	3	38	18	7
Percentage %	61.9	33.3	4.8	60.3	28.6	11.1

Table 5 shows the degree of pain relief. Regarding pain relief at rest, 61.9% of the patients reached the perfect level while there were 33% for a good level and 4.8% on average. For the degree of pain relief on slight movement, the highest figure was for the perfect and good levels with 60.3% and 28.8% respectively. The average level accounted for the lowest with only 11.1%.

Table 6. Side effects

Side effects	**n**	**Percentage %**
PONV	4	6.3
Pruritus	1	1.6
PONV and Pruritus	2	3.2
Total	**7**	**11.1**

The percentage of patients suffering from side effects after surgery was not high, at 11.1% (Table 6). PONV accounted for the highest rate, with 6.3%, and pruritus for the lowest, with 1.6%. The rate of both PONV and pruritus was 3.2%. There were no cases of respiratory depression in this study. All patients, therefore, were satisfied with the quality of pain relief in the first 24 hours postoperatively.

IV. DISCUSSION

Many researchers have demonstrated the effectiveness of pain relief using a dose of 300 µg of intrathecal morphine for different types of operations. The VAS score found by Mark V. Koning et al. for laparoscopic segmental colonic resection was 1.5 (from 0-4) [8]. Further research by Amit Merchea et al. about the use of intrathecal morphine for colorectal surgery showed that median pain scores at 4, 8, 16, 24, and 48 hours were 3, 2, 3, 4, and 3, respectively. The pain relief even prolonged for 48 hours with the average pain score at 3 [2]. Zoran Slavkovic studied the effectiveness of pain relief at rest, on exercise and coughing after gastrectomy. The result indicated all patients were satisfied with pain relief during 72 hours [14]. In our study, the VAS at rest and on slight movement in 24 hours after surgery were low. The patients experienced almost no pain after surgery. The average VAS score was < 2 for 24 hours. The average duration of analgesia was 27.1 hours. These results were positive. In comparison with previous studies, the average analgesic duration varied from 18-24 hours [5]. The shortest analgesic duration was 13.8 hours. The longest analgesic duration was 72 hours [7], [9], [13]. In general, our results are similar to the aforementioned studies.

There was a significant difference in PONV rate. Only 9.5% of patients had postoperative nausea and vomiting (including cases of nausea and pruritus) in our study while the rate ranged from 21-52 in other studies. In addition, 4.8% of the patients experienced pruritus (including cases with nausea and pruritus), which was much lower than Wongyingsinn M. (8%) [13], Khaled M. Fares (20%) [6], Mark V. Koning (41%) [8], Joo-Hyun Jun (37.5%) [4]. This reason can be explained by our routine use of antiemetic ondansetron 8 mg before the completion of the surgery. Therefore, postoperative nausea and vomiting and pruritus rate were lower in our study. Kalindi A DeSousa [5] also suggested that ondansetron could treat pruritus caused by spinal morphine. We also realized that the patients did not experience sedation and motor block. Most patients had a level of sedation Ramsay 2 (Patient is cooperative, oriented, and tranquil). For mobility, all patients had Bromage 0 level (full flexion of knee and feet) from the second hour after surgery. Urinary retention was not mentioned because the urinary catheter was placed 24 hours in the recovery room to facilitate care and monitoring.

V. CONCLUSIONS

A dose of 300 µg intrathecal morphine after laparoscopic colorectal cancer surgery in 24 hours had an analgesic effect at rest of 95.2%. The effectiveness of pain relief on slight movement reached 88.9% with VAS ≤ 3. The rate of side effects was low. Postoperative nausea and vomiting accounted for 6.3%, pruritus (1.6%), and both pruritus and PONV (3.2%).

REFERENCES

1. Akram Rasheed, et al. (2018) Ramsay Sedation Scale and Richmond Agitation Sedation Scale (RASS): A Cross Sectional Study, *Health Sci Journal*, Vol.12. No.6: 604
2. Amit Merchea, et al. (2018), Efficacy and outcome of intrathecal analgesia as part of an Enhanced Recovery Pathway in colon and rectal surgical patients, *Surgery Research and Practice.*
3. Jefferson Zhi Jie Tang (2019), A literature review of intrathecal morphine analgesia in patients undergoing major open hepatopancreatic-biliary (HPB) surgery, *Anesthesia Pain Medicine*, 9(6).
4. Joo-Hyun Jun, et al. (2017), Comparison of intrathecal morphine and surgical-site infusion of ropivacaine as adjuncts to intravenous patient-controlled analgesia in living-donor kidney transplant recipients, *Singapore Med Journal*, 58(11), pp. 666-673.
5. Kalindi A DeSousa, Rajkumar Chandran (2014), Intrathecal morphine for postoperative analgesia: Current trends, *World J of Anesthesiol*, 3(3), pp. 191-202.
6. Khaled Mohamed Fares, et al. (2014), High dose intrathecal morphine for major abdominal cancer surgery: A prospective double-blind, dose-finding clinical study, Pain Physician, Anesthesia and Intensive Care department, *South Egypt Cancer Institute*, Assiut University.
7. Kong S. K., et al. (2002) Use of intrathecal morphine for postoperative pain relief after elective laparoscopic colorectal surgery, *Anesthesia-perioperative medicine critical care and pain*, volume 57, issue 12, pp. 1168-1173.
8. Mark V. Koning, et al. (2018), Intrathecal morphine for laparoscopic segmental colonic resection as part of Enhanced Recovery Protocol, *Reg Anesth Pain Med*, 43(2), pp. 166-173.

9. Pervez Sultan, et al. (2016) The effect of intrathecal morphine dose on outcome after elective cesarean delivery: A meta-analysis, *Anesthesia-Analgesia*, 123, pp. 154-64.
10. Robert W. Hurley, et al. (2020), Acute postoperative pain, *Miller 9th edit*, pp. 2614-2637.
11. Roger Chou, et al. (2016), Guidelines on the management of postoperative pain, American Pain Society, *The Journal of Pain*, Volume 17, No 2, pp. 131-157.
12. Wojciech Weigl, et al. (2017), Perioperative analgesia after intrathecal fentanyl and morphine or morphine alone for cesarean section, *Medicine (Baltimore)*, 96(48).
13. Wongyingsinn M., et al. (2012), Spinal analgesia for laparoscopic resection using enhanced recovery after surgery programme: better analgesia, but no benefits on postoperative recovery: a randomized control trial, *British Journal of Anesthesia*, 108(5), pp. 850-6.
14. Zoran Slavkovic, et al. (2013), Comparison of analgesic effect of intrathecal morphine alone or in combination with bupivacaine and fentanyl in the patients undergoing total gastrectomy: a prospective randomized, double – blind clinical trial, *Vojnosanit Pregl*, 70(6), 541-557.

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