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Original Research Article

A Prospective Randomized Comparative Study: Efficacy of Intravenous Ibuprofen Infusion Used as Pre-Emptive Analgesia in Patients Undergoing Elective Laparoscopic Cholecystectomy

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Abstract:

Background: Post-operative pain following laparoscopic cholecystectomy remains a common clinical concern, often necessitating opioid use that may result in undesirable side effects. Pre-emptive administration of non-steroidal anti-inflammatory drugs (NSAIDs) has been proposed as an effective opioid-sparing strategy.

Aim and Objective: To evaluate the efficacy of intravenous (IV) ibuprofen compared with placebo when used as pre-emptive analgesia in patients undergoing elective laparoscopic cholecystectomy under general anaesthesia.

Materials and Methods: This prospective, randomized, double-blinded, placebo-controlled study was conducted at SVBP Hospital, LLRM Medical College, Meerut, from May 2023 to April 2025. Sixty ASA I–II patients aged 20–60 years scheduled for elective laparoscopic cholecystectomy were enrolled and randomly allocated into two groups (n = 30 each). Group B received IV ibuprofen 400 mg in 100 ml saline, while Group C received 100 ml saline (placebo), both administered 30 minutes before induction. Standardized anaesthetic protocols were followed. Post-operative pain was assessed using the Visual Analogue Scale (VAS) at intervals up to 12 hours. Rescue analgesia with IV Tramadol (2 mg/kg) was administered if VAS >3, and total opioid consumption was recorded. Hemodynamic parameters and adverse events were also documented.

Results: VAS scores were significantly lower in the ibuprofen group compared to placebo at 15 min, 30 min, 1 hr, 4 hr, 10 hr, and 12 hr postoperatively ($p < 0.05$). No significant differences were observed at 2 hr, 6 hr, and 8 hr. Mean Tramadol consumption was significantly reduced in the ibuprofen group (223 ± 43 mg) versus placebo (290 ± 30.5 mg; $p = 0.0037$). Hemodynamic parameters (pulse rate, SBP, DBP, MAP, SpO_2) remained stable in both groups, and adverse effects were minimal and comparable.

Conclusion: Pre-emptive IV ibuprofen significantly reduces post-operative pain scores and opioid requirements compared to placebo, without compromising hemodynamic stability or safety. It represents a safe and effective component of multimodal analgesia for laparoscopic cholecystectomy.

Keywords: Ibuprofen, Pre-Emptive Analgesia, Laparoscopic Cholecystectomy, Opioid-Sparing, Post-Operative Pain

Introduction

Pre-emptive analgesia involves administering analgesics before surgical stimuli to prevent central sensitization and thereby reduce the severity of post-operative pain. [1] Post-operative pain remains a common and challenging issue, often managed with opioids. However, opioids are associated with adverse effects such as respiratory depression, sedation, urinary retention, delayed bowel recovery, nausea, and vomiting. [2] Effective post-operative analgesia is essential, as it reduces complications, decreases the risk of chronic pain, and improves patient satisfaction. [3] Uncontrolled pain may lead to hypertension, tachycardia, immobility, prolonged hospital stays, and dissatisfaction. Despite advancements in pain management, up to 80% of patients report moderate pain, and 31–37% report severe pain postoperatively. [4]

Several alternative strategies have been explored, including patient-controlled analgesia (PCA), epidural analgesia, and peripheral nerve blocks. However,

each carries limitations, such as contraindications in spinal deformities or coagulopathies. Pre-emptive systemic analgesics given with general anaesthesia can block nociceptive transmission, reduce intraoperative anaesthetic requirements, and hasten recovery. [5] By preventing central sensitization, these agents also minimize post-operative hyperalgesia. [6] Laparoscopic surgery is associated with less pain compared to open techniques, yet nearly one-third of patients still require substantial analgesics postoperatively. [7]

Non-steroidal anti-inflammatory drugs (NSAIDs) are an important component of multimodal analgesia owing to their opioid-sparing effect and fewer opioid-related side effects. [8] Among these, intravenous (IV) ibuprofen has gained attention for its effectiveness in reducing post-operative pain severity and lowering opioid requirements. [9] Studies have demonstrated its ability to provide consistent analgesia without significant hemodynamic compromise.

