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Research Article

Opioid-Free Multimodal Analgesia versus Conventional Opioid-Based Analgesia in Adults Undergoing Laparoscopic Cholecystectomy: A Prospective Randomized Controlled Trial.

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Abstract

Background: Laparoscopic cholecystectomy is associated with postoperative pain that may require systemic analgesia. Although opioids provide effective analgesia, their use is associated with adverse effects such as nausea, vomiting, sedation, pruritus, and respiratory depression. Multimodal analgesia using non-opioid agents may provide adequate postoperative pain control while reducing opioid exposure. The present study compared opioid-free multimodal analgesia with conventional opioid-based analgesia in adults undergoing laparoscopic cholecystectomy. **Methods:** This prospective randomized controlled study was conducted in the Department of Anaesthesiology, Subbaiah Medical College and Research Center, over a period of two years from August 2023 to August 2025. A total of 80 adult patients undergoing elective laparoscopic cholecystectomy were randomly allocated into two equal groups. Group A (n=40) received opioid-free multimodal analgesia, while Group B (n=40) received conventional opioid-based analgesia. Postoperative pain was assessed using the Numerical Rating Scale at predetermined time points. Time to first rescue analgesia, total rescue analgesic consumption during 24 hours, postoperative adverse effects, haemodynamic parameters, patient

satisfaction, and duration of hospital stay were also assessed. **Results:** The two groups were comparable with respect to demographic and baseline clinical characteristics. At 24 hours, the mean postoperative pain score was significantly lower in the opioid-free group compared with the opioid-based group (1.2 ± 0.5 vs. 1.6 ± 0.6; p=0.002). Rescue analgesia was required by 45.0% of patients in the opioid-free group compared with 72.5% in the opioid-based group (p=0.015). The time to first rescue analgesia was significantly longer in the opioid-free group (8.4 ± 3.2 vs. 5.7 ± 2.8 hours; p<0.001), while total rescue analgesic consumption was significantly lower (52.5 ± 38.4 vs. 96.3 ± 44.7 mg; p<0.001). The incidence of nausea and/or vomiting (15.0% vs. 37.5%; p=0.028), sedation (7.5% vs. 27.5%; p=0.025), and overall adverse effects (22.5% vs. 52.5%; p=0.006) was significantly lower in the opioid-free group. Patient satisfaction was higher (90.0% vs. 75.0%; p=0.048), and mean hospital stay was shorter (27.4 ± 6.8 vs. 31.2 ± 8.1 hours; p=0.026). **Conclusion:** Opioid-free multimodal analgesia provided effective postoperative pain control and reduced the requirement for rescue analgesics compared with conventional opioid-based analgesia in patients undergoing laparoscopic cholecystectomy. It was also associated with fewer opioid-related adverse effects, greater patient satisfaction, and shorter postoperative hospital stay. Opioid-free multimodal analgesia may therefore represent a useful component of enhanced recovery strategies following laparoscopic cholecystectomy.

Keywords: Opioid-free anaesthesia; multimodal analgesia; laparoscopic cholecystectomy; postoperative pain; rescue analgesia; postoperative nausea and vomiting; opioid-sparing analgesia.

Introduction

Laparoscopic cholecystectomy is a commonly performed minimally invasive procedure associated with faster recovery than open surgery, but patients frequently experience clinically significant postoperative pain arising from abdominal wall trauma, visceral manipulation, diaphragmatic irritation from pneumoperitoneum, and inflammatory responses. Effective perioperative analgesia is therefore essential for early mobilization and enhanced recovery after surgery.

Opioids remain a mainstay of perioperative analgesia but are associated with nausea, vomiting, sedation, respiratory depression, pruritus, and delayed gastrointestinal recovery, prompting efforts to reduce unnecessary perioperative opioid exposure. Multimodal analgesia, combining non-

opioid agents such as paracetamol and NSAIDs with regional or local anaesthetic techniques, targets multiple points in the nociceptive pathway to reduce opioid requirements and related adverse effects. Opioid-free anaesthesia (OFA) extends this approach by avoiding opioids altogether, combining agents such as dexmedetomidine, ketamine, lidocaine, magnesium, dexamethasone, and NSAIDs to maintain analgesia and haemodynamic stability without opioid-related morbidity.

