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Research Article

# EFFICACY OF INTRATHECAL MORPHINE COMBINED WITH 0.75% ROPIVACAINE HEAVY FOR POST-OPERATIVE ANALGESIA IN LAPAROSCOPIC CHOLECYSTECTOMY-A RANDOMIZED CONTROLLED TRIAL

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**ABSTRACT**

**Objective:** The advent of laparoscopy has been a boon in a diverse range of surgeries, nonetheless the associated post-operative visceral pain significantly contributes to delayed hospital discharge and consequent ill effects. Hence, this research was planned to assess the effect of intrathecal Morphine combined with 0.75% Ropivacaine heavy on post-operative analgesia post-operatively in subjects undergoing laparoscopic cholecystectomy. The objective is to determine the duration of post-operative analgesia and the need for rescue analgesics within the first 24 h following the surgery.

**Methods:** A total of 102 subjects who consented to participate in the research and were scheduled for elective laparoscopic cholecystectomy were enrolled and assigned to two groups through computer-generated randomization. Group A received Morphine (200 mcg) combined with 0.75% Ropivacaine, diluted to a total volume of 2 mL, while Group B was administered 0.75% Ropivacaine heavy (2 mL). Post-operative assessments included the total duration of analgesia, the overall dose of rescue analgesics utilized, and any complications, which were subsequently compared between the two groups.

**Results:** The length of post-operative analgesia recorded in Group A was 23.28±5.33 h and 6.56±5.19 h for Group B. The rescue analgesics required in Group A was 17.45±36.102 mg whereas for Group B was 135.49±59.977 mg. The p-value was significant (p≤0.001) for both parameters. Lower visual analog scale score was recorded inpatient receiving morphine as compared to that of control No significant difference was seen in demographic data between the two groups. No statistical significance was recorded between the two groups with respect to any of the complications except for urinary retention which was 31.5% in our study.

**Conclusion:** The deduction that we reached was lower dose of Morphine as an adjunct added to intrathecal Ropivacaine significantly increases post-operative analgesia with diminished analgesic requirement in subjects undergoing laparoscopic cholecystectomy.

**Keywords:** Intrathecal, Opioids, Local anesthetic/spinal anesthesia, Laparoscopy, Analgesia/post-operative pain

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## INTRODUCTION

Laparoscopic cholecystectomy is the preferred surgical treatment for cholelithiasis due to its advantages over open cholecystectomy, such as reduced post-operative ileus, shorter hospital stays, decreased blood loss, and quicker recovery times. Inadequate pain management can disrupt sleep and physical activity and negatively impact the patient's well-being [1]. Effective post-operative pain management can help lower complications and accelerate recovery.

Various multimodal analgesic approaches have been investigated for alleviating post-operative pain, including subarachnoid block, epidural infusion, intravenous (IV) opioids and non-steroidal anti-inflammatory drugs (NSAIDs), intraperitoneal instillation of local anesthetics, and the use of intrathecal opioids [1]. Intrathecal morphine (ITM) offers multiple benefits including cost-effectiveness, easy administration, and less technical failures [2]. The analgesic effects can be up to 20–48 h [3].

This research focused on evaluating the effectiveness of ITM in combination with 0.75% Ropivacaine heavy for post-operative pain relief in patients undergoing laparoscopic cholecystectomy. The primary goal was to determine the efficacy of this analgesic regimen during the post-operative phase. In addition, the study aimed to achieve several secondary objectives: Assessing the total amount of rescue analgesics used in the first 24 h examining the occurrence of side effects such as pruritus, post-operative nausea and vomiting, and respiratory depression, evaluating the satisfaction score of anesthesiologists, and determining any residual motor block present.

## METHODS

Following the principles of the Declaration of Helsinki, after approval from the Institutional Ethics Committee (KIIT/KIMS/IEC/971/2022) and registration with Clinical Trial Registry India (CTRI/2022/08/045034) patient selection and recruitment was started. Informed written consent was obtained from all participating subjects scheduled to undergo laparoscopic cholecystectomy. The research work has been designed in line with the guidelines of Consolidated Standards of Reporting Trials (consort Diagram Fig. 1), where subjects were assessed for eligibility for inclusion, followed by allocation, follow-up, and analysis.