Placebo-controlled trials remain crucial to evaluate the true efficacy of newer agents. A direct comparison of IV ibuprofen with placebo in laparoscopic cholecystectomy patients allows a clear assessment of its analgesic benefits, opioid-sparing potential, and safety. This study was therefore designed to evaluate the efficacy of IV ibuprofen used as preemptive analgesia compared with placebo in patients undergoing elective laparoscopic cholecystectomy.

Methods and Materials

This study was conducted to evaluate the efficacy of intravenous (IV) ibuprofen infusion, used as preemptive analgesia, in comparison with placebo in patients undergoing elective laparoscopic cholecystectomy under general anaesthesia. Institutional Ethics Committee approval was obtained (Approval No./SC-1/2024/3626, dated 16/05/2024), and the study was registered in the Clinical Trial Registry of India (CTRI/2024/10/074976).

Place and Duration of Study: The trial was carried out at SVBP Hospital associated with LLRM Medical College, affiliated with Chaudhary Charan Singh University, Meerut, Uttar Pradesh. The duration of the study was 24 months, from May 2023 to April 2025.

Study Design: This was a prospective, randomized, double-blinded, placebo-controlled comparative study. A total of 60 patients of either sex, aged 20–60 years, belonging to the American Society of Anaesthesiologists (ASA) physical status I or II, scheduled for elective laparoscopic cholecystectomy, were enrolled after detailed pre-anaesthetic evaluation and routine preoperative investigations. Patients were included if they were ASA grade I or II, aged 20–60 years, and provided written informed consent. Exclusion criteria were refusal to participate, pregnancy, asthma, chronic lung or heart disease, renal failure, coagulopathy, history of gastrointestinal bleeding, uncontrolled hypertension, anaemia, warfarin therapy, first- to third-degree heart block, allergy to NSAIDs, or chronic analgesic use.

Informed Consent and Sample Size: All participants were informed verbally and in writing about the research protocol, and written consent was obtained before enrolment. A total of 60 patients were included, with 30 patients in each group. The sample size was calculated to provide 80% power to detect clinically meaningful differences in post-operative pain scores between IV ibuprofen and placebo at a 5% level of significance.

Randomization and Allocation: Randomization was performed by the sealed envelope method. Patients were allocated into two groups: Group B received 400 mg IV ibuprofen in 100 ml normal saline, and Group C received 100 ml normal saline (placebo), both administered 30 minutes before induction. Both the patients and the investigators assessing outcomes were blinded to group allocation.

Anaesthetic Technique: In the preoperative area, intravenous access was secured with an 18-G cannula, and patients received premedication with IV midazolam (0.1 mg/kg). On arrival in the operating theatre, standard monitors were applied. Anaesthesia was induced with IV fentanyl (2 mcg/kg) and IV propofol (2.5 mg/kg), and endotracheal intubation was facilitated with IV vecuronium (0.1 mg/kg). Maintenance of anaesthesia was achieved with isoflurane in a mixture of nitrous oxide and oxygen, and intraoperative analgesia was supplemented with IV fentanyl (1 mcg/kg) as needed. At the end of surgery, residual neuromuscular blockade was reversed with IV glycopyrrolate (0.01 mg/kg) and IV neostigmine (0.05 mg/kg), followed by extubation after thorough suctioning. Patients were subsequently transferred to the post-anaesthesia care unit for monitoring and further assessment.

Statistical Analysis: All collected data were compiled and analyzed using SPSS version 26.0. Continuous variables such as age, BMI, hemodynamic parameters, and VAS scores were expressed as mean ± standard deviation (SD) and compared between groups using analysis of variance (ANOVA) or independent t-test as appropriate. Categorical variables such as gender distribution and incidence of adverse effects were presented as frequencies and percentages, and compared using the chi-square test or Fisher's exact test. Rescue analgesic consumption (Tramadol dose) was analyzed using ANOVA. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics: The baseline demographic variables were comparable between the two study groups. The mean age was 36.7 ± 11.1 years in Group B (IV Ibuprofen) and 36.0 ± 10.9 years in Group C (Placebo), with no statistically significant difference ($p = 0.896$). Female participants constituted 28.9% in Group B and 31.1% in Group C, while male representation was minimal (4.4% and 2.2% respectively), showing no significant difference ($p > 0.05$). The mean BMI was 24.10 ± 2.33 kg/m² in Group B and 22.78 ± 2.86 kg/m² in Group C ($p = 0.06$) (Table 1).

