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Original Article

Intraperitoneal Versus Intravenous Dexamethasone for Prevention of Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy: A Prospective, Randomised, Double-Blinded Study

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ABSTRACT

Background: Postoperative nausea and vomiting (PONV) is a frequent complication following laparoscopic cholecystectomy, occurring in 52–80% of cases. Dexamethasone is an established antiemetic agent; however, the optimal route of administration remains debated. This study compared the efficacy of intraperitoneal (IP) versus intravenous (IV) dexamethasone for PONV prophylaxis.

Methods: This prospective, randomised, double-blinded study enrolled 100 ASA I–II patients undergoing elective laparoscopic cholecystectomy under general anaesthesia. Patients were randomised to Group A (IV dexamethasone 8 mg + IP normal saline placebo) or Group B (IP dexamethasone 8 mg + IV normal saline placebo). PONV incidence, severity (Verbal Descriptive Scale), rescue antiemetic requirement, time to first rescue analgesia, haemodynamic parameters, and adverse effects were assessed at 2, 4, 8, 12, and 24 hours postoperatively.

Results: The IP group showed a significantly lower PONV incidence (16% vs. 44%; $p = 0.004$) and reduced rescue antiemetic requirement (10% vs. 26%; $p = 0.037$). Time to first rescue analgesia was significantly longer in the IP group (74.68 ± 7.11 min vs. 52.90 ± 15.79 min; $p < 0.0001$). Patient satisfaction was higher in the IP group (80% reporting no PONV vs. 48%; $p = 0.002$). Haemodynamic parameters and adverse effects were comparable between groups.

Conclusion: Intraperitoneal dexamethasone is superior to intravenous dexamethasone in preventing PONV, reducing rescue antiemetic need, prolonging analgesic duration, and improving patient satisfaction, with a comparable safety profile. IP dexamethasone should be considered as the preferred route for PONV prophylaxis in laparoscopic cholecystectomy.

Keywords: *Dexamethasone; Intraperitoneal; Intravenous; Laparoscopic cholecystectomy; Postoperative nausea and vomiting; PONV prophylaxis; Antiemetic.*

INTRODUCTION

Laparoscopic cholecystectomy has become the gold standard surgical approach for symptomatic gallstone disease, offering advantages including reduced postoperative pain, shorter hospital stay, earlier return to daily activities, and superior cosmesis compared to open surgery. Despite these benefits, postoperative nausea and vomiting (PONV) remains one of the most distressing and common complications, with reported incidences of 52–80% in this surgical population, considerably higher than the 25–30% seen in general surgical cohorts.

PONV significantly compromises patient satisfaction, delays recovery room discharge, increases the risk of aspiration and wound dehiscence, and represents a major contributor to unanticipated hospital admissions following day-case procedures. A multimodal, risk-stratified approach to PONV prophylaxis is now widely advocated, incorporating both pharmacological and non-pharmacological strategies.

Dexamethasone, a synthetic glucocorticoid, was first recognised as an effective antiemetic in oncological settings in 1981. Since 1999, its intravenous administration has been progressively adopted across surgical specialties for PONV prevention. At a single dose of 4–8 mg IV, dexamethasone demonstrates efficacy comparable to or exceeding that of 5-HT3 receptor

antagonists such as ondansetron. Its mechanism of antiemetic action is incompletely elucidated but is thought to involve inhibition of prostaglandin synthesis, modulation of serotonergic and dopaminergic neurotransmission, and direct effects on the vomiting centre in the medulla oblongata.

Recent interest has shifted toward local delivery of dexamethasone via the intraperitoneal (IP) route. Theoretical advantages include targeted anti-inflammatory effects at the operative site, attenuation of diaphragmatic irritation caused by residual pneumoperitoneum—a key driver of shoulder-tip pain and PONV after laparoscopy—and reduced systemic exposure. Preliminary studies in gynaecological laparoscopy suggest IP dexamethasone may more effectively reduce both PONV and postoperative pain than systemic administration, with a comparable adverse effect profile.