Following the ethics committee's approval, this research was conducted at Pradyumna Bal Memorial Hospital, Kalinga Institute of Medical Sciences, Odisha, India, from August 2022 to July 2024. The study involved consenting participants aged 18–60 years who were scheduled for laparoscopic cholecystectomy under general anesthesia, classified as American Society of Anesthesiologists physical status I and II. Exclusion criteria encompassed individuals aged 70 years and older, those with allergies to local anesthetics, opioids, morphine, NSAIDs, or paracetamol, contraindications to spinal anesthesia, use of abdominal drains for specific procedural reasons, surgeries lasting over 3 h, a body mass index of 30 kg/m$^2$ or higher, and those requiring intensive care unit admission.

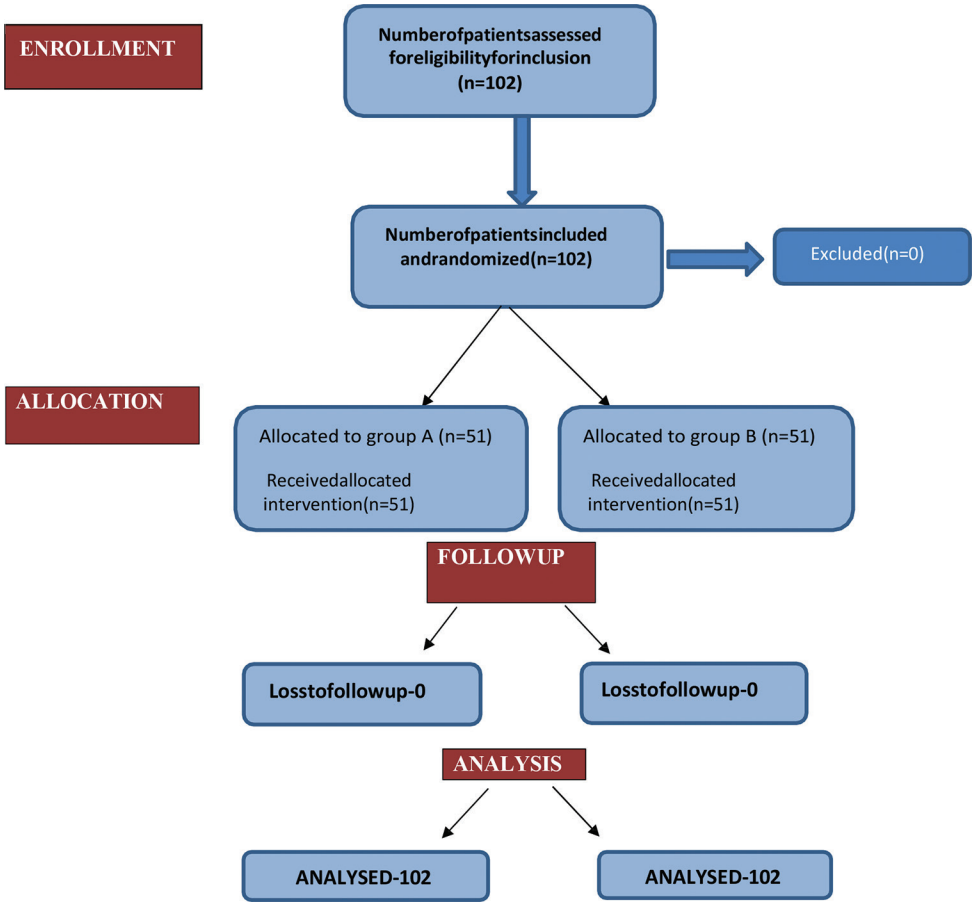


**Fig. 1: Consolidated standards of reporting trials (consort) diagram**

Randomization was achieved using computer-generated tables, and eligible participants were assigned to two groups through an opaque sealed envelope method to minimize bias. A double-blind approach was implemented, ensuring that both the patients and the primary investigator were unaware of the drug assignments. An anesthesiologist not involved in the study prepared the medications according to the designated groups.