Table 1: Baseline Demographic Characteristics

Variable	Group B (Ibuprofen)	Group C (Placebo)	p-value
Age (years, mean ± SD)	36.7 ± 11.1	36.0 ± 10.9	0.896
Female (%)	28.9	31.1	0.134
Male (%)	4.4	2.2	
BMI (kg/m², mean ± SD)	24.10 ± 2.33	22.78 ± 2.86	0.06

Hemodynamic Parameters: Intraoperative monitoring of pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) revealed no statistically significant differences between Group B and Group C at any perioperative time point (all $p > 0.05$). Both groups maintained stable values within physiological limits, indicating hemodynamic neutrality of IV Ibuprofen compared with placebo.

Post-operative Pain Scores (VAS): Post-operative pain was assessed using the VAS at multiple intervals up to 12 hours. Group B (IV Ibuprofen) consistently demonstrated lower pain scores compared to Group C (Placebo) during most of the post-operative period. Statistically significant differences were observed at 15 min, 30 min, 1 hr, 4 hr, 10 hr, and 12 hr ($p < 0.05$). At 2, 6, and 8 hours, no significant difference was noted between the groups.

Table 2: Mean VAS Scores at Different Time Intervals

Time	Group B (Ibuprofen)	Group C (Placebo)	p-value
15 min	2.7 ± 1.02	8.2 ± 0.89	<0.001
30 min	3.63 ± 1.13	2.73 ± 0.45	0.002
1 hr	2.67 ± 1.73	1.77 ± 1.10	0.003
2 hr	0.97 ± 0.72	1.30 ± 0.79	0.31
4 hr	2.23 ± 0.86	2.87 ± 1.20	0.024
6 hr	2.3 ± 0.86	2.87 ± 1.20	0.107
8 hr	2.3 ± 2.10	1.13 ± 1.38	0.164
10 hr	1.53 ± 1.13	2.17 ± 1.26	0.036
12 hr	2.4 ± 1.33	3.8 ± 1.61	0.001

These results indicate that IV Ibuprofen provided superior early analgesia and also maintained significant efficacy during the later post-operative hours compared with placebo (Table 2).

Rescue Analgesia Requirement: The mean total dose of rescue Tramadol required was significantly higher in the placebo group (290 ± 30.5 mg) compared to the Ibuprofen group (223 ± 43 mg), with a p-value of 0.0037 (Table 3).

Table 3: Total Tramadol Consumption

Group	Mean dose (mg) ± SD	95% CI	p-value
B (Ibuprofen)	223 ± 43.0	207–239	0.0037
C (Placebo)	290 ± 30.5	279–301	

Adverse Effects: Adverse events were minimal and comparable between the two groups. Nausea was reported in 2 patients (2.2%) each in Group B and Group C, with no statistical difference ($p = 1.0$). No cases of vomiting, abdominal pain, or bleeding were reported in either group (Table 4).

Table 4: Adverse Effects Profile

Adverse Effect	Group B (Ibuprofen)	Group C (Placebo)	p-value
Nausea	2 (2.2%)	2 (2.2%)	1.0
Vomiting	0	0	–
Abdominal pain	0	0	–
Bleeding	0	0	–

Discussion

In this prospective randomized, double-blinded, placebo-controlled study, we evaluated the efficacy of intravenous (IV) ibuprofen used as pre-emptive analgesia in patients undergoing elective laparoscopic cholecystectomy. The demographic variables, including age, sex distribution, and BMI, were comparable between the two groups, indicating that these baseline factors did not influence the outcomes. The mean age of our participants was approximately 36 years, consistent with previous studies by Sharma et al. [10], Juwita et al. [11], Garg et al. [12], and Zafar et al. [13], who reported a similar age profile in patients undergoing laparoscopic cholecystectomy with pre-emptive analgesia. These findings support the generalisability of our results, as age was not found to affect analgesic efficacy or opioid consumption in the literature significantly.

The gender distribution in our study showed a female predominance, reflecting the known higher prevalence of gallbladder disease in women. This finding is in line with reports by Cao et al. [14] and Juwita et al. [11], who observed a greater proportion of female patients in laparoscopic cholecystectomy cohorts. As gender-related differences in pain perception and opioid sensitivity have been documented in some studies, the balanced distribution across groups in our trial ensured that this factor did not confound the analgesic outcomes. Similarly, BMI did not differ significantly between the groups and did not appear to influence post-operative analgesic requirements. Previous studies, including those by Garg et al. [12], Dönmez et al. [15], and Sharma et al. [10], also concluded that BMI was not a determinant of analgesic efficacy in laparoscopic surgeries, corroborating our results.

