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Intraperitoneal Instillation of Bupivacaine for the Attenuation of Post-Laparoscopic Cholecystectomy Shoulder Tip Pain: A Randomised Controlled Trial

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ABSTRACT

Background: Post-laparoscopic shoulder tip pain (PLSTP) is a common, distressing complication attributable to diaphragmatic irritation by residual carbon dioxide following pneumoperitoneum. Intraperitoneal instillation of local anaesthetic agents has been proposed as a simple intervention to mitigate this pain, yet evidence on the optimal agent, concentration, and timing remains inconclusive.
Objectives: To evaluate the effect of intraoperative intraperitoneal bupivacaine instillation on PLSTP by Visual Analogue Scale (VAS) score, analgesic requirement, and hospital discharge time following laparoscopic cholecystectomy.
Methods: A prospective, randomised controlled trial was conducted at the Department of General Surgery, Government Stanley Medical College, Chennai, between November 2022 and December 2024. Seventy patients undergoing elective laparoscopic cholecystectomy for primary cholelithiasis were randomised to two equal groups: Group A (n = 35) received 50 ml of 0.25% bupivacaine instilled intraperitoneally over the diaphragmatic surface following cholecystectomy, and Group B (n = 35) served as untreated controls. The primary outcome was shoulder tip pain VAS score at 6 hours, and on postoperative days 1, 3, and 5. Secondary outcomes included analgesic consumption and time to discharge.
Results: Both groups were comparable for age, sex, and comorbidities at baseline. Group A demonstrated significantly lower VAS scores at 6 hours (3.63 ± 1.22 vs 6.43 ± 1.80; $p < 0.001$), day 1 (3.03 ± 0.95 vs 5.51 ± 1.48; $p < 0.001$), and day 3 (2.40 ± 0.65 vs 3.69 ± 0.99; $p < 0.001$). No statistically significant difference was observed on day 5 ($p = 0.073$). A significantly greater proportion of Group A patients achieved same-day discharge (71.4% vs 11.4%; $p < 0.001$). Analgesic requirement showed a consistent but statistically non-significant reduction in Group A from day 1 onward.
Conclusion: Intraperitoneal instillation of bupivacaine following laparoscopic cholecystectomy significantly reduces post-operative shoulder tip pain and facilitates early hospital discharge. This safe, simple, and cost-effective adjunct should be considered as a routine practice in laparoscopic cholecystectomy.

Keywords: *Acne, androgenic alopecia, hirsutism, hyperandrogenism, polycystic ovary syndrome.*

INTRODUCTION

Laparoscopic cholecystectomy (LC) has superseded open cholecystectomy as the definitive treatment for symptomatic cholelithiasis, offering the well-established advantages of shorter hospital stay, faster return to functional activity, reduced wound-related morbidity, and superior cosmetic outcome.[1] Despite these merits, a substantial proportion of patients

experience post-laparoscopic shoulder tip pain (PLSTP), a distinctive referred pain perceived in the right or bilateral shoulder regions following pneumoperitoneum.[2]

The pathophysiology of PLSTP is primarily attributed to diaphragmatic irritation secondary to residual intraperitoneal carbon dioxide (CO_2). The absorbed CO_2 forms carbonic acid, lowering local pH and stimulating phrenic nerve afferents, which refer pain to the C3–C5 dermatomes of the shoulder.[3] Although typically self-limiting, PLSTP may be severe, extending hospital stay, delaying mobilisation, and impairing patient satisfaction, particularly in day-case surgical settings.