Participants were divided into two groups: Group A received Morphine (200 µg) combined with 0.75% Ropivacaine heavy, diluted to a total volume of 2 mL, while Group B received only 0.75% Ropivacaine heavy (2 mL).

**Procedure**

Following the pre-operative checkup, risk-benefit counseling was done, and informed written consent was acquired after which the patients were transferred inside the operation theatre. After connecting monitors, basal hemodynamic parameters were noted. All the patients enrolled received an intrathecal injection before the commencement of general anesthesia. For intrathecal injection, patients were placed in a sitting position skin was sterilized with chlorhexidine, and sterile draping was placed over the lumbar area. After infiltrating the skin with 2% lidocaine, the dural puncture was done by a27G Quincke's needle in the L3-L4 or L2-L3 intervertebral space, and the drug was administered as per the group of the patient. After intrathecal injection was administered, pre-oxygenation was done for 3 min with a bag and mask using 100% oxygen was administered. Pre-medication was administered with injection (Inj) Glycopyrrolate (0.04 mg/kg), injection Fentanyl (2 µg/kg) Induction was done with injection Propofol (1.5–2 mg/kg) titrated to loss of verbal response and IV vecuronium (0.1 mg/kg). Orotracheal intubation was accomplished with an appropriate-size cuffed endotracheal tube and bolus dose of Vecuronium (0.1 mg/kg). General anesthesia was maintained with oxygen, nitrous oxide, and Isoflurane along with intermittent doses of injection Vecuronium (0.02 mg/kg). Controlled ventilation was done and $EtCO_2$ was maintained between 35 and 45 mmHg. IV Paracetamol infusion of 15 mg/kg was given before closure of the skin port incision site. Adequate spontaneous ventilation and neuromuscular recovery were ensured, then patients were reversed with injection Neostigmine 0.05 mg/kg and injection Glycopyrrolate 0.01 mg/kg. IV and trachea was extubated.

All participants were moved to the post-anesthesia care unit for observation. Both primary and secondary outcomes were evaluated, with visual analog scale (VAS) scores recorded at different time intervals.

Hemodynamic parameters, including systolic and diastolic blood pressure in mmHg, heart rate in beats per minute, and $SpO_2$ levels, were continuously monitored during the intraoperative phase and post-operatively at 30-min intervals for the first 2 h, followed by assessments at 4, 8, 12, and 24 h.

Post-operative monitoring for respiratory depression was conducted, with oxygen supplementation provided through a Hudson face mask at a rate of 4 L/min when $SpO_2$ levels dropped below 94% and the respiratory rate fell below 12 breaths/min. This ensured timely intervention for any respiratory complications.

Patient satisfaction was evaluated using an anesthesiologist satisfaction score, which considered factors, such as the ability to take oral pain relief medications, mobility, and normal bowel and bladder function. This assessment utilized a 5-point Likert scale ranging from "Very dissatisfied" (1) to "Very satisfied" (5). In keeping with post-operative

analgesia protocol i.v. Ketorolac (30 mg) was administered, after 4 h of administration of paracetamol. Injection Tramadol (1.5 mg/kg) was administered as rescue analgesia, in 100 mL normal saline over 15 min whenever the VAS score was equal to or more than 4 and the maximum dose was not to exceed 100 mg. The duration for the first rescue analgesic as well as the analgesic dose requirement for the first 24 h was noted.

**Outcome measures**

The primary outcome was to observe post-operative pain score using the NRS scale and the time of the first dose of rescue analgesia in hours (from T0– time of arrival in post-anesthetics care unit). Injection Tramadol 1.5 mg/kg will be administered as a rescue analgesic in 100 mL normal saline over 15 min, maximum dose not to exceed 100 mg.

