

A Comparative Study Between Single Shot Intrathecal Morphine with Multimodal Analgesia Versus Currently Ongoing Multimodal Analgesia alone For Postoperative Pain Management in Hepatobiliary and Pancreatic Surgery

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ABSTRACT

Background: Major hepatobiliary and pancreatic surgeries cause significant postoperative pain. Single-shot intrathecal morphine may improve pain control and reduce rescue analgesic requirements when added to multimodal analgesia. This study compared intrathecal morphine plus multimodal analgesia with multimodal analgesia alone for postoperative pain, rescue analgesic use, and adverse effects. **Methods & Materials:** This prospective comparative study included 60 patients undergoing elective major hepatobiliary and pancreatic surgery. Patients were equally assigned to single-shot intrathecal morphine plus multimodal analgesia or multimodal analgesia alone. Postoperative pain, rescue analgesic requirement, adverse effects, and patient satisfaction were assessed. Data were analyzed using Statistical Package for the Social Sciences version 25, with $p < 0.05$ considered statistically significant. **Results:** Sixty patients were included, with 30 in each group. Baseline characteristics and surgical procedures were comparable ($p > 0.05$). Postoperative VAS scores were significantly lower in Group A at 2–48 hours ($p \leq 0.001$). Group A had a longer time to first rescue analgesia (14.8 ± 5.1 vs. 7.6 ± 3.4 hours, $p < 0.001$) and fewer rescue doses (1.30 ± 0.79 vs. 2.23 ± 0.90 , $p < 0.001$). Pruritus was more frequent in Group A (23.3% vs. 3.3%, $p = 0.023$), with no respiratory depression. Patient satisfaction was higher in Group A (8.3 ± 1.1 vs. 6.9 ± 1.4 , $p < 0.001$). **Conclusion:** Single-shot intrathecal morphine improved postoperative pain control, prolonged the time to rescue analgesia, reduced analgesic requirements, and increased patient satisfaction, with pruritus as the main adverse effect and no clinically significant respiratory depression. It may therefore be considered an effective adjunct to multimodal analgesia for hepatobiliary and pancreatic surgery.

Keywords: Intrathecal morphine, Multimodal analgesia, Hepatobiliary surgery, Pancreatic surgery, Postoperative pain, Rescue analgesia, Patient satisfaction.

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INTRODUCTION

Major open hepato-pancreato-biliary (HPB) surgeries are increasingly performed for hepatocellular and pancreatic cancers. Despite relatively low perioperative mortality, postoperative complications and morbidity remain substantial^[1,2]. Effective perioperative analgesia is an essential component of enhanced recovery after surgery (ERAS), reducing pain and physiological stress while facilitating early mobilization, shortening hospital stay, reducing postoperative complications, and promoting functional recovery^[2,3]. However, extensive tissue manipulation and large abdominal incisions associated with HPB surgery often result in significant postoperative pain. Excessive systemic opioid use may further cause sedation, nausea, vomiting, ileus, respiratory depression, and delayed recovery^[4,5].

Multimodal analgesia is therefore central to ERAS pathways, combining analgesic agents and techniques with different mechanisms to improve pain control while minimizing opioid requirements. Intrathecal opioids and regional analgesic techniques are recommended components, although epidural analgesia may be associated with hypotension and delayed mobilization^[5]. ERAS pathways for pancreatic surgery similarly emphasize opioid-sparing analgesia, early mobilization, and accelerated recovery^[6,7]. Single-shot intrathecal morphine (ITM) provides prolonged and potent postoperative analgesia and may reduce systemic opioid requirements. In major HPB surgery, ITM has been associated with effective pain relief, reduced fluid requirements, and shorter hospital stay compared with epidural analgesia, although evidence in pancreatoduodenectomy

remains limited^[8,9]. Recent evidence further suggests that ITM incorporated into multimodal analgesia can reduce postoperative opioid consumption and improve acute pain control following HPB surgery^[10].