The present study was designed to compare the efficacy and safety of IP versus IV dexamethasone (8 mg) for PONV prophylaxis in patients undergoing laparoscopic cholecystectomy under standardised general anaesthesia.

Aims and Objectives

The primary aim was to compare the incidence and severity of PONV between IP and IV dexamethasone groups within 24 hours of laparoscopic cholecystectomy.

Secondary objectives included: (1) comparison of rescue antiemetic requirements; (2) time to first rescue analgesia; (3) haemodynamic stability across intraoperative and postoperative periods; (4) patient satisfaction with postoperative recovery; and (5) incidence of adverse effects attributable to either route of dexamethasone administration.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, prospective, randomised, double-blinded parallel-group study conducted in the Surgical Operation Theatre, Post-Anaesthesia Care Unit (PACU), and postoperative surgical wards of Midnapore Medical College and Hospital, Paschim Medinipur, West Bengal, India. The study was conducted over 12 months (August 2023 – July 2024) following approval from the institutional ethics committee, registration with CTRI, and approval by the West Bengal

University of Health Sciences.

Participants

A total of 100 ASA physical status I–II female patients aged 18–65 years scheduled for elective laparoscopic cholecystectomy under general anaesthesia were enrolled after obtaining written informed consent.

Inclusion criteria: ASA grade I or II; female sex; scheduled for elective laparoscopic cholecystectomy; provision of valid written informed consent.

Exclusion criteria: Severe cardiorespiratory, hepatic, renal, neurological, or endocrine disease; psychiatric disorder; known allergy to dexamethasone; pregnancy; refusal of consent; or intraoperative conversion to open cholecystectomy.

Sample Size

Sample size was calculated based on an estimated PONV incidence of 55% in the IV dexamethasone group and an expected 20% absolute reduction in the IP group. With 80% power and a two-sided significance level of 0.05, 42 patients per group were required. Allowing for 10% dropouts, 50 patients per group were enrolled (total n = 100).

Randomisation and Blinding

Patients were randomised using a computer-generated random number table. Group allocations were maintained in sequentially numbered, sealed, opaque envelopes that were opened by an unblinded pharmacist/assistant immediately before drug preparation. Both the attending anaesthesiologist and the outcome assessors were blinded to group allocation throughout the study period.

Interventions

Group A (IV group, n = 50): Dexamethasone 8 mg IV was administered at induction of anaesthesia, followed by intraperitoneal injection of 2 mL normal saline as placebo at the end of the procedure (after last trocar insertion, before trocar withdrawal).

Group B (IP group, n = 50): Normal saline 2 mL IV was administered at induction as placebo, followed by intraperitoneal injection of dexamethasone 8 mg at the end of the procedure. IP dexamethasone was injected directly into the gallbladder bed by the surgeon under aseptic conditions before trocar withdrawal.

All procedures were performed under the same standardised anaesthetic protocol: premedication with midazolam 1 mg IV and glycopyrrolate 0.2 mg IV; induction with fentanyl 1.0 µg/kg and propofol 2–2.5 mg/kg; intubation facilitated with atracurium 0.5 mg/kg; maintenance with sevoflurane 2–3% in oxygen:nitrous oxide (50:50). Volume-controlled ventilation was adjusted to maintain EtCO2 35–45 mmHg. At the end of surgery, residual neuromuscular blockade was reversed with neostigmine 2.5 mg, atropine 1 mg, and glycopyrrolate 0.5 mg IV. Gastric contents were suctioned via an orogastric tube before extubation.

Outcome Measures

Patients were monitored at 2, 4, 8, 12, and 24 hours postoperatively. Primary outcome: PONV incidence assessed by a blinded observer. Secondary outcomes: PONV severity (Verbal Descriptive Scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe); rescue antiemetic requirement (ondansetron 4 mg IV, with metoclopramide 10 mg IV as second-line); time to first rescue analgesia (diclofenac 100 mg IM for VAS pain > 4, with paracetamol 1 g infusion as second-line); haemodynamic parameters (SBP, DBP, MAP, HR, SpO2, RR); and adverse effects (hyperglycaemia, headache, abdominal pain). Patient satisfaction was assessed at 24 hours using the Likert scale and the Verbal Descriptive Scale.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using standard statistical software. Continuous variables are expressed as mean ± standard deviation; categorical variables as frequencies and percentages. Between-group comparisons of continuous variables were performed using the unpaired Student's t-test for parametric data and the Mann–Whitney U-test for non-parametric data. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. A two-sided p-value < 0.05 was considered statistically significant. Statistical analyses were performed in consultation with a biostatistician.