The secondary outcomes were to measure the total dose of rescue analgesia consumed in 24 h in mg, possible adverse effects, such as pruritus, post-operative nausea, vomiting, and respiratory depression ($SPO_2$ <94% and respiratory rate <12 breaths/min). Anesthesiologist satisfaction and residual motor weakness were assessed using a 5-point Likert score and a modified Bro mage scale, respectively. An observer who was blinded to the group allocation recorded the outcome variables.

**Statistical analysis**

Data analysis was conducted using IBM Statistical Package for the Social Sciences software version 23. Continuous variables were reported as mean±standard deviation (SD), while categorical variables were presented as frequency and percentage. A $p<0.05$ was deemed statistically significant. The Independent t-test was utilized for comparing continuous variables, and the Chi-square test was employed to assess the association between categorical variables.

To evaluate the impact of hemodynamic parameters over time, a repeated measures analysis of variance was applied, allowing for a comparison between the two groups. This statistical approach facilitated a comprehensive understanding of the data trends and relationships. Overall, the analysis provided valuable insights into the variables under study, ensuring that the results were both statistically robust and clinically relevant. The methodologies employed were appropriate for the nature of the data and the research questions posed.

**Sample size collection**

From the previous study by Koo *et al*. (2022) [4], by considering the mean and SD values of VAS in post-anesthetics care unit (30 min) for both groups i.e. 6.1±2.6 and 4.1±2.9, at the level of significance 5%, and 95% power the minimum required sample size for each group is 51 i.e. 102 in total.

**RESULTS**

In all 102 subjects who matched the inclusion criteria were randomized into two groups. Demographic characteristics were comparable between the two groups (Table 1) and no significant difference was observed.

Table 1 shows the demographic parameters (Age, height, weight, and Body mass index) of patients in Groups A and B. On analysis, no significant difference was found in the data demographically between the two groups [1].

Table 2 shows the outcomes (primary and secondary) of the study. There was a significant statistical difference in the duration of analgesia between the two groups with a ($p<0.001$). Statistical analysis revealed a significant difference in the total tramadol dose received between the two groups ($p<0.001$) [2].

Table 1 shows no significant difference between demographic data between the two groups. Table 2 shows the analgesic duration for Group A was 23.28±5.33 h and for Group B 6.56±5.19 h. The total dose of tramadol received within 24 h post-operatively for Group A was 17.45±36.102 mg whereas for Group B was 135.49±59.977 mg. The VAS scores were lower in patients who received Morphine with Ropivacaine intrathecally as compared with Ropivacaine alone as shown in Fig. 2.

There was not much significance on comparing the post-operative hemodynamic parameters between the two groups as shown in Figure.

Fig. 2 shows the VAS score calculated at different time period post-operatively. It showed significance at 90 min, 120 min, 4 h, 8 h, 12 h, and 24 h post-operatively. Fig. 3 shows statistical significance at 120 min between the two groups.

Table 3 shows the incidence of adverse events in the post-operative period. Statistically, no significance is seen between the groups with respect to any of the complications except for urinary retention.

**Table 1: Comparison of demographic data (age, height, weight, and BMI)**

| Demographic parameters | Group A n=51 | Group B n=51 | p-value |
|---|---|---|---|
| Age (years) | 43.37±11.48 | 39.94±13.64 | 0.17 |
| Height (cm) | 164.69±7.41 | 163.96±7.75 | 0.63 |
| Weight (kg) | 61.39±9.04 | 65.00±8.72 | 0.14 |
| BMI ($kg/m^2$) | 22.02±2.90 | 23.71±2.87 | 0.06 |

BMI: Body mass index

**Table 2: The primary outcomes of the study were comparable between the two groups**

| Parameter | Group A n=51 | Group B n=51 | p-value |
|---|---|---|---|
| Duration of analgesia (hours) | 23.28±5.33 | 6.56±5.19 | <0.001 |
| Total dose of tramadol received in 24 h (mg) | 17.45±36.10 | 135.49±59.97 | <0.001 |