Several randomized trials support the efficacy of opioid-free techniques in laparoscopic cholecystectomy. Regimens combining esketamine, dexmedetomidine, and lidocaine, or ketamine and dexmedetomidine, have shown lower rescue analgesic consumption and effective postoperative analgesia compared with opioid-based anaesthesia. Beyond pain scores, opioid-free anaesthesia has been associated with improved quality of recovery and fewer opioid-related adverse effects, including lower rates of nausea and vomiting, without compromising overall pain control. However, the optimal drug combination remains uncertain and may vary by procedure and protocol; recent evidence suggests opioid-free anaesthesia can achieve pain control non-inferior to opioid-sparing approaches while improving selected recovery parameters.

This study was therefore undertaken to compare opioid-free multimodal analgesia with conventional opioid-based analgesia in adults undergoing laparoscopic cholecystectomy, focusing on postoperative pain, rescue analgesic requirements, adverse effects, haemodynamic stability, and overall recovery.

Objectives

Primary Objective

To compare the effectiveness of **opioid-free multimodal analgesia** with **conventional opioid-based analgesia** for postoperative pain control in adults undergoing laparoscopic cholecystectomy.

Secondary Objectives

Secondary objectives were to compare, between groups: postoperative pain intensity at predetermined time points; time to first rescue analgesic requirement; total 24-hour rescue analgesic consumption; incidence of opioid-related adverse effects (nausea, vomiting, sedation, dizziness, pruritus, respiratory depression); postoperative haemodynamic parameters; patient satisfaction; and duration of hospital stay.

Methodology

Study Design

A **prospective, randomized, controlled, parallel-group clinical trial** was conducted to compare opioid-free multimodal analgesia with conventional

opioid-based analgesia in adult patients undergoing laparoscopic cholecystectomy.

Study Setting

The study was conducted in the **Department of Anaesthesiology, Subbaiah Medical College and Research Center**.

Study Duration

The study was conducted over a period of **2 years, from August 2023 to August 2025**.

Study Population

The study included adult patients scheduled to undergo **elective laparoscopic cholecystectomy under general anaesthesia**.

Sample Size

A total of **80 patients** fulfilling the eligibility criteria were included in the study. Patients were randomly allocated into two groups of 40 participants each:

- **Group A (n=40):** Opioid-free multimodal analgesia group
- **Group B (n=40):** Conventional opioid-based analgesia group

Inclusion Criteria

Patients fulfilling the following criteria were included: adults aged 18–65 years scheduled for elective laparoscopic cholecystectomy under general anaesthesia, ASA physical status I or II, and willing to provide written informed consent.

Exclusion Criteria

Patients were excluded if they were aged <18 or >65 years; had ASA status III or above; had a known allergy or contraindication to any study medication; had chronic opioid use, chronic pain, or previous substance abuse/opioid dependence; had significant hepatic, renal, cardiovascular, respiratory, or neurological disease; had psychiatric illness or cognitive impairment affecting pain assessment; required conversion to open cholecystectomy; or were unable or unwilling to provide informed consent.

Ethical Considerations

The study was conducted after obtaining approval from the **Institutional Ethics Committee of Subbaiah Medical College and Research Center**. Written informed consent was obtained from all participants before enrolment. Patient confidentiality was maintained throughout the study, and participation was voluntary.

Randomization

After confirming eligibility and obtaining informed consent, participants were randomly allocated in a **1:1 ratio** to either the opioid-free multimodal analgesia group or the conventional opioid-based analgesia group. Randomization was performed using a computer-generated randomization sequence. Allocation concealment was maintained until enrolment.

Preoperative Assessment

All patients underwent a detailed pre-anaesthetic evaluation, including demographic characteristics, medical and

surgical history, baseline vital signs, airway assessment, routine laboratory investigations, ASA physical status classification, and assessment of previous analgesic/opioid exposure.

Baseline pain assessment was performed using the **Numerical Rating Scale (NRS)**, where 0 represented no pain and 10 represented the worst imaginable pain.