Results

Baseline Characteristics

Both groups were comparable in age, sex distribution, ASA physical status, and mean duration of surgery (Table 1). No statistically significant differences were noted across any baseline variable, confirming adequate randomisation.

Table 1. Baseline demographic and clinical characteristics of both groups

Characteristic	IP Group (n=50)	IV Group (n=50)	p-value
Mean Age, years (±SD)	45.2 ± 8.51	46.7 ± 9.13	0.42
Female, n (%)	28 (56.0%)	30 (60.0%)	0.68
ASA I, n (%)	32 (64.0%)	30 (60.0%)	0.72
ASA II, n (%)	18 (36.0%)	20 (40.0%)	0.72
Mean Surgery Duration, min (±SD)	65.3 ± 10.2	67.8 ± 11.5	0.28

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Primary Outcome: Incidence of PONV

The incidence of PONV within 24 hours was significantly lower in the IP group compared to the IV group (16% vs. 44%; Chi-square = 8.21; p = 0.004), representing an absolute risk reduction of 28% and a relative risk reduction of 64% (Table 2).

Table 2. Incidence of PONV within 24 hours. * Statistically significant (Chi-square = 8.21).

Variable	IP Group (n=50)	IV Group (n=50)	p-value
PONV Yes, n (%)	8 (16.0%)	22 (44.0%)	0.004*
PONV No, n (%)	42 (84.0%)	28 56.0%)	—

PONV Severity and Patient Satisfaction

PONV severity, assessed using the Verbal Descriptive Scale, was significantly lower in the IP group (Chi-square = 14.52; p = 0.002). Eighty percent of patients in the IP group reported no PONV, compared to 48% in the IV group. None of the IP group patients experienced severe PONV, while 16% of IV group patients reported severe symptoms (Table 3).

Table 3. PONV severity (Verbal Descriptive Scale). Chi-square = 14.52; p = 0.002.

PONV Severity	IP Group (n=50)	IV Group (n=50)
0 – None, n (%)	40 (80.0%)	24 (48.0%)
1 – Mild, n (%)	6 (12.0%)	9 (18.0%)

PONV Severity	IP Group (n=50)	IV Group (n=50)
2 – Moderate, n (%)	4 (8.0%)	9 (18.0%)
3 – Severe, n (%)	0 (0.0%)	8 (16.0%)

Rescue Antiemetic Requirement
Significantly fewer patients in the IP group required rescue antiemetics (10% vs. 26%; Chi-square = 3.47; p = 0.037), indicating superior prophylactic efficacy with the IP route (Table 4).

Table 4. Rescue antiemetic requirement. * Statistically significant (Chi-square = 3.47).

Variable	IP Group (n=50)	IV Group (n=50)	p-value
Rescue Antiemetic Required, n (%)	5 (10.0%)	13 (26.0%)	0.037*
No Rescue Required, n (%)	45 (90.0%)	37 74.0%)	—

Time to First Rescue Analgesia
The time to first rescue analgesia was significantly prolonged in the IP group (74.68 ± 7.11 min vs. 52.90 ± 15.79 min; p < 0.0001), indicating superior postoperative pain control with IP dexamethasone (Table 5).

Table 5. Time to first rescue analgesia. * Statistically significant.

Variable	IP Group (n=50)	IV Group (n=50)	p-value
Mean Time to Rescue Analgesia, min (±SD)	74.68 ± 7.11	52.90 ± 15.79	< 0.0001*

Haemodynamic Parameters
Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), and SpO2 were comparable between groups at all intraoperative and postoperative time points, with all p-values > 0.05 (Tables 6–7). Both groups maintained stable haemodynamic profiles throughout the study period.