Conventional multimodal analgesia may include paracetamol, NSAIDs, systemic opioids, local anesthetic techniques, and patient-controlled analgesia. Wound infiltration and transversus abdominis plane (TAP) blocks may further reduce opioid requirements and support recovery, although their effectiveness can vary according to surgical approach and technique^[5,11]. Other systemic and regional analgesic strategies have also shown potential benefits following hepatobiliary and pancreatic surgery^[12–14]. Nevertheless, significant postoperative pain remains an important challenge after major HPB procedures, highlighting the need for

effective and opioid-sparing analgesic strategies.

In Bangladesh, evidence evaluating the additional benefit of single-shot ITM when added to established multimodal analgesia for HPB surgery remains limited. Therefore, this study aims to compare single-shot ITM plus multimodal analgesia versus multimodal analgesia alone regarding postoperative pain, rescue analgesic requirements, and analgesia-related adverse effects.

METHODS & MATERIALS

Study Design and Setting

This was a prospective comparative interventional study conducted in the Department of Anaesthesiology in collaboration with the Department of Hepatobiliary, Pancreatic and Gastrointestinal Surgery at the National Gastroenterology Institute & Hospital, Mohakhali, Dhaka. The study was conducted over a period of one year, from March 2023 to February 2024. The study was designed to compare the effectiveness and safety of single-shot intrathecal morphine combined with multimodal analgesia with multimodal analgesia alone for postoperative pain management following hepatobiliary and pancreatic surgeries.

Study Population

Patients scheduled for elective major hepatobiliary and pancreatic surgeries under general anaesthesia during the study period were considered for inclusion. A total of 60 patients fulfilling the eligibility criteria were enrolled and allocated equally into two groups of 30 patients each. Patients were included if they were aged 18–70 years, belonged to ASA physical status I–III, and were scheduled for elective hepatobiliary or pancreatic surgery. Patients with contraindications to spinal/neuraxial techniques, allergy or hypersensitivity to morphine, pre-existing chronic opioid use, significant respiratory disease, coagulopathy, infection at the proposed puncture site, altered mental status, or inability to reliably assess postoperative pain were excluded.

Group Allocation and Intervention

The enrolled patients were divided into two equal groups:

- Group A (n=30): Received single-shot intrathecal morphine in addition to the institutional multimodal analgesia protocol.
- Group B (n=30): Received the institutional multimodal analgesia protocol alone.

For patients in Group A, intrathecal morphine was administered as a single-shot neuraxial injection before induction of

general anaesthesia, using an aseptic technique. The dose was selected according to the institutional anaesthesia protocol. Group B did not receive intrathecal morphine. Both groups received the same perioperative multimodal analgesic regimen apart from the study intervention to minimize differences in background analgesic management.

Anaesthetic and Perioperative Management

All patients underwent standard preoperative assessment, including medical history, physical examination, routine laboratory investigations, and ASA physical status classification. General anaesthesia was administered according to standard institutional practice. Intraoperative monitoring included non-invasive blood pressure, electrocardiography, pulse oximetry, and end-tidal carbon dioxide, with additional monitoring as clinically indicated.

The type of hepatobiliary or pancreatic procedure, duration of surgery, and relevant intraoperative parameters were recorded. Postoperatively, patients were managed in the recovery unit and subsequently in the appropriate surgical ward or high-dependency area according to their clinical condition. Both groups continued to receive the same multimodal analgesic regimen postoperatively.

Assessment of Postoperative Pain

Postoperative pain was assessed using the Visual Analogue Scale (VAS), ranging from 0 to 10, where 0 indicated no pain and 10 indicated the worst imaginable pain. Pain scores were recorded at 2, 6, 12, 24, and 48 hours after surgery.

For descriptive analysis, pain severity at 24 hours was categorized as mild (VAS 0–3), moderate (VAS 4–6), and severe (VAS ≥7).

Rescue Analgesia

Rescue analgesia was administered when patients reported inadequate pain relief despite the scheduled multimodal analgesic regimen. The time from completion of surgery to the first requirement for rescue analgesia was recorded. The number of rescue analgesic doses required during the first 24 postoperative hours was also documented and compared between the two groups.