Anaesthetic Management

All patients underwent standardized general anaesthesia, with standard intraoperative monitoring including electrocardiography, non-invasive blood pressure, pulse oximetry, end-tidal carbon dioxide, respiratory rate, and heart rate.

Anaesthesia was induced and maintained according to the institutional protocol. The surgical procedure and perioperative care were standardized as far as possible between the two groups.

Group A: Opioid-Free Multimodal Analgesia

Patients in Group A received a **multimodal analgesic regimen without perioperative opioids**. The analgesic strategy consisted of appropriately dosed non-opioid analgesic agents and/or adjuvant analgesic techniques according to the institutional study protocol.

The multimodal approach was designed to target different pain pathways and reduce the requirement for rescue analgesics. **No opioid was administered as part of the planned intraoperative analgesic regimen.**

Specifically, patients in Group A received intravenous ketamine 0.3 mg/kg and intravenous lidocaine 1.5 mg/kg as part of the multimodal analgesic protocol.

Group B: Conventional Opioid-Based Analgesia

Patients in Group B received **conventional opioid-based perioperative analgesia** according to the institutional anaesthesia protocol. Opioids were used as the primary intraoperative analgesic component, with additional non-opioid analgesics administered when appropriate.

Specifically, patients in Group B received intravenous ketamine 0.3 mg/kg and intravenous fentanyl 2 mcg/kg as part of the intraoperative analgesic protocol.

All patients underwent bilateral ultrasound guided ESP block at T7 vertebral level after induction (each side- 20ml of 0.2% ropivacaine) and port site incision was infiltrated with 5ml of 0.1% lidocaine.

Postoperative Analgesia

Following surgery, both groups received standardized postoperative care. Pain was assessed using the **Numerical Rating Scale (NRS; 0–10)**.

Pain assessment was performed immediately after recovery from anaesthesia and at 1, 2, 4, 6, 12, and 24 hours postoperatively.

Pain was assessed both **at rest and, where feasible, during movement**.

Rescue Analgesia

Rescue analgesia (inj. parecoxib sodium 40 mg IV) was administered if NRS ≥4 within the first 24 hours postoperatively.

The following parameters were recorded: whether rescue analgesia was required, time from completion of surgery to first rescue analgesic administration, number of rescue doses administered, and total dose of rescue analgesic required during the first 24 postoperative hours.

Assessment of Postoperative Adverse Effects

Patients were monitored for opioid- and analgesic-related adverse effects during the first 24 postoperative hours.

The following adverse events were recorded: nausea, vomiting, sedation, dizziness, pruritus, respiratory depression, hypotension, bradycardia, and other clinically significant adverse events.

The severity and frequency of these events were documented and compared between the two groups.

Haemodynamic Monitoring

Heart rate and blood pressure were recorded at baseline and at predefined intraoperative and postoperative intervals. Any clinically significant haemodynamic changes requiring intervention were documented.

Patient Satisfaction

Patient satisfaction with postoperative pain management was assessed before discharge using a standardized satisfaction scale. Patients were asked to rate their overall satisfaction with pain control and the adequacy of analgesia received.

Duration of Hospital Stay

The duration of postoperative hospitalization was recorded for each participant and compared between the two groups.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were expressed as frequency and percentage. The normality of continuous variables was assessed before selecting the appropriate statistical test. Comparison of continuous variables between the two groups was performed using the independent-samples t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate.

Repeated postoperative pain scores and haemodynamic parameters were analyzed using an appropriate repeated-measures statistical method, with adjustment for multiple comparisons where required. A p-

value <0.05 was considered statistically significant.