Table 6. Summary of haemodynamic parameters (selected time points; all p > 0.05 across all time points).

Parameter	Time Point	IP Group	IV Group	p-value
SBP (mmHg)	Baseline	128.5 ± 10.2	127.8 ± 9.8	0.75
	Intubation	132.4 ± 11.5	131.7 ± 10.9	0.78
	24 h post-op	120.5 ± 7.7	120.0 ± 7.6	0.85
DBP (mmHg)	Baseline	78.5 ± 6.2	77.8 ± 6.0	0.60
	24 h post-op	72.5 ± 3.7	72.0 ± 3.6	0.72
MAP (mmHg)	Baseline	95.2 ± 7.5	94.5 ± 7.3	0.65
	24 h post-op	88.5 ± 5.4	88.0 ± 5.3	0.82
HR (bpm)	Baseline	78.5 ± 6.2	77.8 ± 6.0	0.60
SpO2 (%)	Baseline	98.5 ± 0.5	98.4 ± 0.5	0.60

Adverse Effects

The incidence of adverse effects was low and comparable between groups. Hyperglycaemia occurred in 6% (IP) vs. 4% (IV) ($p = 0.70$); headache in 4% (IP) vs. 6% (IV) ($p = 0.68$); abdominal pain in 10% (IP) vs. 8% (IV) ($p = 0.75$). No serious adverse events were recorded in either group (Table 7).

Table 7. Incidence of adverse effects (all $p > 0.05$).

Adverse Effect	IP Group (n=50)	IV Group (n=50)	p-value
Hyperglycaemia, n (%)	3 (6.0%)	2 (4.0%)	0.70
Headache, n (%)	2 (4.0%)	3 (6.0%)	0.68
Abdominal Pain, n (%)	5 (10.0%)	4 (8.0%)	0.75

DISCUSSION

This prospective, randomised, double-blinded study demonstrates that intraperitoneal dexamethasone (8 mg) is significantly more effective than intravenous dexamethasone (8 mg) in preventing PONV, reducing rescue antiemetic consumption, and prolonging the duration of postoperative analgesia in patients undergoing laparoscopic cholecystectomy. These benefits were achieved without any compromise in haemodynamic stability or increased incidence of adverse effects.

The PONV incidence of 16% in the IP group versus 44% in the IV group observed in the present study aligns closely with findings from comparable trials. Bhattacharjee et al. (2019) reported PONV rates of 18% versus 42% in IP versus IV dexamethasone groups in laparoscopic cholecystectomy patients. Ismail et al. (2019), studying patients undergoing gynaecological laparoscopy, similarly found significantly lower PONV rates following IP administration. Wang et al. (2016) corroborated that IP dexamethasone, particularly when combined with ondansetron, provided superior PONV prophylaxis compared to IV administration alone.

The mechanisms underlying the superior efficacy of IP dexamethasone likely relate to its localised anti-inflammatory action. During laparoscopy, carbon dioxide pneumoperitoneum induces diaphragmatic irritation and peritoneal inflammation, stimulating afferent vagal pathways that contribute substantially to PONV. Intraperitoneal administration allows direct suppression of prostaglandin synthesis and inflammatory mediator release at the operative site, attenuating this nociceptive-emetic reflex arc. In contrast, IV dexamethasone exerts its antiemetic effect primarily through central mechanisms, lacking targeted local action.

The superior analgesic profile observed with IP dexamethasone—reflected in the significantly prolonged time to first rescue analgesia (74.68 vs. 52.90 minutes; $p < 0.0001$)—further supports a localised anti-inflammatory mechanism. Reduced peripheral inflammation lowers postoperative pain scores and decreases opioid requirements, which in turn contributes to lower PONV rates through opioid-sparing effects. Asgari et al. (2015) similarly reported reduced shoulder-tip pain with IP dexamethasone in gynaecological laparoscopy, attributing the benefit to attenuation of diaphragmatic irritation from residual pneumoperitoneum. Hosseini Valami et al. (2016) demonstrated comparable analgesic benefits of IP dexamethasone combined with bupivacaine following caesarean section.