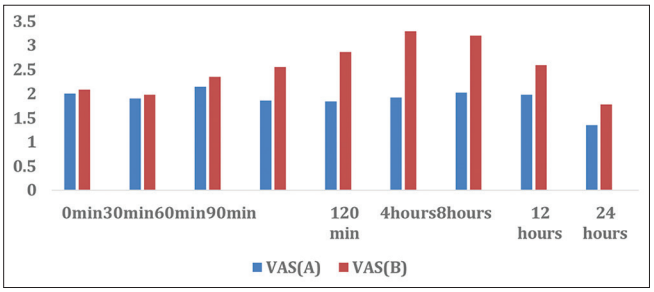


**Fig. 2: Bar chart comparing the visual analog scale score between two groups [1]**

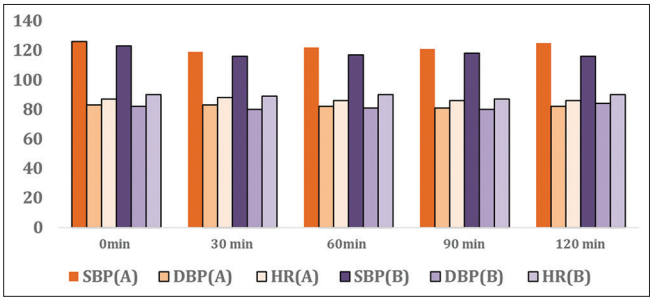


**Fig. 3: Bar chart comparing the intraoperative hemodynamic parameters between two groups [2]**

**Table 3: Incidence of side effects, such as pruritus, urinary retention, respiratory depression, post-operative nausea, and vomiting [2]**

| Complications | Group A (n=51) (%) | Group B (n=51) (%) | p-value |
|---|---|---|---|
| Urinary retention | | | |
| Present | 16 (31.4) | 0 (0) | 0.002 |
| Not present | 35 (68.6) | 51 (100) | |
| Post-operative nausea and vomiting | | | |
| Present | 6 (11.8) | 8 (15.7) | 0.56 |
| Not present | 45 (88.2) | 43 (84.3) | |
| Respiratory depression | | | |
| Present | 1 (2.0) | 0 (0.0) | 1 |
| Not present | 50 (98.0) | 51 (100) | |
| Pruritus | | | |
| Present | 3 (5.9) | 0 (0) | 0.24 |
| Not present | 48 (94.1) | 51 (100) | |

Fig. 4 shows no statistical difference between the two groups Table 3 shows the incidence of 31.4% incidence of urinary retention in group A as compared to group B.

## DISCUSSION

Spinal anesthesia provides a basic component of acute pain management when an adjuvant is added to the local anesthetic and thus reduces overall NSAIDs and opioid consumption, early recovery, and shorter hospital stays. The administration of opioids by the central neuraxial route provides adequate pain relief. [4] ITM has gained acceptance due to its proven effectiveness in managing moderate-to-severe degree of post-operative pain [5,6]. However, ITM is associated with worrisome side effects, such as pruritus, nausea, vomiting, and delayed respiratory depression [7]. Studies conducted have shown that a reduced dose of ITM (100–200 mcg) provides optimal analgesia [8,9]. Morphine intrathecally is associated with reduced side effects with a dose <0.3 mg. A study revealed in their meta-analysis the same to be reduced [10]. Cummings *et al*., recommended dose 0.1–0.2 mg intrathecally for both intraoperative and post-operative analgesia [10,11]. This study has depicted that a small dose for both of ITM (200 mcg) provides very good analgesia post-operatively during the first 24 h after laparoscopic cholecystectomy.

Given that pain is a subjective experience without reliable objective evidence, we rely on patients' self-reported pain levels, traditionally measured using a VAS score. The VAS consists of a 10 cm line with endpoints labeled as "No pain" and "Worst possible pain."

