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Effect of Intraperitoneal Bupivacaine Irrigation on Postoperative Pain Following Laparoscopic Cholecystectomy: A Randomised Controlled Trial

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Abstract

Background: Postoperative pain remains a significant challenge after laparoscopic cholecystectomy, particularly in resource-limited settings. Local anaesthetic instillation into the liver bed has been proposed as a simple technique to reduce visceral pain and facilitate early recovery. The objective of this study was to evaluate the effectiveness of 0.5% bupivacaine irrigation into the gallbladder bed in reducing postoperative pain severity following laparoscopic cholecystectomy.

Methods: This was a two-arm, double-blind, prospective randomised controlled trial conducted at the Federal Government Polyclinic Hospital, Islamabad, from March to September 2020. Sixty-two patients aged 18–65 years undergoing elective laparoscopic cholecystectomy were randomised equally into intervention (bupivacaine irrigation) and control (standard care without local anaesthetic irrigation) groups. Randomisation used folded paper allocation and was performed by surgical residents; outcome assessors and patients were blinded. The primary outcome was the proportion of patients reporting severe pain at 24 hours postoperatively using a 10-point visual analogue scale (VAS). Secondary outcomes included pain severity stratified by age and gender.

Results: At 24 hours, none of the patients in the bupivacaine group reported severe pain, compared with five (16.1%) in the control group ($p = 0.036$). Younger patients (≤30 years) in the intervention group had significantly lower pain scores compared to controls ($p<0.001$). No significant differences were observed by gender. No adverse events were reported.

Conclusions: Irrigation with 10 ml of 0.5% bupivacaine into the liver bed during laparoscopic cholecystectomy significantly reduced the severity of postoperative pain at 24 hours. This simple intervention may enhance recovery and facilitate early discharge, especially in low-resource settings. Further multicentre trials are recommended to inform standardised postoperative analgesia protocols.

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Introduction

Abdominal pain is one of the most frequently encountered complaints in both emergency and outpatient surgical departments. It may arise from any of the nine anatomical quadrants, each offering clinical clues to its underlying cause. Among these, pain in the right hypochondrium is commonly due to gallstones, making cholecystectomy one of the most frequently performed surgical procedures. Laparoscopic cholecystectomy is now widely regarded as the gold standard treatment for cholelithiasis [1]. The British Association of Day Surgery (BADS) recommends same-day discharge in at least

60 percent of laparoscopic cholecystectomy cases, reflecting its role as a safe, minimally invasive procedure associated with better cosmesis, earlier ambulation, reduced postoperative pain, and shorter hospital stays [2]. The introduction of laparoscopic techniques has revolutionised biliary surgery, including in cases of acute cholecystitis, with improved outcomes reported in clinical practice [3].

Despite these advances, postoperative pain remains a persistent and significant concern. Numerous clinical trials have investigated the efficacy of intravenous, oral, and local drug administration strategies to address pain following laparoscopic surgery. Among these, instillation of local anaesthetics into the liver bed has emerged as a promising approach due to its simplicity, safety, and effectiveness in enhancing postoperative pain control [4]. In laparoscopic procedures, multiple adjunct techniques are employed to minimise pain, including wound infiltration with local anaesthetic agents, reduced pneumoperitoneum pressure, and targeted operative site analgesia [5–7]. A recent study evaluating the intraperitoneal use of 0.5% bupivacaine following laparoscopic cholecystectomy demonstrated a substantial reduction in analgesic requirement. In that study, only 28 percent of patients receiving bupivacaine required further pain relief, compared with 71 percent in the control group [8].

The rationale for this study is to evaluate the effectiveness of bupivacaine instillation into the gallbladder fossa in reducing postoperative pain following laparoscopic cholecystectomy, particularly in a resource-limited healthcare setting. There is a relative paucity of evidence from countries with low human development indices, and current local studies are insufficient to inform systematic reviews or meta-analyses. Reducing the severity of postoperative pain may help facilitate early discharge, support recovery, and alleviate bed occupancy pressures in under-resourced hospitals. The findings of this study may contribute to the body of evidence needed to develop standardised postoperative pain management protocols and support the safe implementation of laparoscopic cholecystectoy as a day-case procedure.

