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Original Research Article

Intraperitoneal Bupivacaine for Early Postoperative Pain Control after Laparoscopic Cholecystectomy: A Prospective Comparative Study

Dhivakar Ramasamy[1], A.K. Malhotra[2], Subimal Gupta[3], Gopal Vijayakumar Koulagi[4], Thirumalai Jothi G.[5], Tapas Sarkar[6]

[1]Senior Resident, Department of General Surgery, Central Hospital, South Eastern Railway
[2]Principal Chief Consultant, General Surgery, Central Hospital, South Eastern Railway
[3]Chief Consultant, General Surgery, Central Hospital, South Eastern Railway
[4]ADMO, General Surgery, Central Hospital, South Eastern Railway
[5]MBBS, General Private Practitioner
[6]DNB General Surgery, Central Hospital, South Eastern Railway

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Corresponding author: Dr. Dhivakar Ramasamy
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Abstract

Background: Despite the minimally invasive nature of laparoscopic cholecystectomy, postoperative pain remains an important factor affecting patient comfort and recovery. Intraperitoneal administration of local anesthetics may reduce visceral and referred pain while decreasing the requirement for additional analgesics. This study evaluated the efficacy of intraperitoneal bupivacaine for postoperative pain control following laparoscopic cholecystectomy.

Methods: This prospective comparative study was conducted at Central Hospital, South Eastern Railway, Kolkata, India, from May 2023 to April 2024. Sixty adult patients with uncomplicated gallstone disease and American Society of Anesthesiologists physical status I or II undergoing elective laparoscopic cholecystectomy were included. Patients were allocated into two groups of 30 each. The intervention group received intraperitoneal 0.25% bupivacaine at a dose of 2 mg/kg, with a maximum dose of 100 mg, following gallbladder extraction and achievement of hemostasis. The control group received no intraperitoneal instillation. Postoperative pain was assessed using the Visual Analog Scale at 30 minutes and 1, 3, 6, 12, 18, and 24 hours after surgery. Rescue analgesia requirement during the first 24 hours was also recorded. Continuous variables were compared using the Mann–Whitney U test and categorical variables using the chi-square test or Fisher's exact test, as appropriate.

Results: The baseline characteristics of the two groups were comparable. Mean age was 34.77 ± 12.25 years in the control group and 34.93 ± 13.62 years in the bupivacaine group ($p = 0.970$). Mean body weight was 66.47 ± 12.47 kg and 65.77 ± 15.56 kg, respectively ($p = 0.859$). There was no significant difference in sex distribution ($p = 0.796$).

Patients receiving intraperitoneal bupivacaine had significantly lower postoperative pain scores at 30 minutes (2.23 vs 2.87; $p < 0.001$), 1 hour (2.60 vs 3.77; $p = 0.001$), 3 hours (2.47 vs 3.10; $p = 0.020$), and 12 hours (2.37 vs 2.63; $p = 0.034$). No statistically significant difference was observed at 6, 18, or 24 hours. Rescue analgesia was required by 16 patients (53.33%) in the bupivacaine group compared with 25 patients (83.33%) in the control group ($p = 0.012$).

Conclusion: Intraperitoneal instillation of 0.25% bupivacaine at a dose of 2 mg/kg was associated with reduced early postoperative pain and a significantly lower requirement for rescue analgesia following laparoscopic cholecystectomy. Its analgesic benefit appeared to be most prominent during the early postoperative period.

Keywords: Bupivacaine; Intraperitoneal Instillation; Laparoscopic Cholecystectomy; Postoperative Pain; Visual Analog Scale; Multimodal Analgesia.

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Introduction

Laparoscopic cholecystectomy is the standard surgical treatment for symptomatic gallstone disease and offers several advantages over open surgery, including reduced tissue trauma, shorter recovery, and decreased postoperative morbidity. Nevertheless, postoperative pain remains a clinically relevant concern even after minimally invasive surgery.[1,2] Pain following laparoscopic

cholecystectomy is multifactorial. Visceral pain may result from surgical manipulation and irritation of the peritoneum, whereas parietal pain arises from trocar insertion and abdominal wall trauma. Pneumoperitoneum and diaphragmatic irritation may additionally contribute to refer shoulder pain. Consequently, effective postoperative analgesia often requires a multimodal approach.[1,2]

Intraperitoneal administration of local anesthetic is an attractive technique because it can directly target visceral and peritoneal nociceptive pathways.