Assessment of Adverse Effects

Patients were monitored for opioid- and analgesia-related adverse effects during the first 48 postoperative hours. The recorded adverse effects included nausea, vomiting, pruritus, urinary retention, excessive sedation, hypotension requiring treatment, and respiratory depression. Respiratory status and level of consciousness were routinely monitored during the postoperative period.

Patient Satisfaction

Patient satisfaction with postoperative pain management was assessed before discharge using a 10-point satisfaction scale, where 0 represented complete dissatisfaction and 10 represented complete satisfaction. Patients with a score indicating satisfaction or high satisfaction were categorized as satisfied/very satisfied.

Outcome Measures

- The primary outcome was postoperative pain intensity as measured by VAS at predefined postoperative time points.
- The secondary outcomes included time to first rescue analgesia, total rescue analgesic requirement during the first 24 hours, postoperative adverse effects, and patient satisfaction with pain management.

Statistical Analysis

Data were entered, processed, and analyzed using Statistical Package for the Social Sciences (SPSS-25). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The independent-samples t-test was used to compare normally distributed continuous variables between the two groups. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients undergoing hepatobiliary and pancreatic surgeries were included in the study. The patients were equally divided into two groups, with 30 patients receiving single-shot intrathecal morphine in addition to multimodal analgesia (Group A), and 30 patients receiving multimodal analgesia alone (Group B).

Table I shows the baseline demographic and clinical characteristics of the study participants. The mean age was 48.7 ± 11.2 years in Group A and 47.9 ± 10.8 years in Group B. Male patients constituted 60.0% and 56.7% of the groups, respectively. The mean BMI was also comparable between Group A and Group B (24.1 ± 2.8 vs. 23.8 ± 2.6 kg/m²). Most patients in both groups were classified as ASA II. No statistically significant difference was observed between the groups regarding age, sex, BMI, or ASA physical status ($p > 0.05$ for all), indicating comparable baseline characteristics.

Table I

Baseline demographic and clinical characteristics of the study participants (n=60).

Variable	Group A (n=30), n (%)	Group B (n=30), n (%)	p-value
Age (years), mean $\pm$ SD	48.7 $\pm$ 11.2	47.9 $\pm$ 10.8	0.779
Male	18 (60.0)	17 (56.7)	0.793
Female	12 (40.0)	13 (43.3)	
BMI (kg/m ²), mean $\pm$ SD	24.1 $\pm$ 2.8	23.8 $\pm$ 2.6	0.668
ASA II	17 (56.7)	18 (60.0)	0.792
ASA III	2 (6.7)	2 (6.7)	

Table II presents the distribution of different hepatobiliary and pancreatic surgical procedures. Open cholecystectomy was the most common procedure, accounting for 26.7% of patients in Group A and 30.0% in Group B. Whipple

procedure was performed in 23.3% and 20.0% of patients, while hepatectomy was performed in 20.0% and 16.7% of patients in Groups A and B, respectively. Biliary reconstruction and other major hepatobiliary and pancreatic procedures

were similarly distributed between the groups. The difference in the distribution of surgical procedures was not statistically significant (p=0.951).

Table II

Distribution of types of surgery among the study participants (n=60).

Type of surgery	Group A (n=30)	Group B (n=30)	p-value
Whipple procedure	10 (23.3)	9 (20.0)	0.951
Extended cholecystectomy	5 (26.7)	6 (30.0)	
Hepatectomy	6 (20.0)	5 (16.7)	
Biliary reconstruction	5 (16.7)	6 (20.0)	
Other HPB surgeries	4 (13.3)	4 (13.3)	

Table III shows postoperative pain scores assessed using the Visual Analogue Scale (VAS) at different time points. Patients in the intrathecal morphine group consistently reported lower pain scores throughout the postoperative period. At 2 hours after

surgery, the mean VAS score was 2.1 ± 0.9 in Group A compared with 3.6 ± 1.1 in Group B. Similarly, at 6, 12, 24, and 48 hours, the mean VAS scores were 2.4 ± 1.0 , 2.8 ± 1.1 , 3.1 ± 1.2 , and 2.6 ± 1.1 , respectively, in Group A, compared with

4.2 ± 1.2 , 4.5 ± 1.3 , 4.6 ± 1.3 , and 3.7 ± 1.2 , respectively, in Group B. The differences in VAS scores between the two groups were statistically significant at all postoperative assessment points (p $\leq$ 0.001).