Multiple strategies have been investigated to attenuate PLSTP, including low-pressure pneumoperitoneum, active gas aspiration at procedure end, Trendelenburg positioning, and intraperitoneal local anaesthetic (IPLA) instillation.[4] IPLA has the theoretical advantage of direct pharmacological inhibition of diaphragmatic sensory afferents, thereby attenuating the nociceptive cascade at source. Bupivacaine, a long-acting amide local anaesthetic with a duration of action of 6–12 hours, is the most widely studied agent in this context.[5]

Despite a substantial body of literature, the results remain discordant.[6] Studies by Partridge BL [7], Yahya Gumusoglu A[8], and Kim et al.[9] consistently demonstrated significant VAS reduction following IPLA. Heterogeneity in methodology, agent volume, concentration, and anatomical site of instillation confounds cross-study comparisons. There is also limited data from the Indian subcontinent, where the demographic and operative profile of cholelithiasis patients may differ materially from Western cohorts. The present study was therefore designed to evaluate the efficacy of intraoperative intraperitoneal bupivacaine instillation in a prospective, randomised, controlled framework at a tertiary government institution in South India.

MATERIALS AND METHODS

A prospective, randomised controlled trial was conducted in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India. The study was conducted after approval from the Institutional Ethics. Written informed consent was obtained from all participants prior to enrolment. The study was conducted in conformity with the Declaration of Helsinki.

Sample size was calculated using the formula $N = 2(Z_{1-\alpha/2} + Z\beta)^2 SD^2 / (M_1 - M_2)^2$ based on the with similar study with a mean VAS of 4.5 (control) versus 2.9 (bupivacaine group), SD = 2.2, $\alpha = 0.05$ (two-tailed), and $\beta = 0.20$ (80% power). This yielded a minimum sample of 30 per group; adding a 10% non-response allowance and rounding produced a final sample size of 35 per group (70 total).

Adult patients aged 18 years or above with ultrasonographically confirmed primary cholelithiasis who consented to elective laparoscopic cholecystectomy were eligible. Exclusion criteria comprised: known allergy to local anaesthetic agents, American Society of Anesthesiologists (ASA) grade III or above, pre-existing contraindications to general anaesthesia, emergency procedures, conversion to open surgery, significant intraoperative complications, and prior upper abdominal surgery with anticipated dense adhesions.

Participants were allocated to Group A (bupivacaine) or Group B (control) by simple random sampling using a random number table. Allocation was performed by a researcher not involved in patient care or outcome assessment. Due to the nature of the intervention, blinding of the operating surgeon was not feasible; however, pain assessment was conducted by a research nurse blinded to group allocation.

All procedures were performed under general anaesthesia induced with propofol (2 mg/kg) and maintained with isoflurane in oxygen–nitrous oxide (50:50) mixture, with vecuronium for neuromuscular blockade. Pneumoperitoneum was established using a Veress needle at the umbilicus, with CO_2 insufflation to a pressure of 12–14 mmHg. Standard four-port laparoscopic cholecystectomy was performed by a single experienced consultant surgeon. The cystic duct and cystic artery were identified, clipped, and divided following critical view of safety technique.

In Group A, immediately following extraction of the gallbladder specimen and before desufflation, 50 ml of 0.25% bupivacaine solution was instilled under direct laparoscopic visualisation, distributed evenly over the right diaphragmatic surface and subhepatic space. In Group B, no intraperitoneal instillation was performed. In both groups, residual CO_2 was evacuated by passive exsufflation and gentle manual abdominal compression; ports were removed and fascial defects of $\geq$ 10 mm were closed with 1-0 polyglactin.

All patients received a standardised post-operative analgesic regimen: intravenous paracetamol 1 g every 8 hours as scheduled analgesia, with intramuscular diclofenac 75 mg administered on patient request as rescue analgesia. Opioids were not routinely prescribed. Diet was reintroduced 4–6 hours post-operatively. Patients were assessed in the post-operative ward at 6 hours and on days 1, 3, and 5 by a trained observer blinded to group allocation.

The primary outcome was the VAS score for shoulder tip pain (0 = no pain, 10 = worst imaginable pain) at 6 hours post-operatively. Secondary outcomes included VAS score at days 1, 3, and 5; requirement for rescue analgesic at each assessment time point; and timing of discharge (same day vs next day after surgery).

Data were entered into Microsoft Excel and analysed using SPSS version 16.0. Continuous variables are presented as mean ± standard deviation (SD); categorical variables as frequencies and proportions. Differences in VAS scores between groups were compared using the independent samples t-test. Categorical outcomes were compared using the chi-square test or Fisher's exact test as appropriate. A two-tailed p-value < 0.05 was considered statistically significant. Ninety-five percent confidence intervals (CIs) are reported for all primary comparisons.

