The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 4, Issue 6, 2026

COMPARISON OF THE OUTCOME OF SINGLE-DOSE PREEMPTIVE INTRAVENOUS IBUPROFEN VERSUS PLACEBO IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY AT A TERTIARY CARE HOSPITAL, KARACHI

Pawan Kumar[*1], Syed Farjad Sultan[2], Dr. Pirbhoo Mal[3], Amir Khan[4], Kanchan[5], Mahnoor Umar[6]

*[*1,5,6]Postgraduate Resident, Department of Anesthesia Dow Medical College (DMC), Dow University of Health Sciences (DUHS), Karachi, Pakistan*
[2]Associate Professor, Department of Anesthesia Dow Medical College (DMC), Dow University of Health Sciences (DUHS), Karachi, Pakistan
[3]Postgraduate Resident, Department of AnesthesiaDow University of Health Sciences (DUHS), Karachi, Pakistan
[4]Senior Registrar, Department of Anesthesia Dow Medical College (DMC), Dow University of Health Sciences (DUHS), Karachi, Pakistan

DOI: https://doi.org/10.5281/zenodo.20759630

Keywords
Preemptive analgesia, Intravenous ibuprofen, Laparoscopic cholecystectomy, Hemodynamic response, Postoperative pain

Article History
Received: 22 April 2026
Accepted: 04 June 2026
Published: 19 June 2026

Corresponding Author: *
Pawan Kumar

Abstract

Objective: To compare the hemodynamic and analgesic outcomes of single-dose preemptive intravenous ibuprofen versus placebo in patients undergoing laparoscopic cholecystectomy.Methodology:This randomized controlled trial was conducted at the Department of Anesthesia, Civil Hospital Karachi over six months. A total of 110 patients (ASA I–II, aged 40–80 years) undergoing elective laparoscopic cholecystectomy were enrolled and randomly allocated into two groups (n=55 each). Group A received intravenous ibuprofen (400 mg) 15 minutes prior to induction, while Group B received placebo (normal saline). Hemodynamic parameters (SBP, DBP, MAP, heart rate) were recorded at 30 minutes postoperatively. Pain was assessed using the Visual Analog Scale, and time to first analgesic requirement was noted. Data was analyzed using SPSS version 20.Results:Baseline characteristics were comparable between the groups ($p>0.05$). The ibuprofen group demonstrated significantly lower systolic blood pressure (122.6 ± 15.6 vs 130.8 ± 15.7 mmHg, $p=0.007$), diastolic blood pressure (74.5 ± 10.1 vs 83.4 ± 9.5 mmHg, $p<0.001$), mean arterial pressure (91.1 ± 9.5 vs 99.0 ± 9.0 mmHg, $p<0.001$), and heart rate (73.8 ± 10.6 vs 78.9 ± 11.8 beats/min, $p=0.019$). The mean time to first analgesic requirement was significantly prolonged in the ibuprofen group (594.7 ± 98.2 vs 228.4 ± 81.3 minutes, $p<0.001$), while rescue tramadol consumption was significantly reduced (59.1 ± 16.5 vs 85.9 ± 20.9 mg, $p<0.001$).Conclusion:Preemptive intravenous ibuprofen significantly improves postoperative analgesia and hemodynamic stability while reducing opioid requirements in patients undergoing laparoscopic cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy has emerged as the gold standard of symptomatic gallstone disease treatment because of its minimally invasive nature, shorter recovery, lower morbidity, and decreased hospitalization; however, postoperative

pain still is a critical clinical issue, which has impacted patient recovery, satisfaction, and overall outcomes of surgery. Pain after laparoscopic cholecystectomy is multifactorial in nature and includes visceral pain because of the carbon dioxide insufflation, parietal pain which results out of the trocar insertion, and finally referred shoulder pain which is a result of the irritation of the diaphragm.

Physiological response to postoperative pain is not only a subjective event but a complicated neuroendocrine and inflammatory process. Peripheral sensitization and central nervous system hyperexcitability are triggered by surgical trauma and can intensify pain perception unless it is managed properly and consequently may result in heightened sympathetic activity, tachycardia, hypertension, poor pulmonary function, slowness, and thromboembolic issues.