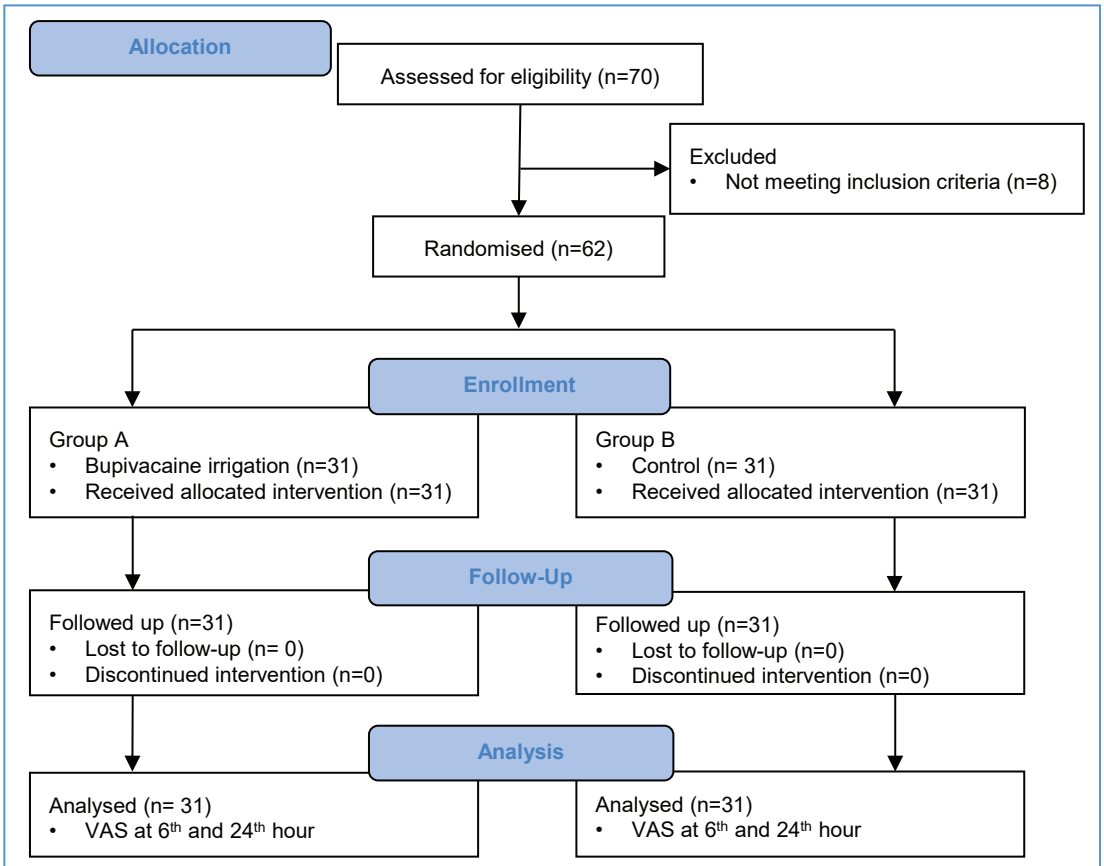

Figure 1: Consort Diagram. (VAS: Visual analogue scale).

Table 1: Comparison of post-cholecystectomy pain severity in both groups on VAS at 24th hour after surgery.

	Group A	Group B	P-value
Mild Pain	20 (64.5%)	13 (41.9%)	
Moderate Pain	11 (35.5%)	13 (41.9%)	
Severe Pain	0 (0%)	5 (16.1%)	0.036
Total	31	31	

Methods

Study Design and Setting

This was a two-arm prospective randomised controlled trial conducted in the Department of General Surgery at the Federal Government Polyclinic Hospital, Islamabad, Pakistan. The study was carried out between 13 March 2020 and 12 September 2020, following approval from the institutional ethical review board. The trial was not registered on a clinical trial registry due to the unavailability of expertise within the hosting institute at the time.