Bupivacaine is a long-acting amide local anesthetic that has been extensively investigated for postoperative analgesia following laparoscopic cholecystectomy. Earlier meta-analyses demonstrated a reduction in early postoperative pain, opioid consumption, and rescue analgesic requirements, although substantial clinical heterogeneity was noted among trials.[1-3]

A subsequent Cochrane review including 85 completed trials and 4957 participants found that intraperitoneal local anesthetic may reduce pain up to 24 hours and probably produces a small reduction in length of hospital stay; however, the certainty of evidence for several clinically important outcomes was low or very low, largely because of risk of bias and variation in the technique of instillation.[4]

More recent network meta-analysis has further suggested that the type, timing, and method of intraperitoneal local anesthetic administration may influence opioid consumption, while differences in overall pain scores between delivery strategies remain uncertain.[5]

The present prospective comparative study was undertaken to evaluate whether intraperitoneal instillation of bupivacaine reduces postoperative pain and the requirement for rescue analgesia in patients undergoing laparoscopic cholecystectomy.

Materials and Methods

Study Design and Setting: This was a prospective comparative study conducted in the Department of General Surgery at Central Hospital, South Eastern Railway, and Kolkata, India. The study was performed over 12 months, from May 2023 to April 2024.

Ethical Considerations: The study protocol was submitted for institutional ethical review before commencement. Written informed consent for participation was obtained from all included patients. Important for final submission:

The institutional ethics committee/Hospital Review Committee approval number and approval date should be inserted here if available.

Participants: A total of 60 patients undergoing laparoscopic cholecystectomy for uncomplicated gallstone disease were included.

Inclusion Criteria

1. Were aged 18–60 years.
2. Had uncomplicated gallbladder disease requiring laparoscopic cholecystectomy.
3. Had ASA physical status I or II.
4. Were able to understand and use the Visual Analog Scale.
5. Provided informed consent.

Exclusion Criteria

- Complicated gallbladder disease, including gallbladder perforation or choledocholithiasis.
- Inability to use the Visual Analog Scale.
- Pregnancy.
- Conversion to open cholecystectomy.
- Concurrent surgical procedures.
- Known allergy to local anesthetics or study analgesics.
- Chronic analgesic use for more than 3 weeks before surgery.
- History of substance abuse.

Sample Size: The calculated sample size was 60 patients, with 30 patients in each group. The calculation was based on a two-sided significance level of 5%, study power of 90%, an assumed pooled standard deviation of 5, and a clinically significant difference of 4.2 in the pain score at extubation.

Study Groups: Control group: No intraperitoneal bupivacaine was administered. Bupivacaine group: Patients received intraperitoneal instillation of 0.25% bupivacaine at a dose of 2 mg/kg, with a maximum total dose of 100 mg.

The thesis describes patient selection as nonprobability consecutive sampling and group allocation using a slip system.

Perioperative Procedure: All patients underwent standard four-port laparoscopic cholecystectomy under general anesthesia. Following gallbladder extraction and confirmation of hemostasis, patients in the intervention group received intraperitoneal bupivacaine. The drug was instilled into the hepatodiaphragmatic space, gallbladder bed, and hepatoduodenal ligament before trocar removal. The control group received no intraperitoneal instillation.

All patients underwent port-site infiltration with 10 mL of 2% lignocaine. Study drugs were prepared by an anesthesiologist not otherwise involved in the study, and the thesis reports that the anesthesiologist and surgeon were blinded to study group allocation.

Postoperative Analgesic Protocol: All patients received standard postoperative analgesia consisting of diclofenac sodium 75 mg intramuscularly and paracetamol 1 g intravenously immediately after surgery and subsequently according to the study protocol for 24 hours.

Rescue analgesia consisted of tramadol 100 mg intravenously when the Visual Analog Scale score exceeded 3.

Outcome Measures: The primary outcome was postoperative pain intensity measured using the Visual Analog Scale.

Pain scores were recorded at:

- 30 minutes
- 1 hour
- 3 hours
- 6 hours
- 12 hours
- 18 hours
- 24 hours

The secondary outcome was the requirement for rescue analgesia during the first 24 postoperative hours. Postoperative pain assessments and analgesic requirements were recorded by nursing staff who were unaware of group allocation.

Statistical Analysis: Categorical variables were expressed as frequency and percentage and compared using Pearson's chi-square test or Fisher's exact test, as appropriate.

Continuous variables were summarized using mean, median, and standard deviation. Since the data were considered non-normally distributed, comparisons between groups were performed using the Mann–Whitney U test.