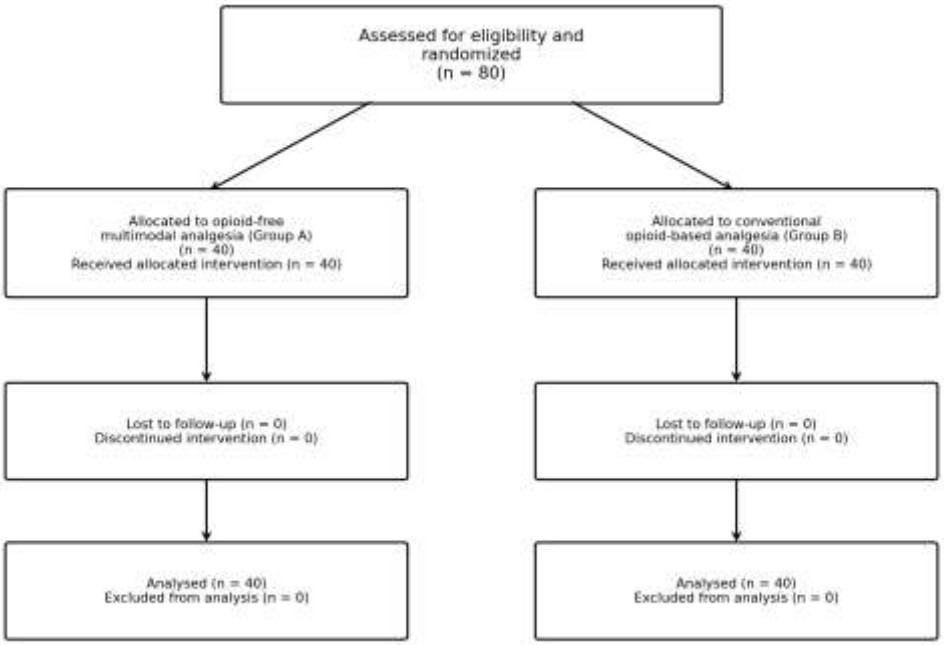

Figure 1. CONSORT flow diagram of patient enrolment, allocation, follow-up, and analysis.

Results

Table 1. Demographic and baseline clinical characteristics

Variable	Opioid-free group (n=40)	Opioid-based group (n=40)	*p* value
Age (years), Mean ± SD	42.3 ± 10.2	43.1 ± 9.8	0.72
Age group, n (%)			
18–30	7 (17.5)	6 (15.0)	0.93
31–40	11 (27.5)	10 (25.0)	
41–50	13 (32.5)	14 (35.0)	
51–60	7 (17.5)	8 (20.0)	
61–65	2 (5.0)	2 (5.0)	
Sex, n (%)			
Male	16 (40.0)	17 (42.5)	0.82
Female	24 (60.0)	23 (57.5)	
BMI (kg/m²), Mean ± SD	24.8 ± 2.9	25.1 ± 3.1	0.65
ASA I, n (%)	26 (65.0)	25 (62.5)	0.81
ASA II, n (%)	14 (35.0)	15 (37.5)	
Duration of surgery (min)	67.4 ± 12.6	69.1 ± 13.4	0.56
Duration of anaesthesia (min)	82.3 ± 14.1	84.5 ± 15.2	0.51

Table 1 shows that the two groups were comparable for age, sex, BMI, ASA status, and duration of surgery/anaesthesia (all p>0.05), confirming adequate randomization.

Table 2. Postoperative pain scores

Postoperative time	Pain at rest: Opioid-free	Pain at rest: Opioid-based	*p* value	Pain on movement: Opioid-free	Pain on movement: Opioid-based	*p* value
1 hour	3.5 ± 1.0	3.4 ± 1.0	0.65	4.5 ± 1.2	4.7 ± 1.3	0.48
2 hours	3.1 ± 0.9	3.2 ± 0.9	0.62	4.0 ± 1.1	4.3 ± 1.2	0.25
4 hours	2.7 ± 0.8	2.9 ± 0.9	0.3	3.4 ± 1.0	3.8 ± 1.1	0.09
6 hours	2.3 ± 0.7	2.6 ± 0.8	0.08	2.9 ± 0.9	3.4 ± 1.0	**0.024**
12 hours	1.7 ± 0.6	2.1 ± 0.7	**0.009**	2.1 ± 0.7	2.6 ± 0.8	**0.004**
24 hours	1.2 ± 0.5	1.6 ± 0.6	**0.002**	1.5 ± 0.6	2.0 ± 0.7	**0.001**

Table 2 shows comparable pain scores at rest and during movement during the early postoperative period, with significantly lower scores in the opioid-free group from 6–24 hours (rest: p=0.009–0.002; movement: p=0.024–0.001), indicating more effective analgesia later in the postoperative course.