Participants

Eligible participants were patients of either gender, aged 18 to 65 years, undergoing elective laparoscopic cholecystectomy for cholecystitis, cholelithiasis, or gallbladder polyp greater than 1 cm, with no other abdominal pathology. Patients were excluded if they were unable or unwilling to provide informed consent, including due to a language barrier. Additional exclusions included individuals with gallstones receiving chronic pain treatment for unrelated conditions, and those with malignancy, coagulopathy, cirrhosis, ascites, prior abdominal surgery, hepatitis B or C positivity, or conversion from laparoscopic to open cholecystectomy. These exclusions were applied to reduce clinical variability and avoid confounding, as management in patients with chronic or comorbid conditions may differ.

Sample Size and Recruitment

A formal sample size calculation was not conducted prior to the study. Instead, a pragmatic target of 70 patients was chosen based on expected recruitment capacity over the 6-month study period. These patients were approached through non-probability consecutive sampling in the surgical outpatient department and then the exclusion criteria applied. Written informed consent was obtained from all patients after they were provided with details about the purpose, methods, risks and benefits of the study.

Randomisation and Allocation

Participants were randomly assigned to one of two groups in a 1:1 ratio. Randomisation was carried out using a simple method involving folded papers marked 'A' or 'B'. Allocation was determined by postgraduate surgical residents in the order of admission, and assignments were recorded in Excel sheets. Once data had been entered, the allocation cards were discarded. The resulting data sheets remain available for reference. The allocation sequence was concealed using sealed envelopes provided to the operating surgeon before each procedure.

Blinding

This was a double-blind study. The operating consultant surgeons were aware of group allocation in order to perform the assigned intervention. However, patients and outcome assessors, who were registrar-level surgical staff, remained blinded to treatment assignment.

Intervention

All patients underwent laparoscopic cholecystectomy in the morning elective theatre list. In the intervention group, following gallbladder removal, 10 ml of 0.5%

Table 2: Age wise distribution of post-operative pain in both groups

Age	Group	Mild pain	Moderate Pain	Severe Pain	P-value
< 30 years	Group A	5 (83.3%)	1 (16.7%)	0 (0%)	
	Group B	2 (28.6%)	3 (42.9%)	2 (28.6%)	<0.001
31-40 years	Group A	4 (66.7%)	2 (33.3%)	0 (.0%)	
	Group B	2 (66.7%)	1 (33.3%)	0 (.0%)	1
41-50 years	Group A	2 (28.6%)	5 (71.4%)	0 (.0 %)	
	Group B	4 (36.4%)	5 (45.5 %)	2 (18.2 %)	0.393
> 50 years	Group A	9 (75.0%)	3 (25.0%)	0 (.0%)	
	Group B	7 (50.0%)	4 (40.0%)	1 (10.0%)	0.346

bupivacaine was irrigated into the liver bed using a laparoscopic irrigation-suction set. These patients were then placed in a right tilt Trendelenburg position for five minutes to facilitate drug distribution. The control group received standard care without bupivacaine irrigation.

Outcome Assessment and Follow-Up

Pain assessment was carried out at 6 and 24 hours postoperatively using a 10-point visual analogue scale by blinded surgical registrars. Patients were asked to categorise their pain by using a visual analog scale as mild (0-3), moderate (4-6), or severe (7-10) on a scale of 1-10. All patients received the same postoperative analgesic regimen, including NSAIDs. Rescue analgesia in the form of intravenous ketorolac 15 mg (single dose) was administered to patients experiencing severe pain at 6 hours. Those with continuing severe pain at 24 hours remained hospitalised for additional observation, while those with mild to moderate pain were discharged with oral medications and reviewed on postoperative day five.