Hemodynamic stability is an important consideration during anaesthesia and post-operative recovery. In our study, perioperative parameters including pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) remained stable. They showed no statistically significant differences between the ibuprofen and placebo groups. These findings indicate that IV ibuprofen did not adversely affect cardiovascular or respiratory stability. Similar results were reported by Albuquerque et al. [16], Sharma et al. [10], and Cao et al. [14], who highlighted that IV ibuprofen, when used pre-emptively, provided adequate analgesia without compromising hemodynamic safety.

The most important finding of our study relates to post-operative pain assessment using the Visual Analogue Scale (VAS). Patients in the ibuprofen group reported significantly lower pain scores compared to the placebo group at multiple time points, particularly at 15 minutes, 30 minutes, 1 hour, 4 hours, 10 hours, and 12 hours postoperatively. These results are consistent with the findings of Asheghvatan et al. [17], who demonstrated superior analgesic efficacy of IV ibuprofen compared to placebo in the early post-operative period. Likewise, Nasr et al. [18] and Zafar et al. [13] reported that ibuprofen reduced post-operative pain intensity and improved patient comfort following laparoscopic procedures. Interestingly, at some intervals (2 hours, 6 hours, and 8 hours), no significant difference was observed, suggesting a possible waning or overlapping effect during the intermediate post-operative period. This finding is in agreement with Dönmez et al. [15], who noted that ibuprofen may be most effective in the immediate post-operative period but shows variable efficacy during later phases depending on the type of surgery.

Another key outcome of our study was the opioid-sparing effect of IV ibuprofen. The mean total Tramadol requirement was significantly lower in the ibuprofen group compared to placebo (223 mg vs 290 mg, $p = 0.0037$). This reduction in opioid consumption is clinically relevant, as it minimizes the risks of opioid-related side effects such as nausea, vomiting, sedation, and delayed bowel recovery. Our results are consistent with those of Albuquerque et al. [16] and Sharma et al. [10], who also reported lower opioid requirements with NSAID-based pre-emptive analgesia. Nasr et al. [18] similarly highlighted the advantage of ibuprofen in reducing opioid use, particularly in abdominal surgeries where inflammatory pain contributes substantially to post-operative discomfort.

About adverse effects, the incidence of nausea was low and comparable between the two groups, while vomiting, abdominal pain, and bleeding were not reported in either group. These findings underscore the safety and tolerability of IV ibuprofen in the perioperative setting. Previous studies by Sharma et al. [10] and Albuquerque et al. [17] also observed minimal gastrointestinal or bleeding complications with pre-emptive use of ibuprofen, supporting its favorable safety profile when used in appropriate doses and patient populations.

Strengths and Limitations: The strengths of this study include its prospective, randomized, double-blinded design and the use of a standardized anaesthetic technique, which minimized bias. The placebo-controlled comparison provides robust evidence of the true efficacy of IV ibuprofen. However, some limitations must be acknowledged. First, the study had a relatively small sample size (30 patients per group), which may limit the power to detect differences in secondary outcomes such as adverse events. Second, the follow-up period was restricted to the first 12 hours postoperatively; longer-term outcomes, including the risk of chronic post-operative pain, were not assessed. Third, the study was conducted in a single center, which may limit external validity.

Clinical Implications: Our study supports the incorporation of IV ibuprofen into multimodal analgesic protocols for laparoscopic cholecystectomy. Its efficacy in reducing post-operative pain and opioid requirements, along with its safety and hemodynamic neutrality, make it a valuable option for enhancing recovery and patient satisfaction. Given the growing emphasis on opioid-sparing strategies, IV ibuprofen provides an effective and safe alternative for post-operative analgesia.

Conclusion

This study demonstrates that pre-emptive intravenous ibuprofen, provides superior post-operative pain relief compared to placebo, particularly in the early and late post-operative periods. It was also associated with significantly reduced rescue opioid (Tramadol) consumption, highlighting its opioid-sparing effect. Importantly, IV ibuprofen was well tolerated, with no significant adverse effects or hemodynamic instability observed. These findings support the role of pre-emptive IV ibuprofen as a safe and effective component of multimodal analgesia for laparoscopic cholecystectomy, contributing to improved post-operative outcomes and enhanced patient recovery.

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