Table 3. Rescue analgesic requirement and consumption

Parameter	Opioid-free group (n=40)	Opioid-based group (n=40)	*p* value
Patients requiring rescue analgesia, n (%)	18 (45.0)	29 (72.5)	**0.015**
Time to first rescue analgesia (hours)	8.4 ± 3.2	5.7 ± 2.8	**<0.001**
Median time to first rescue analgesia (hours)	8	5.5	**<0.001**
Number of rescue doses	0.7 ± 0.6	1.3 ± 0.8	**<0.001**
Total rescue analgesic consumption in 24 h (mg)	52.5 ± 38.4	96.3 ± 44.7	**<0.001**

Table 3 shows that rescue analgesia was required less often (45.0% vs. 72.5%, p=0.015), later (8.4±3.2 vs. 5.7±2.8 h, p<0.001), and in lower total dose (52.5±38.4 vs. 96.3±44.7 mg, p<0.001) in the opioid-free group.

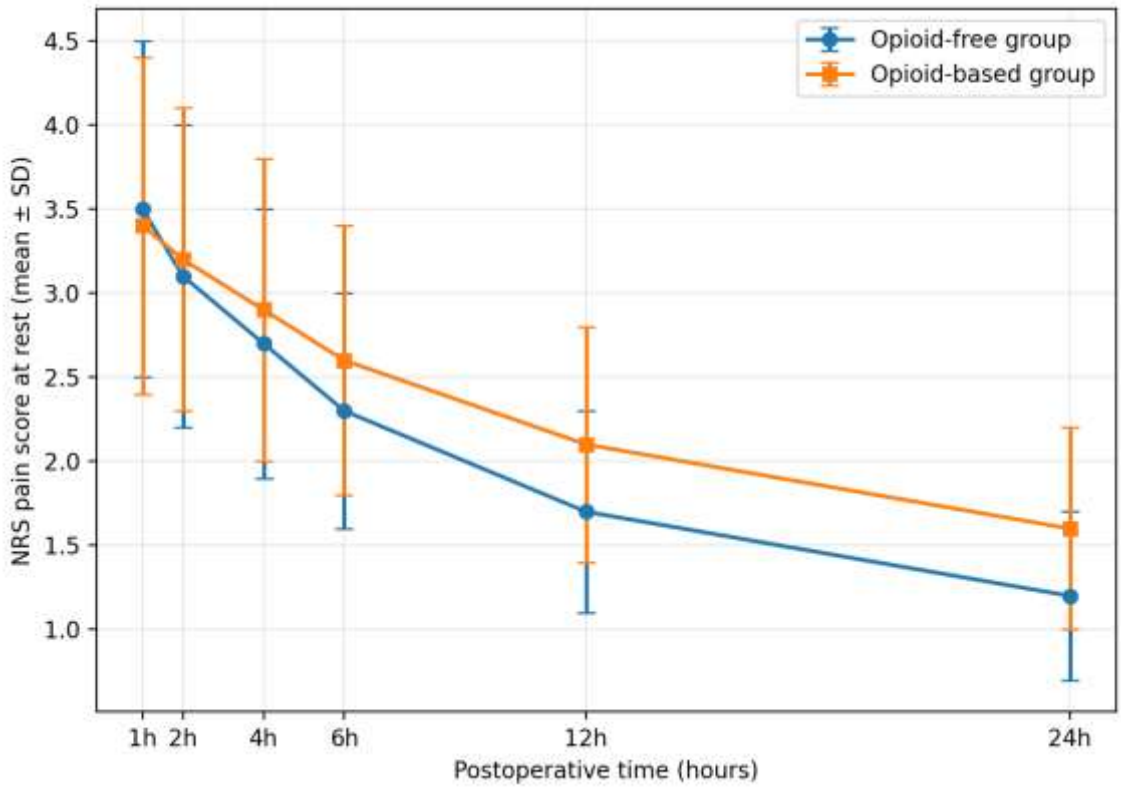

Figure 2. Postoperative pain scores (at rest) over time, by group.