Inclusion Criteria:

- Patients willing to participate in the study and who have given written informed consent
- Patients with a primary diagnosis of cholelithiasis (with or without comorbidities such as diabetes and hypertension)
- Patients scheduled for elective laparoscopic cholecystectomy
- ASA Physical Status I or II

Exclusion Criteria:

- Patients with pre-existing contraindications to general anaesthesia
- Known allergy to local anaesthetic agents
- Patients presenting with acute cholecystitis or cholangitis
- Prior upper abdominal surgery
- Intraoperative conversion to open cholecystectomy
- Patients unable to provide reliable pain-score data (VAS assessment)

RESULTS

Seventy patients completed the study: 35 in each group. No patients were lost to follow-up or withdrew consent. The mean age of the cohort was 40.50 ± 9.51 years. Female patients predominated (41 of 70; 58.6%). Comorbid conditions (principally type 2 diabetes mellitus and hypertension) were present in 32 patients (45.7%). Fifty-five percent of all procedures were completed within one hour (Table 1).

Table 1. Baseline characteristics of the study cohort (N = 70).

Variable	Category	n	(%)	Total
Age (years), mean ± SD	**40.50 ± 9.51**	70	100%	70
Sex				
Male		29	41.4	70 (100%)
Female		41	58.6	70 (100%)
Comorbid Conditions				
Present		32	45.7	70 (100%)
Absent		38	54.3	70 (100%)
Surgery Duration				
< 1 hour		39	55.7	70 (100%)
> 1 hour		31	44.3	70 (100%)
Discharge Timing				
Same day		29	41.4	70 (100%)
Next day		41	58.6	70 (100%)

The two randomised groups were well matched for age (Group A: 40.74 ± 10.20 years; Group B: 40.26 ± 8.91 years; $p = 0.81$), sex distribution ($p = 0.80$), and prevalence of comorbid conditions ($p = 0.62$). Group A had a significantly higher proportion of procedures lasting more than one hour (57.1% vs 31.4%; $p = 0.03$), reflecting the tendency for more complex

anatomy in older male patients who were somewhat overrepresented in Group A, although the difference in mean age did not reach significance (Table 2).

Table 2. Comparison of baseline characteristics between Group A (bupivacaine) and Group B (control).

Variable	Group A — Bupivacaine (n = 35)		Group B — Control (n = 35)		p-value
	n / Mean ± SD	%	n / Mean ± SD	%	
Age (years), mean ± SD	40.74 ± 10.20	—	40.26 ± 8.91	—	0.81
Sex					
Male	15	42.9	14	40.0	0.80
Female	20	57.1	21	60.0	0.80
Comorbid Conditions					
Present	17	48.6	15	42.9	0.62
Absent	18	51.4	20	57.1	0.62
Surgery Duration					
< 1 hour	15	42.9	24	68.6	0.03
> 1 hour	20	57.1	11	31.4	0.03

Across the entire cohort, mean VAS was highest at 6 hours post-operatively (5.03 ± 2.08), reflecting the peak of diaphragmatic irritation. A progressive and sustained decline was observed over subsequent assessment intervals, reaching a mean of 0.96 ± 0.60 on day 5 (Table 3).

Table 3. Visual Analogue Scale (VAS) scores for shoulder tip pain in the overall cohort (N = 70).