Table III

Postoperative pain scores at different time points.

Time after surgery	Group A Mean $\pm$ SD	Group B Mean $\pm$ SD	p-value
2 hours	2.1 $\pm$ 0.9	3.6 $\pm$ 1.1	<0.001
6 hours	2.4 $\pm$ 1.0	4.2 $\pm$ 1.2	<0.001
12 hours	2.8 $\pm$ 1.1	4.5 $\pm$ 1.3	<0.001
24 hours	3.1 $\pm$ 1.2	4.6 $\pm$ 1.3	<0.001
48 hours	2.6 $\pm$ 1.1	3.7 $\pm$ 1.2	0.001

Table IV shows the time to first rescue analgesia and total rescue analgesic requirement during the first 24 postoperative hours. The mean time to first rescue analgesia was significantly longer in

Group A than in Group B (14.8 ± 5.1 vs. 7.6 ± 3.4 hours, p<0.001). Rescue analgesia was required by 25 (83.3%) patients in Group A and all 30 (100%) patients in Group B (p=0.022).

Furthermore, the mean number of rescue analgesic doses required during the first 24 hours was significantly lower in Group A than in Group B (1.30 ± 0.79 vs. 2.23 ± 0.90 doses, p<0.001).

Table IV

Time to first rescue analgesia and 24-hour rescue analgesic requirement.

Variable	Group A (n=30)	Group B (n=30)	p-value
Time to first rescue analgesia (hours), mean $\pm$ SD	14.8 $\pm$ 5.1	7.6 $\pm$ 3.4	<0.001
Patients requiring rescue analgesia, n (%)	25 (83.3)	30 (100.0)	0.022
Rescue doses in 24 h, mean $\pm$ SD	1.30 $\pm$ 0.79	2.23 $\pm$ 0.90	<0.001

Table V shows postoperative adverse effects occurring within the first 48 hours. Nausea occurred in 30.0% of patients in Group A and 20.0% in Group B, while vomiting occurred in 13.3% and 10.0%,

respectively. Pruritus was significantly more frequent among patients receiving intrathecal morphine (23.3% vs. 3.3%, p=0.023). Urinary retention and excessive sedation were also slightly more frequent

in Group A, although the differences were not statistically significant. No patient in either group developed clinically significant respiratory depression.

Table V
Postoperative adverse effects within 48 hours.

Adverse effects	Group A (n=30)	Group B (n=30)	p-value
Nausea	9 (30.0)	6 (20.0)	0.371
Vomiting	4 (13.3)	3 (10.0)	0.688
Pruritus	7 (23.3)	1 (3.3)	0.023
Urinary retention	4 (13.3)	2 (6.7)	0.389
Excessive sedation	2 (6.7)	1 (3.3)	0.554
Respiratory depression	0 (0.0)	0 (0.0)	—

Table VI shows patient satisfaction with postoperative pain management. The mean satisfaction score was significantly higher in Group A than in Group B (8.3 ± 1.1 vs.

6.9 ± 1.4 , $p < 0.001$). Overall, 86.7% of patients in Group A were satisfied or very satisfied with their postoperative pain management compared with 60.0% in

Group B, and this difference was statistically significant ($p = 0.020$).

Table VI
Patient satisfaction with postoperative pain management.