Table 4. Postoperative haemodynamic parameters

Time point	HR: Opioid-free	HR: Opioid-based	*p*	SBP: Opioid-free	SBP: Opioid-based	*p*
Baseline	79.2 ± 8.4	80.1 ± 8.7	0.64	124.6 ± 10.8	125.8 ± 11.2	0.63
End of surgery	82.6 ± 7.9	86.8 ± 8.6	**0.028**	121.8 ± 10.2	119.4 ± 11.0	0.31
1 hour	80.8 ± 7.5	84.9 ± 8.2	**0.024**	120.6 ± 9.7	118.7 ± 10.1	0.39
2 hours	79.6 ± 7.1	82.7 ± 7.8	0.067	121.9 ± 9.4	119.8 ± 9.8	0.33
4 hours	78.8 ± 6.9	80.9 ± 7.2	0.18	122.4 ± 9.2	120.7 ± 9.5	0.42
6 hours	78.1 ± 6.7	79.8 ± 7.0	0.27	123.1 ± 9.1	121.8 ± 9.3	0.53

Table 4 shows comparable baseline haemodynamics; heart rate was modestly higher in the opioid-based group at the end of surgery and at 1 hour (p=0.028, p=0.024), with no other significant differences in heart rate or systolic blood pressure

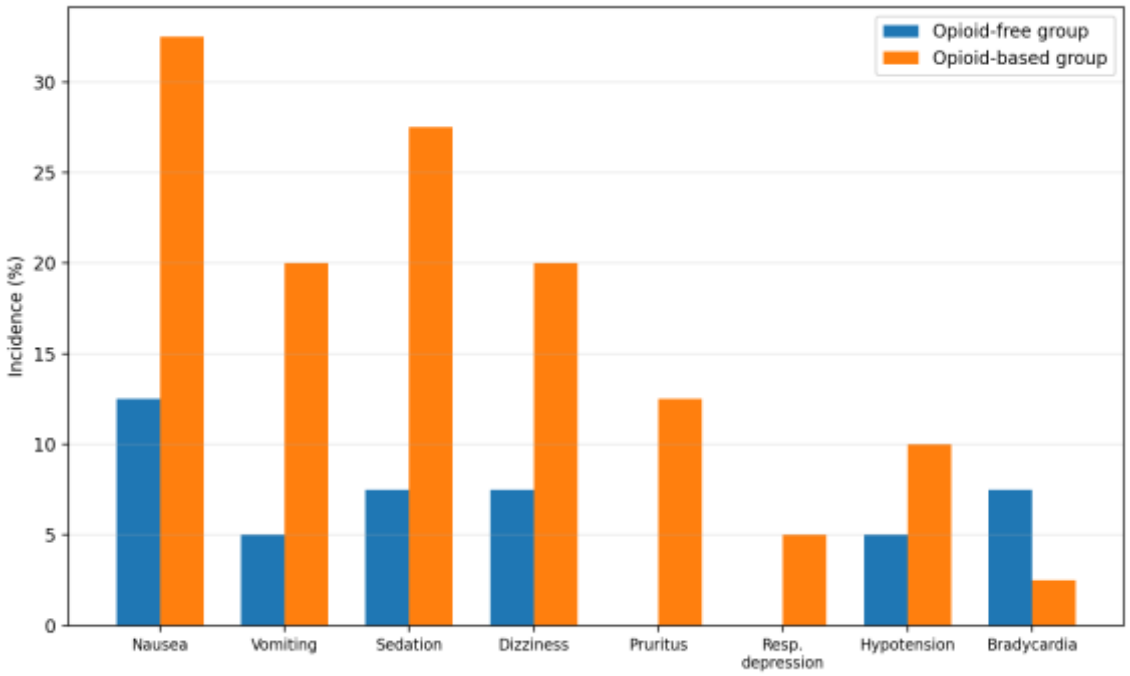

Figure 3. Incidence of postoperative adverse effects by group.