Preemptive analgesia, the administration of analgesic measures before the surgical incision, is conceptualized as the ability to prevent central sensitization and decrease the intensity of postoperative pain as well as lower analgesic requirements during the postoperative stage. Research has shown that preemptive analgesia does not only work better in controlling pain but also better in improving the recovery profiles and decreasing the hospital stay.

Non-steroidal anti-inflammatory drugs (NSAIDs) are common in the use of perioperative pain treatment because of their analgesic, anti-inflammatory, and opioid-sparing efficacy. The propionic acid derivative intravenous ibuprofen has a more desirable safety profile, with the least possible risk of respiratory depression, sedation, and postoperative nausea and vomiting compared to opioids.

Recent studies indicate that intravenous ibuprofen as a component of a multimodal analgesic regimen can have a significant impact in the reduction of postoperative pain scores and opioid use. Southworth et al. also found that intravenous ibuprofen was an effective analgesic in reducing the intensity of postoperative pain and analgesic needs in a randomized controlled trial, as well as Gago-Martinez et al. in a placebo-controlled trial.

Preoperative use of intravenous ibuprofen can be an extra advantage in the conditions of laparoscopic cholecystectomy since it could stabilize the intraoperative hemodynamic parameters. The pain and stress associated with surgery might result in some changes in blood pressure and heart rate that might negatively influence patient outcomes, especially in people with comorbidity. The decrease of the inflammatory process and nociceptive conduction can also be achieved with the help of ibuprofen and has the potential of improving the hemodynamic stability during and after surgery.[11].

Although there is increasing evidence that intravenous ibuprofen can be used in perioperative analgesia, not much information is available in the local healthcare environment in Pakistan. The different patient demographics, surgical procedures, and healthcare resources require research specific to the regions to confirm the effectiveness and safety of such interventions. Moreover, the process of introducing preemptive analgesia into the everyday clinical practice needs solid evidence to prove its positive effects on the quality of analgesia and hemodynamic results.

Thus, this paper seeks to draw a comparison between the impact of a single dose of preemptive intravenous ibuprofen and a placebo on the postoperative pain and hemodynamic variables among patients who undergo laparoscopic cholecystectomy in a tertiary care hospital in Karachi. The results of the research will help to optimize the perioperative pain management plan, advance opioid-sparing methods, and improve patient recovery and surgical outcomes.

METHODOLOGY

This prospective randomized controlled trial was conducted in the Department of Anesthesiology, Civil Hospital Karachi, for six months following the approval from the College of Physicians and Surgeons Pakistan (CPSP) and the ethical review committee of the institution .

Using a non-probability consecutive sampling procedure, 110 patients scheduled for elective laparoscopic cholecystectomy were included in

this study. A sample size of 110 patients was calculated using OpenEpi software, based on reported differences in mean diastolic blood pressure (DBP) between ibuprofen group and placebo group (80.7 ± 12.9 vs 73.7 ± 13.3) with 95% confidence and 80% power, to include 55 patients in each group.

Patients aged 40 to 80 years of either gender with American Society of Anesthesiologists (ASA) physical status I or II were included. History of epilepsy, conduction defects, renal disease, chronic liver disease, chronic obstructive lung disease, asthma, hypothyroidism, stroke, and congestive cardiac failure were excluded.

Patients were divided into two groups using opaque envelopes. Patients in Group A received 400 mg of intravenous ibuprofen diluted with 100 ml of normal saline 15 minutes before induction of anesthesia and Group B was given 100 ml normal saline as a placebo. The patients were blinded to the drug administered and assessment of the outcome was done by an independent anesthesiologist.

Preoperative assessment of all patients was performed as per routine, and patients were instructed on using the Visual Analog Scale (VAS) for pain scoring. In the operating room, initial values of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), heart rate and oxygen saturation were noted. Continuous monitoring of ECG, non-invasive blood pressure, and pulse oximetry was instituted, and patients were secured with an 18-gauge cannula.