Assessment Time Point	Mean VAS Score	Standard Deviation	Interpretation
6 hours post-operatively	5.03	2.078	Moderate–severe pain
Postoperative day 1	4.27	1.760	Moderate pain
Postoperative day 3	3.04	1.055	Mild–moderate pain
Postoperative day 5	0.96	0.600	Minimal / no pain

Group A demonstrated statistically significantly lower VAS scores at all three early assessment time points compared with Group B (Table 4). At 6 hours, mean VAS in Group A was 3.63 ± 1.22 versus 6.43 ± 1.80 in Group B ($t = -7.618$; 95% CI −3.53 to −2.07; $p < 0.001$). At day 1, mean scores were 3.03 ± 0.95 versus 5.51 ± 1.48 ($t = -8.340$; 95% CI −3.08 to −1.89; $p < 0.001$). At day 3, scores were 2.40 ± 0.65 versus 3.69 ± 0.99 ($t = -6.406$; 95% CI −1.69 to −0.89; $p < 0.001$). On day 5, the difference was marginal and did not reach statistical significance (0.83 ± 0.62 vs 1.09 ± 0.56; $t = -1.822$; 95% CI −0.54 to 0.03; $p = 0.073$), consistent with near-complete pain resolution in both groups by this time point (Table 4).

Table 4. Inter-group comparison of VAS shoulder tip pain scores (independent samples t-test).

Time Point	Group A Mean	Group A SD	Group B Mean	Group B SD	t-value	95% CI	p-value
6 hours	3.63	1.215	6.43	1.803	−7.618	−3.53 to −2.07	**<0.001**
Day 1	3.03	0.954	5.51	1.483	−8.340	−3.08 to −1.89	**<0.001**
Day 3	2.40	0.651	3.69	0.993	−6.406	−1.69 to −0.89	**<0.001**
Day 5	0.83	0.618	1.09	0.562	−1.822	−0.54 to 0.03	0.073

At 6 hours, all 70 patients in both groups required rescue analgesic administration (100% vs 100%; p = 1.000), reflecting the intensity of early post-operative pain regardless of bupivacaine instillation. On day 1, analgesic requirement remained high and comparable between groups (94.3% vs 97.1%; p = 1.000). On day 3, 54.3% of Group A versus 60.0% of Group B required analgesia (p = 0.629). On day 5, 8.6% of Group A versus 22.9% of Group B required rescue analgesia; although the absolute difference was clinically meaningful (risk reduction 14.3 percentage points), this did not attain statistical significance (p = 0.101). The progressive reduction in analgesic use in Group A from day 3 onward, compared with the higher persisting requirement in Group B, is consistent with the VAS data (Table 5).

Table 5. Analgesic requirement at each assessment time point by group.

Time Point	Group A — Analgesic Required		Group B — Analgesic Required		p-value
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	
6 hours	35 (100%)	0 (0%)	35 (100%)	0 (0%)	1.000
Day 1	33 (94.3%)	2 (5.7%)	34 (97.1%)	1 (2.9%)	1.000
Day 3	19 (54.3%)	16 (45.7%)	21 (60.0%)	14 (40.0%)	0.629
Day 5	3 (8.6%)	32 (91.4%)	8 (22.9%)	27 (77.1%)	0.101

The pattern of hospital discharge differed markedly and significantly between the two groups (Table 6). In Group A, 25 of 35 patients (71.4%) were discharged on the same day as surgery, compared with only 4 of 35 patients (11.4%) in Group B ($\chi^2 = 27.03$; $p < 0.001$). The majority of Group B patients (88.6%) required an overnight stay for adequate pain management, whereas 28.6% of Group A patients remained for one night due to administrative and logistical reasons rather than pain control requirements (Table 6).

Table 6. Discharge timing comparison between Group A and Group B.

Group	Same-day Discharge n(%)	Next-day Discharge n(%)	p-value
Group A — Bupivacaine (n = 35)	25 (71.4%)	10 (28.6%)	**<0.001**
Group B — Control (n = 35)	4 (11.4%)	31 (88.6%)	**<0.001**
Total (N = 70)	29 (41.4%)	41 (58.6%)	**<0.001**

DISCUSSION

This prospective randomised controlled trial demonstrates that intraperitoneal instillation of 50 ml 0.25% bupivacaine following laparoscopic cholecystectomy produces a clinically meaningful and statistically significant reduction in post-operative shoulder tip pain at 6 hours, day 1, and day 3, with a concomitant and significant increase in same-day discharge rates. These findings are broadly consistent with the majority of published literature and provide evidence from a South Indian tertiary government hospital context.