Table 5. Postoperative adverse effects

Adverse effect	Opioid-free group (n=40)	Opioid-based group (n=40)	*p* value
Nausea	5 (12.5)	13 (32.5)	**0.035**
Vomiting	2 (5.0)	8 (20.0)	**0.046**
Nausea and/or vomiting	6 (15.0)	15 (37.5)	**0.028**
Sedation	3 (7.5)	11 (27.5)	**0.025**
Dizziness	3 (7.5)	8 (20.0)	0.19
Pruritus	0 (0.0)	5 (12.5)	**0.022**
Respiratory depression	0 (0.0)	2 (5.0)	0.49
Hypotension	2 (5.0)	4 (10.0)	0.67
Bradycardia	3 (7.5)	1 (2.5)	0.61
Any adverse effect	9 (22.5)	21 (52.5)	**0.006**

Table 5 shows significantly lower rates of nausea, vomiting, sedation, and pruritus in the opioid-free group, and a lower overall incidence of any adverse effect (22.5% vs. 52.5%, p=0.006); dizziness, hypotension, and bradycardia did not differ significantly.

Table 6. Sedation, patient satisfaction and duration of hospital stay

Parameter	Opioid-free group	Opioid-based group	*p* value
Sedation score			
0 hour	1.8 ± 0.6	2.1 ± 0.7	0.041
1 hour	1.6 ± 0.5	2.0 ± 0.6	**0.002**
2 hours	1.4 ± 0.5	1.8 ± 0.6	**0.001**
4 hours	1.3 ± 0.4	1.5 ± 0.5	0.051
Overall satisfied, n (%)	**36 (90.0)**	**30 (75.0)**	**0.048**
Hospital stay (hours)	27.4 ± 6.8	31.2 ± 8.1	**0.026**

Table 6 shows lower early sedation scores (1 h and 2 h, p≤0.002) and higher patient satisfaction (90.0% vs. 75.0%, p=0.048) in the opioid-free group, together with a shorter hospital stay (27.4±6.8 vs. 31.2±8.1 h, p=0.026).

Table 7. Overall comparison of primary and secondary outcomes

Outcome	Opioid-free group	Opioid-based group	*p* value
NRS pain score at 24 h	1.2 ± 0.5	1.6 ± 0.6	**0.002**
Patients requiring rescue analgesia	18 (45.0%)	29 (72.5%)	**0.015**
Time to first rescue analgesia (h)	8.4 ± 3.2	5.7 ± 2.8	**<0.001**
Total rescue analgesic consumption (mg)	52.5 ± 38.4	96.3 ± 44.7	**<0.001**
Nausea/vomiting	6 (15.0%)	15 (37.5%)	**0.028**
Sedation	3 (7.5%)	11 (27.5%)	**0.025**
Any adverse effect	9 (22.5%)	21 (52.5%)	**0.006**
Satisfied with analgesia	36 (90.0%)	30 (75.0%)	**0.048**
Hospital stay (hours)	27.4 ± 6.8	31.2 ± 8.1	**0.026**

Table 7 summarizes the primary and secondary outcomes: opioid-free multimodal analgesia was associated with lower 24-hour pain scores, reduced rescue analgesic requirement and consumption, fewer adverse effects, higher satisfaction, and shorter hospital stay, while haemodynamic stability was maintained in both groups.

Discussion

This randomized controlled trial compared opioid-free multimodal analgesia with conventional opioid-based analgesia in adults undergoing laparoscopic cholecystectomy. Baseline demographic and clinical characteristics were comparable between groups, supporting the validity of subsequent outcome comparisons.

Postoperative pain

Opioid-free multimodal analgesia provided effective postoperative pain control, with significantly lower pain scores at rest and during movement from 6–24 hours. These findings align with Yu et al., who reported lower rescue analgesic consumption with an esketamine-dexmedetomidine-lidocaine regimen,[13] and Vishnuraj et al., who found reduced early analgesic requirements with ketamine-dexmedetomidine, although differences narrowed by 6 hours.[14] Conversely, Xiong et al. found opioid-free anaesthesia non-inferior but with slightly higher early pain scores than opioid-sparing anaesthesia,[15] suggesting that opioid-free techniques should be interpreted as an effective alternative rather than as universally superior to opioid-containing approaches.