General anesthesia was given per institutional guidelines. Surgeons with experience performed a four-port laparoscopic cholecystectomy. A carbon dioxide pneumoperitoneum was maintained at 10-12 mmHg. Patients were in reverse Trendelenburg position with left tilt. At the conclusion of surgery, anticholinesterase agents neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg) were administered, and the patients extubated once spontaneous ventilation and airway reflexes were acceptable.

Postoperatively, patients were monitored in the post-anesthesia care unit (PACU). Blood pressure (systolic blood pressure [SBP], diastolic blood pressure [DBP], mean arterial pressure [MAP], and heart rate) were measured at 30 minutes after surgery. Postoperative pain was evaluated with the Visual Analog Scale (VAS) and time to first analgesic request was recorded. Rescue analgesia (tramadol 30 mg intravenous) was administered to patients who reported a VAS score of ≥4.

Details of age, sex, duration of surgery, duration of anesthesia, hemodynamic variables, and time to first analgesic request were recorded in a proforma. Potential confounders such as diabetes, hypertension and smoking were also recorded and adjusted for.

Data was analyzed using SPSS version 20. Continuous variables were presented as mean ± standard deviation or median (interquartile range) according to normality evaluated by Kolmogorov Smirnov test. Categorical variables were expressed as number and percentage. Between-group differences were assessed using independent t-test or Mann-Whitney U test and data were stratified for effect modification. Statistical significance was set at $p \leq 0.05$.

RESULTS

The study enrolled 110 patients scheduled for elective laparoscopic cholecystectomy and they were divided into two groups: ibuprofen group (n=55) and placebo group (n=55). All randomized patients completed the study.

The demographic variables were similar between groups. The mean age in the ibuprofen group was 49.2 ± 7.0 years, while in the placebo group it was 50.4 ± 7.0 years (p=0.365). There were no significant differences in gender, ASA score, presence of diabetes mellitus, hypertension, and smoking status, surgical duration, or duration of anesthesia (p>0.05 for all).

At 30 minutes after surgery, those who received preemptive intravenous ibuprofen had greater hemodynamic stability than those who received placebo. Systolic blood pressure was significantly lower in the ibuprofen group (122.6 ± 15.6 mmHg) than in the placebo group (130.8 ± 15.7 mmHg, p=0.007). Diastolic blood pressure was also lower in the ibuprofen group (74.5 ± 10.1 mmHg) than in the placebo group (83.4 ± 9.5 mmHg, p<0.001). The mean arterial pressure was

also significantly lower in patients treated with ibuprofen (91.1 ± 9.5 mmHg) than in those who received placebo (99.0 ± 9.0 mmHg, p<0.001). Finally, heart rate was lower in the ibuprofen group (73.8 ± 10.6 beats/min) than in the placebo group (78.9 ± 11.8 beats/min, p=0.019).

About the analgesic effect, the mean time to first analgesic was significantly longer in the ibuprofen group (594.7 ± 98.2 minutes) than in the placebo group (228.4 ± 81.3 minutes, p<0.001). Also, the mean total 24-hour tramadol requirement was markedly less in the ibuprofen group (59.1 ± 16.5 mg) than in the placebo group (85.9 ± 20.9 mg, p<0.001).

Overall, preemptive intravenous ibuprofen was associated with significantly improved postoperative analgesia and more favorable hemodynamic parameters in comparison with placebo.

Table 1. Baseline characteristics of study participants

Variable	Ibuprofen (n=55)	Placebo (n=55)	p-value
Age (years), mean ± SD	49.2 ± 7.0	50.4 ± 7.0	0.365
Male, n (%)	25 (45.5)	17 (30.9)	0.170
Female, n (%)	30 (54.5)	38 (69.1)	
ASA I, n (%)	35 (63.6)	30 (54.5)	0.438
ASA II, n (%)	20 (36.4)	25 (45.5)	
Diabetes mellitus, n (%)	5 (9.1)	6 (10.9)	1.000
Hypertension, n (%)	16 (29.1)	19 (34.5)	0.682
Active smoker, n (%)	15 (27.3)	10 (18.2)	0.509
Ex-smoker, n (%)	7 (12.7)	7 (12.7)	
Non-smoker, n (%)	33 (60.0)	38 (69.1)	
Duration of surgery (min), mean ± SD	64.3 ± 9.6	67.3 ± 10.1	0.116
Duration of anesthesia (min), mean ± SD	82.2 ± 10.2	85.8 ± 10.5	0.069