Statistical analysis was performed using SPSS version 25. A two-sided p-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics: The two study groups were comparable with respect to age, body weight, and sex distribution. The mean age was 34.77 ± 12.25 years in the control group and 34.93 ± 13.62 years in the bupivacaine group, with no statistically significant difference between groups (p = 0.970). Mean body weight was 66.47 ± 12.47 kg in the control group and 65.77 ± 15.56 kg in the bupivacaine group (p = 0.859). In the control group, 16 patients (53.33%) were female and 14 (46.67%) were male. In the bupivacaine group, 15 patients (50.00%) were female and 15 (50.00%) were male. The difference in sex distribution was not statistically significant (p = 0.796).

Table 1: Baseline Characteristics

Variable	Control (n = 30)	Bupivacaine (n = 30)	p-value
Age, years, mean ± SD	34.77 ± 12.25	34.93 ± 13.62	0.970
Weight, kg, mean ± SD	66.47 ± 12.47	65.77 ± 15.56	0.859
Female, n (%)	16 (53.33)	15 (50.00)	0.796
Male, n (%)	14 (46.67)	15 (50.00)	

Postoperative Pain Scores: The bupivacaine group demonstrated lower mean pain scores during the early postoperative period. At 30 minutes, the mean pain score was 2.23 in the bupivacaine group compared with 2.87 in the control group (p < 0.001). At 1 hour, the corresponding scores were 2.60 and 3.77 (p = 0.001), and at 3 hours they were 2.47 and 3.10 (p = 0.020). At 6 hours, there was no statistically significant difference between groups.

A statistically significant difference was again observed at 12 hours, although the absolute difference in mean scores was small. No significant difference was observed at 18 or 24 hours.

Table 2: Postoperative Visual Analog Scale Scores

Time after surgery	Control: Mean ± SD	Bupivacaine: Mean ± SD	p-value
30 minutes	2.87 ± 0.51	2.23 ± 1.19	<0.001
1 hour	3.77 ± 1.41	2.60 ± 1.22	0.001
3 hours	3.10 ± 1.12	2.47 ± 0.86	0.020
6 hours	2.77 ± 1.07	3.00 ± 1.08	0.339
12 hours	2.63 ± 0.56	2.37 ± 0.76	0.034
18 hours	2.73 ± 0.64	2.40 ± 0.62	0.077
24 hours	1.73 ± 0.64	2.03 ± 0.67	0.082

Rescue Analgesia Requirement: Rescue analgesia was required significantly less frequently in the bupivacaine group. In the control group, 25 of 30 patients (83.33%) required rescue analgesia, compared with 16 of 30 patients (53.33%) in the bupivacaine group. Conversely, 14 patients (46.67%) in the bupivacaine group did not require rescue analgesia compared with only 5 patients

(16.67%) in the control group. The difference was statistically significant (p = 0.012).

Table 3: Requirement for Rescue Analgesia

Rescue analgesia	Control (n = 30)	Bupivacaine (n = 30)	p-value
Required	25 (83.33%)	16 (53.33%)	0.012
Not required	5 (16.67%)	14 (46.67%)	

Discussion

This prospective comparative study evaluated the effect of intraperitoneal bupivacaine on postoperative pain and rescue analgesic requirement following laparoscopic cholecystectomy. The principal finding was that patients receiving intraperitoneal bupivacaine experienced lower pain scores during the early postoperative period and were less likely to require rescue analgesia during the first 24 hours.

The analgesic benefit was most evident at 30 minutes, 1 hour, and 3 hours after surgery. These findings are consistent with the meta-analysis by Boddy et al., which demonstrated a significant reduction in early postoperative abdominal pain, including a pooled reduction in pain at 4 hours after laparoscopic cholecystectomy.[1] Kahokehr et al. subsequently reviewed 30 randomized controlled trials and reported evidence favoring intraperitoneal local anesthetic, with reductions in pain, opioid use, and rescue analgesia despite marked clinical heterogeneity.[2] Our findings therefore add prospective comparative data to the body of evidence suggesting that the principal benefit of intraperitoneal bupivacaine is concentrated in the early postoperative period.

The effect observed in the present study was not sustained consistently throughout the 24-hour postoperative period. No significant difference was observed at 6, 18, or 24 hours. Although a statistically significant difference was observed at 12 hours, the absolute difference between group means was relatively small. This temporal pattern is compatible with findings from randomized studies of intraperitoneal local anesthetic techniques. For example, high-volume, low-concentration intraperitoneal bupivacaine in emergency laparoscopic cholecystectomy was associated with significantly lower early pain scores and analgesic use, while the magnitude and duration of benefit varied across assessment intervals.[6] Conversely, a randomized trial evaluating the addition of intraperitoneal bupivacaine to trocar-site infiltration did not demonstrate a clear additional reduction in pain compared with trocar infiltration alone, emphasizing the importance of the background analgesic regimen and comparator treatment.[7] Overall, our results suggest that intraperitoneal bupivacaine may be most useful as one component of multimodal analgesia rather than as a sole strategy for sustained postoperative pain control.