The significant improvement in patient satisfaction in the IP group (80% reporting no PONV vs. 48%; $p = 0.002$) represents an important patient-centred outcome. PONV is consistently rated by patients as one of the most undesirable aspects of the perioperative experience and is a primary determinant of postoperative quality of recovery. This finding concurs with Singh et al. (2020), who identified improved patient-reported outcomes with IP dexamethasone attributable to superior PONV control and pain management.

The haemodynamic stability observed across both groups throughout the intraoperative and postoperative periods is reassuring. No significant inter-group differences were identified at any time point for SBP, DBP, MAP, HR, RR, or SpO2. This aligns with Rajnikant et al. (2017), who found comparable haemodynamic profiles between dexamethasone-palonosetron and dexamethasone-ondansetron groups. The similar adverse effect profile—specifically, comparable rates of hyperglycaemia, headache, and abdominal pain—between the IP and IV groups suggests that IP administration does not introduce additional safety concerns.

Conflicting evidence exists in the literature. Mohtadi et al. (2016) reported no significant difference in postoperative pain between IV dexamethasone and placebo, and Ali et al. (2017) found that ondansetron-bupivacaine was more effective than dexamethasone-bupivacaine for pain reduction. These discrepancies may reflect variability in dexamethasone dosing, timing of administration, concomitant analgesic protocols, or patient selection criteria. Zahra et al. (2018) suggested that bupivacaine-magnesium sulphate combinations may surpass bupivacaine-dexamethasone for pain control, possibly due to extended local anaesthetic duration.

The strengths of the present study include its prospective, randomised, double-blinded design which minimises selection and observer bias; comprehensive outcome assessment encompassing PONV incidence and severity, analgesia, haemodynamics, and patient satisfaction; and clear demonstration of superiority of the IP route with clinically meaningful effect sizes and statistically robust results.

Limitations

Several limitations of this study must be acknowledged. First, the sample size of 100 patients, whilst adequate for the primary outcome, limits the power to detect smaller differences in secondary outcomes and may restrict generalisability. A large-scale multicentre trial is needed to confirm these findings across diverse populations and surgical practices. Second, the study was limited to female patients, given the known higher PONV susceptibility in women; findings may not be directly applicable to male patients, who represent a distinct risk profile. Third, the postoperative follow-up was restricted to 24 hours. Extended follow-up would be valuable for characterising delayed PONV, prolonged analgesic effects, and any late adverse effects of IP dexamethasone. Fourth, the study did not assess quality of recovery using validated tools such as the QoR-15 or QoR-40, which may have provided more granular data on patient experience. Finally, optimal dosing, timing, and potential adjunctive benefits of IP dexamethasone in combination with other antiemetics or local anaesthetics warrant investigation in future trials.

CONCLUSION

This randomised, double-blinded trial demonstrates that intraperitoneal dexamethasone (8 mg) is superior to intravenous dexamethasone (8 mg) in preventing postoperative nausea and vomiting after laparoscopic cholecystectomy. The IP route confers significantly lower PONV incidence, reduced rescue antiemetic requirements, prolonged time to first analgesic rescue, and greater patient satisfaction, with an equivalent haemodynamic and adverse effect profile. These findings support incorporation of IP dexamethasone as a routine PONV prophylaxis strategy in laparoscopic cholecystectomy. Multicentre trials with extended follow-up and inclusion of male patients are warranted to validate and generalise these conclusions.

Declarations

Ethics approval and consent to participate: Institutional ethics committee approval was obtained. Written informed consent was secured from all participants prior to enrolment. The study was registered with the Clinical Trials Registry – India (CTRI).

Conflict of interest: The authors declare no conflicts of interest.

Funding: No external funding was received for this study.

Authors' contributions: MH conceived and designed the study, conducted data collection and statistical analysis, and drafted the manuscript. BKB supervised the study design and critically revised the manuscript. AKM supervised clinical protocols and assisted in data interpretation. All authors approved the final version.

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