Table 2. Comparison of postoperative hemodynamic parameters at 30 minutes

Parameter	Ibuprofen (n=55) mean ± SD	Placebo (n=55) mean ± SD	p-value
Systolic blood pressure (mmHg)	122.6 ± 15.6	130.8 ± 15.7	0.007
Diastolic blood pressure (mmHg)	74.5 ± 10.1	83.4 ± 9.5	<0.001
Mean arterial pressure (mmHg)	91.1 ± 9.5	99.0 ± 9.0	<0.001
Heart rate (beats/min)	73.8 ± 10.6	78.9 ± 11.8	0.019

Table 3. Comparison of postoperative analgesic outcomes

Variable	Ibuprofen (n=55) mean ± SD	Placebo (n=55) mean ± SD	p-value
Time to first analgesic requirement (min)	594.7 ± 98.2	228.4 ± 81.3	<0.001
24-hour rescue tramadol requirement (mg)	59.1 ± 16.5	85.9 ± 20.9	<0.001

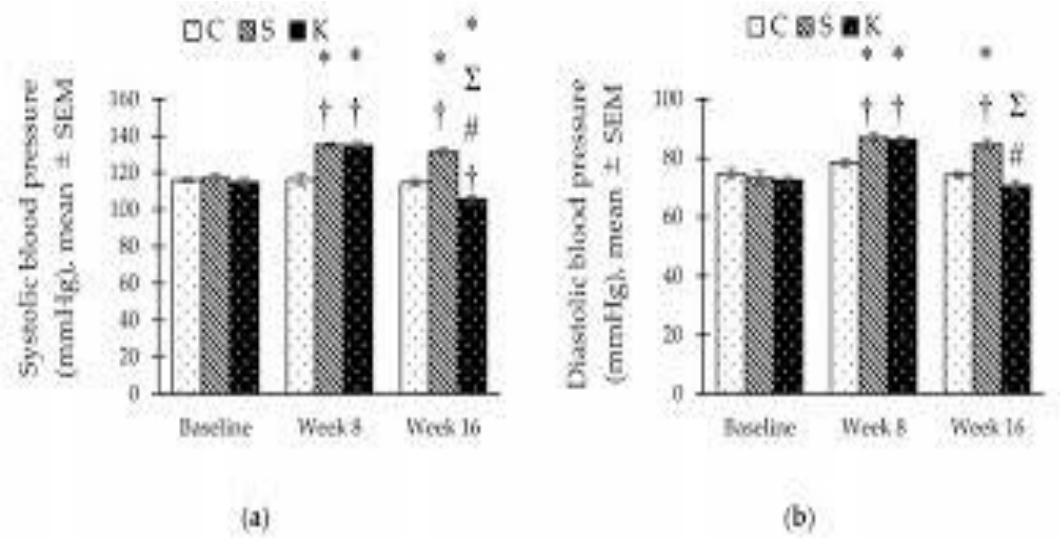
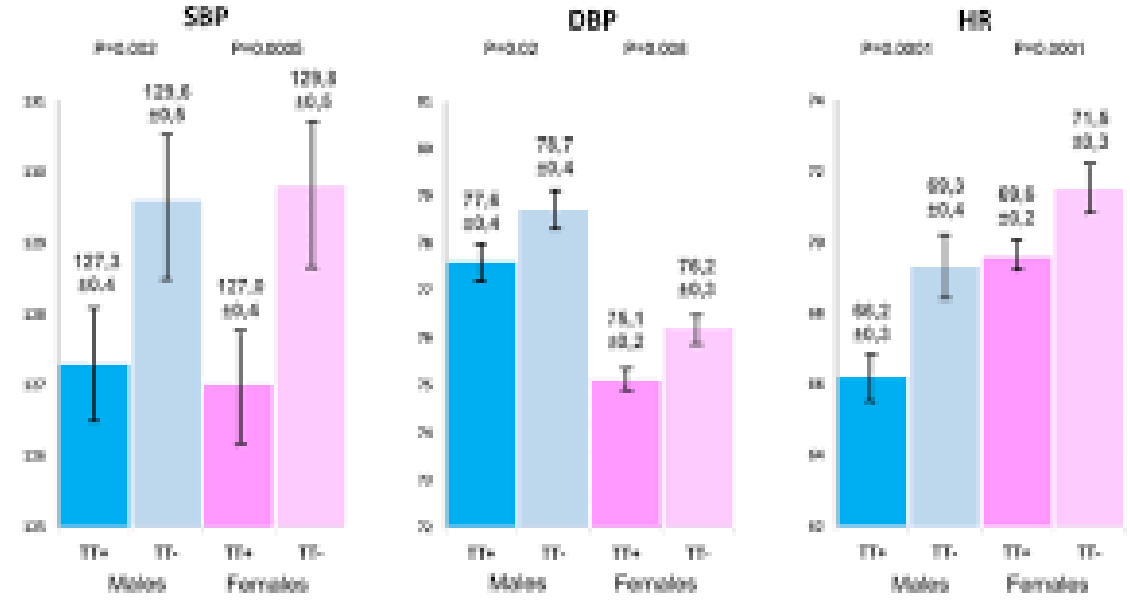