Satisfaction	Group A (n=30)	Group B (n=30)	p-value
Satisfied/very satisfied, n (%)	26 (86.7)	18 (60.0)	0.020
Satisfaction score, mean $\pm$ SD	8.3 ± 1.1	6.9 ± 1.4	< 0.001

Overall, the findings demonstrated that the addition of single-shot intrathecal morphine to multimodal analgesia was associated with lower postoperative pain scores, delayed requirement for rescue analgesia, and reduced rescue analgesic consumption, while patient satisfaction was higher. The main adverse effect associated with intrathecal morphine was an increased incidence of pruritus, whereas no clinically significant respiratory depression was observed.

DISCUSSION

In our study, baseline characteristics were comparable between Group A and Group B. The mean age was 48.7 ± 11.2 and 47.9 ± 10.8 years, respectively, with males comprising 60.0% and 56.7% of the groups. BMI was also comparable, and most patients were ASA II, with no significant between-group differences. A previous randomized controlled study comparing intrathecal and intravenous morphine after hepatectomy reported comparable sex and BMI between groups, although the intrathecal morphine group was younger (56 vs. 63 years, $p = 0.012$) [15]. Thus, the present study showed comparable baseline characteristics, supporting adequate group comparability. In our study, the types of HPB surgery were similarly distributed between groups, with no significant difference. Open cholecystectomy was the most common procedure, followed by Whipple procedure and hepatectomy. A previous randomized controlled study evaluated intrathecal morphine with low-dose bupivacaine for postoperative analgesia after laparoscopic liver resection [16]. This provides further evidence supporting the use of intrathecal morphine in hepatobiliary surgery. In our study, postoperative VAS scores were significantly lower in the intrathecal morphine group at 2, 6, 12, 24, and 48 hours, with reduced additional analgesic

requirements. A previous randomized study also reported lower VAS scores and fewer additional analgesics during the first postoperative day with intrathecal morphine [17]. These findings support the effectiveness of intrathecal morphine in improving early postoperative pain control. In our study, the time to first rescue analgesia was significantly longer in Group A than Group B, while fewer patients required rescue analgesia and fewer rescue doses were required within 24 hours. Previous evidence has demonstrated prolonged analgesia and reduced opioid requirements with intrathecal morphine in major HPB surgery [2,10]. These findings further support the opioid-sparing and prolonged analgesic effects of intrathecal morphine. In our study, nausea, vomiting, urinary retention, and excessive sedation were comparable between groups, whereas pruritus was significantly more frequent with intrathecal morphine. No clinically significant respiratory depression occurred in either group. A previous review reported that multimodal analgesia provides effective postoperative pain control with a favorable safety profile when appropriately monitored [18]. Overall, intrathecal morphine was well tolerated, with pruritus being the main additional adverse effect. In our study, patient satisfaction was significantly higher with intrathecal morphine, with a higher satisfaction score and a greater proportion of satisfied or very satisfied patients. A systematic review reported that multimodal perioperative pain management improves postoperative pain control and short-term recovery after hepatectomy [19]. Improved postoperative analgesia with intrathecal morphine may therefore contribute to greater patient satisfaction. Overall, single-shot intrathecal morphine combined with multimodal analgesia provided superior postoperative pain

control, prolonged the time to rescue analgesia, reduced analgesic requirements, and improved patient satisfaction, with pruritus being the main additional adverse effect.

CONCLUSION

The addition of single-shot intrathecal morphine to multimodal analgesia provided more effective postoperative pain control than multimodal analgesia alone in patients undergoing hepatobiliary and pancreatic surgeries. Patients receiving intrathecal morphine had significantly lower postoperative pain scores, a longer time to first rescue analgesia, and lower rescue analgesic requirements during the first 24 hours. Patient satisfaction with postoperative pain management was also significantly higher in the intrathecal morphine group. Although pruritus occurred more frequently with intrathecal morphine, no clinically significant respiratory depression was observed. Therefore, single-shot intrathecal morphine may be considered an effective adjunct to multimodal analgesia for improving postoperative pain management in hepatobiliary and pancreatic surgery, with appropriate monitoring for opioid-related adverse effects.

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