Laparoscopic cholecystectomy is a minimally invasive procedure, but subjects often suffer from moderate to severe pain in the first 24 h post-surgery. This pain may be attributed to visceral discomfort and the effects of pneumoperitoneum with increased pressure of $CO_2$. ITM is a "one-shot" technique that provides many benefits as it is easy, less expensive, and with less technical difficulties [2]. Due to the morphine's hydrophilic nature and its peak effect time being around 6 h after administration, it may not provide immediate relief [11]. To address this, some studies suggest combining ITM with local anesthetics, such as bupivacaine. For instance, a study found that adding 12.5 mg of bupivacaine to morphine during robot-assisted radical prostatectomy reduced opioid consumption and supported multimodal analgesia [12]. Similarly, another study highlighted that combining adjuvants with local anesthetics improves the efficacy and safety of post-operative pain management [13].

In this study, patients receiving ITM (Group A) reported significantly reduced pain scores and required less rescue analgesic (17.45±36.102 mg) compared to the control group (Group B) (135.49±59.977 mg). These results align with findings by Roy *et al*. [12], who observed a lower requirement of rescue analgesics (sufentanil) in the ITM group compared to the control group during several post-operative periods, with significant statistical differences (p<0.001).

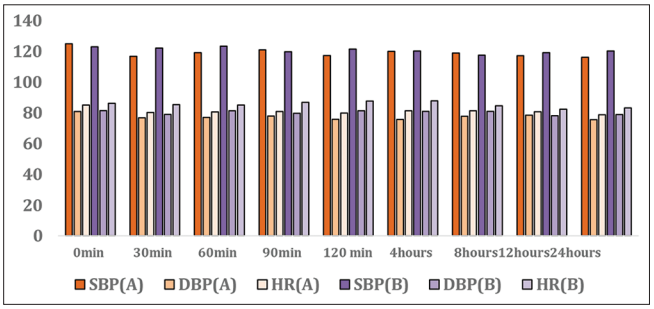


**Fig. 4: Bar chart comparing the post-operative hemodynamic parameters between two groups [1]**

In the study, observed that the mean VAS score at the time of the first rescue analgesic in the post-operative period was 7.5 in the intrathecal bupivacaine group whereas it was 5 in the intrathecal bupivacaine and morphine group and also the time required for the first rescue analgesic was shorter for intrathecal bupivacaine group as compared to intrathecal bupivacaine and morphine group. This result strongly correlates with our study [14].

Another study had noted that a reduced dose of ITM (200 mcg) combined with 0.5% bupivacaine (7.5 mg) provided significant pain relief during the initial 24 h following Robotic-Assisted Laparoscopic Prostatectomy. Patients who were given ITMB had less pain and the requirement for cumulative IV opioids [15]. The intrathecal approach was deemed effective and safe for the management of acute post-operative pain, providing several benefits over epidural or systemic methods, including lower requirement of opioids for pain relief, along with a failure of the procedure. These findings are consistent with our study.

Our study compared the time period of the requirement of the first rescue analgesic between both the groups where the morphine-Ropivacaine group achieved a longer duration of analgesia (23.28±5.33 h) in comparison to the Ropivacaine group (6.56±5.19 h). A study observed similar results where the control group required rescue analgesics earlier than the morphine+ bupivacaine group. They concluded that combining low-dose morphine with local anesthetics can deliver effective pain relief with fewer side effects [5].

A study noted that patients receiving bupivacaine with morphine experienced extended post-operative pain relief compared to those receiving bupivacaine alone [16]. This finding aligns closely with our study, where we have used ropivacaine as a local anesthetic agent due to its early recovery from motor block. In a study performed the onset and regression of sensory block were faster, and duration of motor block was significantly shorter in the ropivacaine as compared to the bupivacaine group [17].

Higher doses of morphine (e.g., >500 mcg) offer superior analgesia but are associated with side effects, such as vomiting, and respiratory depression. ITM at a lower dose (100–200 mcg) combined with a local anesthetic agent can provide effective post-operative analgesia with lesser side effects in subjects undergoing laparoscopic surgeries. A conducted study comparing the efficacy and adverse effects of lower ITM dose in patients undergoing total knee arthroplasty. They found that both 200 mcg and 300 mcg of ITM offered excellent relief of pain with minimal need for additional analgesic within the first 24 h after surgery [18]. No significant difference was seen in post-operative pain scores measured at different time intervals between the two dosage regimens. The dosage of morphine selected for our study corresponds to the one utilized in their investigation.