Data Management and Statistical Analysis

Data were collected on paper forms and entered into Excel spreadsheets to avoid data loss. Statistical analysis was performed using IBM SPSS Statistics version 16. The primary outcome was the proportion of patients experiencing severe pain at 24 hours. Secondary outcomes included analysis of age and gender in relation to pain severity. The chi-square test was used for comparison, with statistical significance set at a p-value of 0.05. In the presentation of baseline characteristics, any reported p-value corresponds specifically to the comparison for severe pain between groups.

Ethics and funding

Ethical approval was granted by the Federal Government Polyclinic Hospital Ethics Review Board. All participants gave written informed consent before taking part in the study. The trial was not registered due to institutional limitations. No external funding was received for this study, as bupivacaine and other resources used were routinely available in the operating theatre.

Results

A total of 62 patients underwent elective laparoscopic cholecystectomy according to the study's inclusion criteria. Of these, 31 were assigned to Group A and 31 to Group B. Group A received 10 ml of 0.5% bupivacaine irrigation in the liver bed after gallbladder removal. Group B received standard care without intraperitoneal irrigation.

Primary Outcome

The primary outcome was the severity of postoperative pain at 24 hours, measured using the visual analogue scale (VAS). In Group A, 20 patients (64.5%) reported mild pain, 11 patients (35.5%) reported moderate pain, and none reported severe pain. In Group B, 13 patients (41.9%) reported mild pain, 13 (41.9%) reported moderate pain, and 5 (16.1%) reported severe pain. The difference in the proportion of patients experiencing severe pain at 24 hours between the two groups was statistically significant, with a p-value of 0.036. These findings suggest that irrigation with 0.5% bupivacaine was associated with a reduction in severe postoperative pain at 24 hours (Table 1).

Table 3: Gender wise distribution of post-operative pain in both groups

Gender	Group	Mild Pain	Moderate Pain	Severe Pain	P-value
Males	Group A	6 (46.2%)	7 (53.8%)	0 (.0%)	
	Group B	5 (41.75)	6 (50.0%)	1 (8.3%)	0.568
Females	Group A	14 (77.8%)	4 (22.2%)	0 (0%)	
	Group B	8 (42.1%)	7 (36.8%)	4 (21.1%)	0.060

Secondary Outcomes

The mean age of participants was 43.64 years (SD ±12.6), with an age range of 18 to 65 years. In Group A, 6 patients were aged below 30, 6 were between 31–40, 7 between 41–50, and 12 were over 50 years. Group B included 7 patients under 30, 3 between 31–40, 11 between 41–50, and 11 over 50. When stratified by age, patients in the younger age group (≤30 years) in Group A experienced lower pain scores compared to those in Group B. Among patients aged ≤30, none in Group A reported severe pain, while 2 patients in Group B did. This age-based comparison showed a statistically significant difference in pain perception between groups for this younger age bracket (p <0.001). In other age categories, differences between groups were not statistically significant (Table 2).

Regarding gender distribution, Group A comprised 13 males (41.9%) and 18 females (58.1%), while Group B had 12 males (38.7%) and 19 females (61.3%). The overall male-to-female ratio across the study population was 0.68:1. Analysis of postoperative pain stratified by gender revealed no statistically significant differences between groups (Table 3).

Discussion

This study demonstrated that the use of 0.5% bupivacaine irrigation in the liver bed following laparoscopic cholecystectomy resulted in a significant reduction in postoperative pain severity. At the 24-hour mark, no patients in the intervention group reported severe pain, while five in the control group did, with a statistically significant p-value of 0.036. These findings support the analgesic benefit of bupivacaine instillation during surgery. Age-stratified analysis showed that participants under 30 years of age in the intervention group had notably better pain outcomes compared to controls (p-value 0.000), although this trend was not observed in older age groups. Gender was not associated with any difference in pain severity. These results are consistent with previous studies, including that by Vijayaraghavalu et al, which reported lower VAS scores at six hours in the bupivacaine group compared to controls (2.45±1.11 vs 4.22±1.26, P = 0.04) [16], and Manan et al, who found a prolonged analgesic duration in bupivacaine recipients, with pain score differences peaking at six hours postoperatively (p < 0.001) [17].