Figure 1: Hemodynamic Comparison



Abbreviations: DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; TT-, tilt-negative; TT+, tilt-positive.

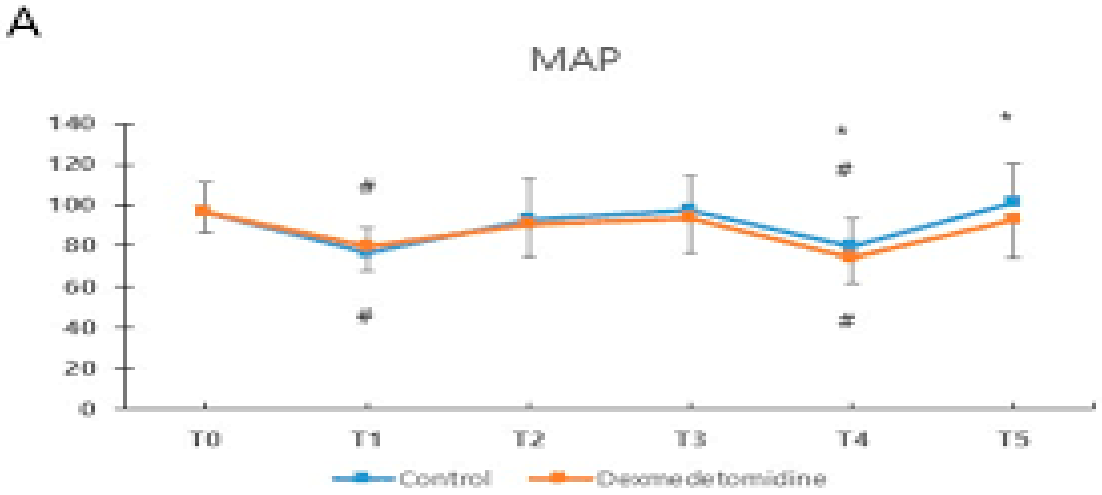


Figure 1: Comparison of Postoperative Hemodynamic Parameters Between Ibuprofen and Placebo Groups

Bar chart showing mean systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate measured at 30 minutes postoperatively. Patients receiving preemptive intravenous ibuprofen demonstrated significantly lower SBP, DBP, MAP, and heart rate compared to placebo ($p<0.05$).