In our study, we observed a significant increase intraoperative systolic blood pressure at 120 min which can be attributed to the lighter plane of anesthesia.

We have also recorded differences between systolic blood pressure, diastolic blood pressure, and heart rate at different time intervals post-operatively probably due to port site pain or residual pneumo peritoneum after surgery. The incidence of urinary retention (31.4% vs. 0) was greater in patients who received ITM along with ropivacaine than ropivacaine alone [18,19].

Two studies observed that patients receiving spinal anesthesia with 0.5% hyperbaric bupivacaine and morphine had higher incidence and longer time of urinary catheterization as compared to patients injected with local anesthetics (1/16 vs. 6/14; p=0.025) only. These results strongly correlate with our study [19,20].

No significant hemodynamic instability or residual motor block was noticed in any of the patients. No significant difference was noted between the two groups in terms of anesthesiologist satisfaction score. Post-dural Puncture Headache (PDPH) was observed in a few patients only even though we used 27G Quincke's needle for administration of sub-arachnoid block.

## CONCLUSION

Therefore, we would like to conclude that advocating a regime of multimodal analgesia using morphine in a dose of 200 µg with intrathecal 0.75% hyperbaric Ropivacaine in patients undergoing laparoscopic cholecystectomy offers efficacious post-operative analgesia, thereby mitigating the use of IV rescue analgesics.

### Limitations of the study

This study has a few drawbacks. (1) It was performed in a single tertiary care hospital. (2) The period for follow-up was 24 h post-operatively but patients experiencing complications, such as PDPH and urinary retention needed follow-up and appropriate post-operative care for an extended period. The use of intrathecal opioids, such as morphine in patients posted for laparoscopic cholecystectomy could have hampered the early discharge of patients.

## ACKNOWLEDGMENT

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Footnotes: The results of the study revealed a significant statistical difference in analgesia duration between the two groups, with a p<0.001. Furthermore, the analysis highlighted a marked difference in the total tramadol dosage given to each group, also with a p-value below 0.001. There was no significant difference in demographic data between the groups. Specifically, the analgesic duration for Group A was recorded at 23.28±5.33 h, while Group B had an average of 6.56±5.19 h. In terms of tramadol administration within the first 24 h post-operatively, Group A received an average of 17.45±36.102 mg, compared to 135.49±59.977 mg for Group B disparity in the total tramadol dosage administered to the two groups, also with a p<0.001.

## CONFLICTS OF INTEREST

NO.

## FUNDING

No.