Gallstone disease is becoming increasingly common, with a global prevalence estimated at 10–20% [9]. Historically managed by open cholecystectomy for over a century, the advent of laparoscopic cholecystectomy has marked a shift towards minimally invasive surgical treatment [10]. Despite its benefits, postoperative pain remains a clinical concern. This pain may originate from the abdominal wall (parietal) or internally (visceral), with causes including pneumoperitoneum-induced stretch, gallbladder bed dissection, and retained CO□. As laparoscopic cholecystectomy is now commonly performed as a day-case procedure, effective pain relief is essential to facilitate same-day discharge [11]. Various strategies have been trialled to manage pain post-cholecystectomy, including local anaesthetic instillation with agents such as bupivacaine [6, 12]. Bupivacaine remains the most widely studied drug for intraperitoneal use to alleviate pain following laparoscopic gallbladder removal [13].

This study had several strengths, including randomised allocation, blinding of outcome assessors, and equal analgesia protocols across groups. A key finding was the significant reduction in severe postoperative pain, particularly among younger participants. The majority of participants were female, in keeping with global patterns in gallstone disease prevalence [2, 14]. The mean

age was slightly younger than in comparable studies 2, [15]. However, not all published trials support the efficacy of intraperitoneal bupivacaine. Studies such as those by Lysander et al reported no significant reduction in pain or analgesic requirement when bupivacaine was used intraperitoneally compared to skin infiltration [19]. The Cochrane review of 48 trials similarly concluded that peritoneal lavage with bupivacaine may not be an effective technique for pain relief after laparoscopic cholecystectomy [20]. These inconsistencies may be due to differences in concentration, administration site, or methodology. In contrast, Parmatha et al found significantly reduced rescue analgesia use and shorter hospital stay in patients receiving bupivacaine irrigation ($p = 0.008$ and $p < 0.001$ respectively) [21], aligning more closely with the current findings.

This study has several limitations that must be acknowledged. First, while the trial was randomised and double-blinded with allocation concealment, it was a single-centre study conducted at a government hospital, which may limit the generalisability of findings to other settings with different surgical practices or patient populations. Second, although a target sample of 70 patients was set, no formal sample size calculation was performed prior to enrolment. The study was therefore not powered based on pre-specified effect size estimates, which limits the strength of statistical inferences, particularly for subgroup analyses such as age and gender. Third, simple randomisation by folded papers, while transparent, may be more prone to imbalance compared to computer-generated or stratified randomisation methods. Additionally, although outcome assessors and patients were blinded, the surgeons were not, which could introduce performance bias, especially in intraoperative care or decision-making. Furthermore, follow-up was limited to 24 hours, with a single scheduled outpatient contact on postoperative day 5. This design does not capture longer-term pain trajectories or complications, which are relevant in evaluating the overall effectiveness of postoperative analgesia strategies. Pain assessment relied on subjective self-reported VAS scores, which are influenced by patient interpretation, although the use of standardised scales and blinded assessors helped mitigate bias. Finally, although the intervention was consistent and clearly described, no placebo irrigation was used in the control group, which may have introduced an unblinded procedural difference between groups during surgery.

While other local anaesthetics such as lidocaine [7], mepivacaine, and ropivacaine [4] have also been tested in this context, bupivacaine remains preferred due to its longer duration of action. Nevertheless, the use of intraperitoneal bupivacaine remains a subject of ongoing debate 20. This study also found no association between the preoperative indication for cholecystectomy and postoperative pain outcomes, in line with previous literature. Given the ongoing controversy around intraperitoneal anaesthetics and the varied findings across studies, future research should focus on standardising the concentration, volume, and technique of administration. Comparative trials of different agents may also be warranted to further clarify their respective roles.

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Author's contribution: AB: Conceived idea, Study design; MM: Data collection, manuscript writing; ZKT: Data collection, manuscript writing; AR: Data analysis, literature review; UM: Data analysis, proofreading; TNH: Data collection

Data sharing: Data sharing available upon request from the author.

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