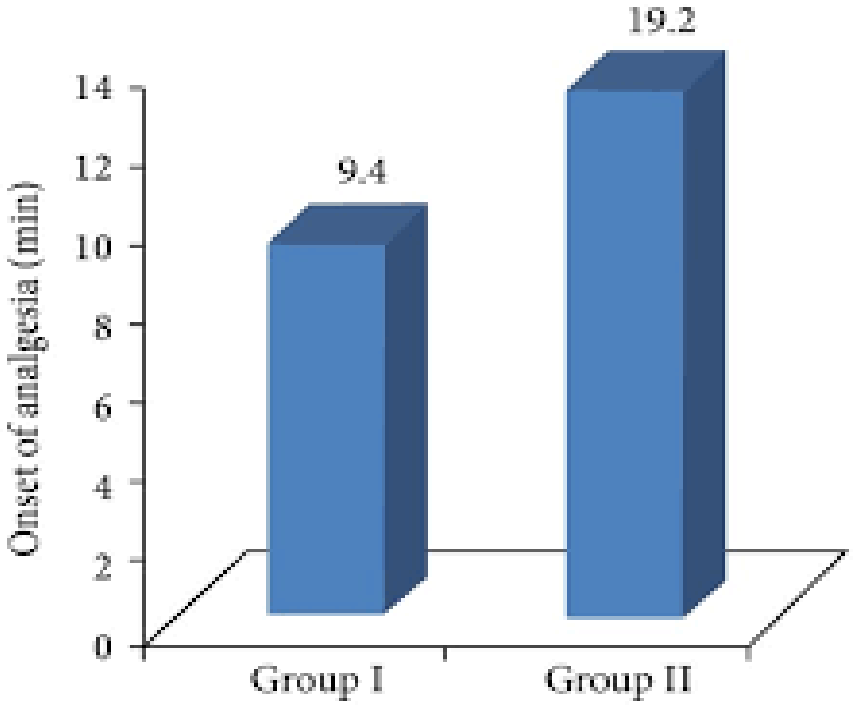
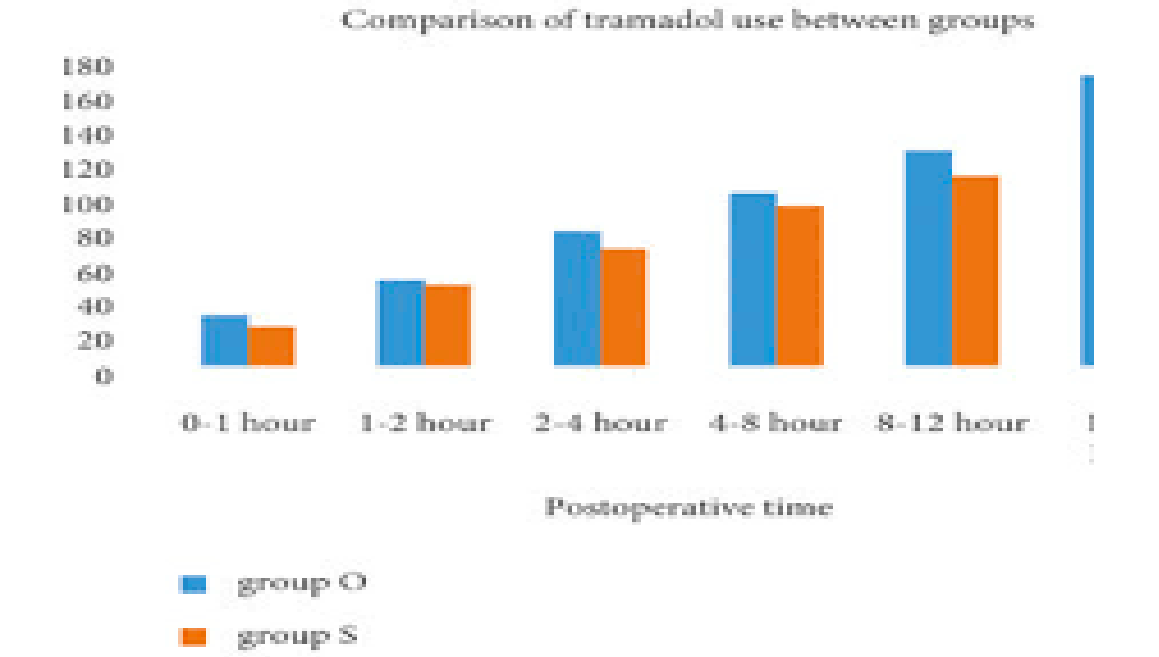