## REFERENCES

1. Saadati K, Razavi MR, Nazemi Salman D, Izadi S. Postoperative pain relief after laparoscopic cholecystectomy: intraperitoneal sodium bicarbonate versus normal saline. Gastroenterol Hepatol Bed Bench. 2016;9(3):189–96.
2. Cook TM, Counsell D, Wildsmith J a. W, Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. Br J Anaesth. 2009 Feb;102(2):179–90.
3. Koning MV, de Vlieger R, Teunissen AJW, Gan M, Ruijgrok EJ, de Graaff JC, et al. The effect of intrathecal bupivacaine/morphine on quality of recovery in robot-assisted radical prostatectomy: a randomised controlled trial. Anaesthesia. 2020 May;75(5):599–608.
4. Ban M, Choi YS, Koo BN. Analgesic Effect of Intrathecal Morphine Combined with Low-Dose Bupivacaine on Postoperative Analgesia after Liver Resection: A Randomized Controlled Study. J Pers Med. 2022 Feb 3;12(2):211.
5. Nikita , Bharti S , Sudama Prasad. International Journal of Current Pharmaceutical Review and Research.To Compare the Pain-Relieving Effectiveness of Butorphanol and Fentanyl in Different Surgical Procedures International Journal of Current Pharmaceutical Review and Research 2024; 16(3); 452-455.
6. Ban M, Choi YS, Koo BN. Analgesic Effect of Intrathecal Morphine Combined with Low- Dose Bupivacaine on Postoperative Analgesia after Liver Resection: A Randomized Controlled Study. J Pers Med. 2022 Feb 3;12(2):211.
7. Kong SK, Onsiong SMK, Chiu WKY, Li MKW. Use of intrathecal morphine for postoperative pain relief after elective laparoscopic colorectal surgery. Anaesthesia. 2002;57(12):1168–73.
8. SINGHAL G, SAXENA AK, BHARADWAJ G. A COMPARISON BETWEEN INTRATHECAL NALBUPHINE AND DEXMEDETOMIDINE AS ADJUVANTS TO HYPERBARIC BUPIVACAINE FOR LOWER LIMB ORTHOPEDIC SURGERIES. Asian J Pharm Clin Res [Internet]. 2023 Sep. 7 [cited 2025 May 31];16(9):29-32.
9. Kwan AS, Lee BB, Brake T. Intrathecal morphine for post-operative analgesia in patients with fractured hips. Hong Kong Med J Xianggang Yi Xue Za Zhi. 1997 Sep;3(3):250–5.
10. Yang T, Breen TW, Archer D, Fick G. Comparison of 0.25 mg and 0.1 mg intrathecal morphine for analgesia after Cesarean section. Can J Anaesth. 1999 Sep;46(9):856-60.doi: 10.1007/BF03012975. PMID: 10490154.
11. Gehling M, Tryba M. Risks and side-effects of intrathecal morphine combined with spinal anaesthesia: a meta-analysis. Anaesthesia. 2009 Jun;64(6):643-51. doi: 10.1111/j.1365- 2044.2008.05817.x. PMID: 19462494.
12. Cummings A, Orgill BD, Fitzgerald BM. Intrathecal Morphine. [Updated 2023 Sep 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
13. Roy JD, Massicotte L, Sassine MP, Seal R, Roy A. A Comparison of Intrathecal Morphine/Fentanyl and Patient-Controlled Analgesia with Patient-Controlled Analgesia Alone for Analgesia After Liver Resection. Anesth Analg. 2006 Oct 1;103:990–4.
14. Krishna Prasad GV, Khanna S, Jaishree SV. Review of adjuvants to local anesthetics in peripheral nerve blocks: Current and future trends. Saudi J Anaesth. 2020;14(1):77–84.
15. Wang Y, Guo X, Guo Z, Xu M. Preemptive analgesia with a single low dose of intrathecal morphine in multilevel posterior lumbar interbody fusion surgery: a double-blind, randomized, controlled trial. Spine J Off J North Am Spine Soc. 2020 Jul;20(7):989–97.
16. Basnet U. A Comparative study of intrathecal hyperbaric Bupivacaine with or without Morphine for Post-Operative Analgesia in Hysterectomy. Nepal J Obstet Gynaecol. 2018 Nov 12;13:34.
17. Shim JW, Cho YJ, Moon HW, Park J, Lee HM, Kim YS, et al. Analgesic efficacy of intrathecal morphine and bupivacaine during the

early postoperative period in patients who underwent robotic-assisted laparoscopic prostatectomy: a prospective randomized controlled study. BMC Urol. 2021 Feb 26;21(1):30.

18. Tomaszewski D, Bałkota M, Truszczyński A, Machowicz A. Intrathecal morphine increases the incidence of urinary retention in orthopaedic patients under spinal anaesthesia. Anaesthesiol Intensive Ther. 2014;46(1):29–33.
19. Bhat SN, Himaldev, Upadya M. Comparison of efficacy and safety of ropivacaine with bupivacaine for intrathecal anesthesia for lower abdominal and lower limb surgeries. Anesth Essays Res. 2013;7(3):381–5.
20. Hassett P, Ansari B, Gnanamoorthy P, Kinirons B, Laffey JG. Determination of the efficacy ad side-effect profile of lower doses of intrathecal morphine in patients undergoing total knee arthroplasty. BMC Anesthesiol. 2008 Sep 24;8(1):5.