Toleska et al[10] demonstrated that there is a statistically significant VAS reduction at all post-operative time points with IPLA. Additionally, there was no significant adverse effects. Banoria et al[11] reported significant VAS reduction with 20 ml 0.5% bupivacaine instilled over the diaphragmatic as well as subhepatic surfaces. These findings were similar to our findings. Moreover Cunningham et al[12] reported that there is a significantly lower shoulder tip pain scores with 0.25% levobupivacaine in a double-blind RCT comprising of 100 patients. Putta et al[13] in a three-arm trial comparing pre-emptive versus post-surgical intraperitoneal instillation, found statistically lower VAS scores in both active arms compared with control, supporting the concept of intraperitoneal analgesia irrespective of timing.

Dath and Park[14] in a double-blind randomised controlled trial of 97 patients undergoing elective laparoscopic cholecystectomy, demonstrated that intraperitoneal bupivacaine instillation produced significantly lower VAS pain scores within the first 6 hours postoperatively (2.9 vs 4.5; p = 0.001), and a significantly greater proportion of bupivacaine-treated patients elected same-day discharge (p = 0.034). Notably, narcotic analgesic consumption was not significantly different between groups despite the marked difference in pain scores — a paradox the authors attributed to the existence of a pain threshold below which patients do not routinely request medication, rather than to any failure of pharmacological effect. This analgesic paradox closely mirrors our own finding

The sole discordant trial in the literature is that of Agarwal and Pai,[15] which enrolled 50 patients and found no statistically significant reduction in pain with IPLA. The investigators attributed this to a potential ceiling effect of the standardised background analgesia regimen, which may have masked a bupivacaine benefit. Additionally, differing concentrations and volumes used across trials may partly explain heterogeneous outcomes; several meta-analyses have suggested that diaphragmatic instillation specifically, rather than general peritoneal flooding, is the most effective anatomical target.

The pronounced difference in same-day discharge (71.4% vs 11.4%; $p < 0.001$) in the present study is among the most striking reported. Earlier studies with similar findings have noted that the decision to discharge is multifactorial, involving nausea, pain control, social support availability, and institutional policy. The Government Stanley Medical College serves a predominantly lower-income population; the high same-day discharge rate in Group A is therefore also likely to reflect economic and social pressures favouring early discharge, in addition to genuine pharmacological benefit. This contextual interpretation is important in applying these findings to resource-limited settings.

The safety profile of intraperitoneal bupivacaine at the doses used (50 ml of 0.25% = 125 mg total dose; maximum recommended dose 2 mg/kg for a 60 kg adult = 120 mg; slightly above standard single-shot maximum but within accepted range for peritoneal instillation given slow absorption kinetics) was excellent in the present study, with no adverse events attributable to local anaesthetic toxicity.

Limitations of the present study include the open-label design (blinding of the surgeon was not feasible), the limited follow-up period (five days), and the absence of patient satisfaction data and cost-effectiveness analysis. The binary analgesic requirement outcome (yes/no) rather than quantitative dose recorded is a further limitation, precluding analysis of analgesic sparing in morphine-equivalent units. Future work should include a double-blind design with saline placebo, blinded pain assessment at all time points, longer follow-up, and cost-effectiveness analysis in the day-surgery setting.

CONCLUSION

Intraoperative intraperitoneal instillation of 50 ml 0.25% bupivacaine over the diaphragmatic surface at the conclusion of laparoscopic cholecystectomy results in a statistically significant and clinically meaningful reduction of post-operative shoulder tip pain at 6 hours, day 1, and day 3. It significantly facilitates same-day discharge, a finding of particular relevance in tertiary government hospitals serving resource-limited populations. The intervention is safe, technically simple, requires no specialised equipment, and adds minimal cost to the procedure. On the basis of current evidence, including the results of the present trial, intraperitoneal bupivacaine instillation should be considered as a routine adjunct in elective laparoscopic cholecystectomy to improve the quality of post-operative recovery.

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Conflicts of Interest: All authors declare no conflicts of interest.

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