An important clinical finding was the reduction in rescue analgesia requirement. Only 53.33% of patients receiving bupivacaine required rescue analgesia compared with 83.33% of patients in the control group. This approximately 30-percentage-point absolute difference supports the potential role of intraperitoneal local anesthetic as part of a multimodal, opioid-sparing analgesic strategy. This interpretation is supported by systematic review evidence showing reductions in opioid consumption and rescue analgesia requirements with intraperitoneal local anesthetic, although the magnitude of benefit varies substantially across trials because of differences in drug, dose, timing, and co-analgesic protocols.[2,4,5]

The present findings are broadly consistent with previous randomized trials and systematic reviews, but direct comparison should be interpreted cautiously. The literature includes placebo-controlled studies, comparisons with no intraperitoneal treatment, and trials in which intraperitoneal administration was evaluated in addition to port-site infiltration or other multimodal analgesic measures.[1-8] These differences are clinically important because the incremental benefit of intraperitoneal bupivacaine may be smaller when effective local or systemic analgesic techniques are already used. The contemporary evidence also indicates that timing and delivery technique remain relevant sources of heterogeneity, with recent network meta-analysis unable to establish a single optimal approach for all laparoscopic procedures.[5]

No adverse effects related to bupivacaine toxicity were reported in the study. Earlier meta-analysis also reported no adverse events attributable to local anesthetic toxicity among the included trials.[1] Nevertheless, the Cochrane review concluded that adverse-event evidence was limited by inadequate reporting and low certainty, and therefore an increase in uncommon complications could not be confidently excluded.[4] Experimental clinical data have also demonstrated measurable plasma concentrations after intraperitoneal bupivacaine administration, reinforcing the importance of adherence to recommended dose limits.[8] Our study used 2 mg/kg of 0.25% bupivacaine with a maximum dose of 100 mg, but the sample size was

not sufficient to establish safety for rare adverse events.

Strengths and Limitations: The strengths of this study include its prospective design, standardized surgical procedure, predefined postoperative pain assessment intervals, blinded postoperative outcome assessment, and use of a standardized rescue analgesic protocol.

Several limitations should be acknowledged. First, the sample size was relatively small, with 30 patients in each group. Second, the study was conducted at a single center. Third, although the thesis describes allocation using a slip system and reports blinding of outcome assessors, the exact allocation concealment procedure and whether a placebo or sham intervention was used are not fully documented. In addition, the control group did not receive an intraperitoneal placebo, which may have implications for interpretation of blinding. Finally, outcomes such as time to ambulation, time to discharge, postoperative nausea and vomiting, shoulder pain, total analgesic consumption, and patient satisfaction were not reported as primary study outcomes.

Larger, well-designed trials using clearly described allocation concealment and placebo-controlled protocols would help define the optimal dose, concentration, timing, and technique of intraperitoneal bupivacaine administration. Future studies should also report total opioid consumption, patient-centered recovery measures, postoperative nausea and vomiting, shoulder pain, time to ambulation, and readiness for discharge. These outcomes would address important gaps highlighted in contemporary evidence syntheses.[4,5]

Conclusion

Intraperitoneal instillation of 0.25% bupivacaine at a dose of 2 mg/kg, with a maximum dose of 100 mg, was associated with improved early postoperative pain control following laparoscopic cholecystectomy. The intervention also significantly reduced the proportion of patients requiring rescue analgesia during the first 24 postoperative hours.

The analgesic effect was predominantly observed during the early postoperative period and was not consistently maintained through 24 hours. Intraperitoneal bupivacaine may therefore be considered as an adjunct to multimodal postoperative analgesia following laparoscopic cholecystectomy.

Declarations

Ethics Approval and Consent to Participate: The study protocol received institutional ethical approval before commencement, and written informed consent was obtained from all participants.

Consent for Publication: Not applicable, as no identifiable patient information is included.

Availability of Data and Materials: The datasets generated and analyzed during the current study are not publicly available but may be available from the corresponding author on reasonable request, subject to institutional policies and ethical approval.

Author Contributions: R. Dhivakar: Study conception and design, data collection, data analysis, interpretation of results, and manuscript preparation.

Other authors: To be finalized according to actual contributions and journal authorship requirements.

All authors should review and approve the final manuscript before submission.

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