Rescue analgesic requirement

Rescue analgesia was required less often, later, and in lower total dose in the opioid-free group, consistent with Yu et al.[13] and Vishnuraj et al.,[14] and with an earlier trial of dexmedetomidine-lidocaine-propofol opioid-free anaesthesia showing similarly reduced fentanyl consumption.[16] This benefit likely reflects the synergistic action of ketamine (NMDA antagonism), dexmedetomidine (α2-adrenergic effects), and local anaesthetic agents acting through complementary non-opioid pathways.

Postoperative nausea and vomiting

Nausea and/or vomiting were significantly less common in the opioid-free group (15.0% vs. 37.5%), consistent with Vishnuraj et al.[14] and Hao et al.,[17] both of whom attributed this benefit to avoidance of perioperative opioids. This is particularly relevant after laparoscopic surgery, where both the procedure itself and opioid use independently increase PONV risk.

Other opioid-related adverse effects

Sedation and pruritus were also significantly less frequent in the opioid-free group, consistent with the known adverse-effect profile of opioids and with Hao et al.[17] Dizziness, hypotension, and bradycardia did not differ significantly, though dexmedetomidine can itself cause bradycardia and hypotension, warranting continued haemodynamic monitoring with opioid-free protocols.

Haemodynamic stability

Heart rate was modestly higher in the opioid-based group immediately postoperatively, while systolic blood

pressure was comparable between groups. Evidence on haemodynamic effects of opioid-free anaesthesia is mixed — Xiong et al. found no intraoperative differences,[15] whereas Hao et al. reported more hypotension with opioid-free anaesthesia[17] — suggesting haemodynamic outcomes depend on the specific agents and doses used rather than opioid avoidance per se.

Sedation and recovery

Early postoperative sedation scores were lower in the opioid-free group. This contrasts with Vishnuraj et al., who found longer times to LMA removal and orientation recovery despite reduced analgesic requirements,[14] highlighting that opioid-free anaesthesia does not automatically equate to faster emergence given the sedative properties of adjuvants such as dexmedetomidine and ketamine.

Patient satisfaction and hospital stay

Patient satisfaction was higher and hospital stay shorter in the opioid-free group, broadly consistent with Hao et al.'s finding of better quality-of-recovery scores.[17] Xiong et al. similarly reported faster bowel recovery with opioid-free anaesthesia, though overall recovery times and satisfaction were otherwise similar,[15] suggesting the benefits of opioid-free approaches are expressed more consistently through reduced opioid exposure than through universally shorter hospitalization.

Overall interpretation

These findings suggest that the opioid-free multimodal regimen used in this study was a feasible alternative to the opioid-containing regimen for laparoscopic cholecystectomy, with lower pain scores at later postoperative time points, delayed and reduced rescue analgesic requirements, fewer opioid-associated adverse effects, and favorable recovery parameters consistent with enhanced recovery after surgery principles. As Xiong et al. demonstrated non-inferiority rather than superiority,[15] the clinical goal should be effective multimodal analgesia with the lowest appropriate opioid exposure rather than opioid elimination at the expense of adequate pain control.

Strengths and limitations

The randomized design with equal allocation and comprehensive multi-domain outcome assessment are key strengths. Limitations include the modest single-centre sample, difficulty blinding opioid-free versus opioid-based techniques, variability in opioid-free protocols across studies limiting comparability, and lack of longer-term outcomes such as persistent pain or prolonged opioid use.

Conclusion

In this randomized controlled trial, the opioid-free multimodal regimen was associated with effective postoperative analgesia, lower pain scores at later time

points, delayed and reduced rescue analgesic requirements, fewer opioid-associated adverse effects (including PONV, sedation, and pruritus), higher patient satisfaction, and shorter hospital stay, while haemodynamic stability was maintained. These findings suggest that the studied opioid-free regimen may be a useful alternative to an opioid-containing regimen for laparoscopic cholecystectomy. However, the results should be interpreted in the context of the specific multimodal protocol used in this study, including the bilateral ESP block and ketamine administration in both groups. Larger, adequately powered multicentre trials with standardized opioid-free protocols are required to confirm these findings.

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