Figure 2: Analgesic Outcome (Primary Endpoint)



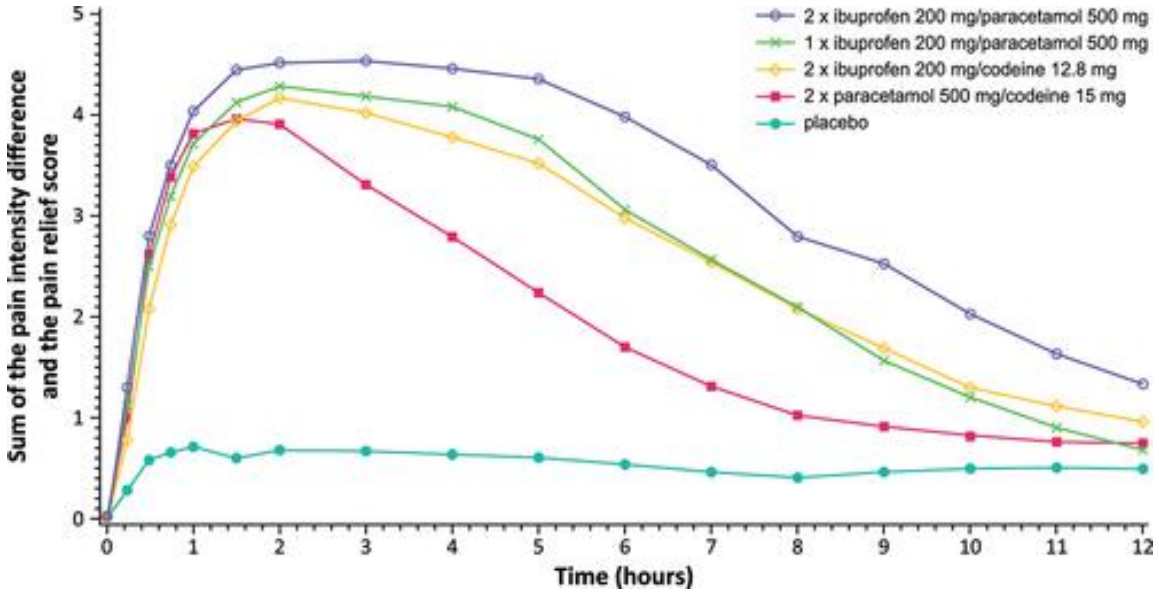


Figure 2: Comparison of Time to First Analgesic Requirement and Rescue Analgesic Consumption

Bar chart illustrating the mean time to first analgesic requirement and total 24-hour tramadol consumption in both groups. The ibuprofen group showed significantly prolonged analgesia duration and reduced rescue analgesic requirement compared
to placebo ($p<0.001$).

DISCUSSION

In this randomized controlled study, a single dose of preemptive intravenous ibuprofen was shown to reduce the need for postoperative pain relief and to improve hemodynamic stability in patients who had laparoscopic cholecystectomy. Ibuprofen recipients took longer to need the first dose of analgesia. They also needed less opioids. They

also had lower postoperative systolic and diastolic blood pressure, which mean arterial pressure and heart rate than patients who received placebo.

Laparoscopic cholecystectomy can produce complex pain. It has visceral, somatic, and referred elements resulting from pneumoperitoneum, stretching of the peritoneum, and trauma to the port sites.[1] Adequate pain management is required for patient comfort. It also diminishes neuroendocrine stress responses that may contribute to recovery.[4] Our study confirms the effectiveness of preemptive analgesia in decreasing these responses.

The delayed need for pain relief in this study suggests that preemptive analgesia works well. It does not set up central sensitization, reducing hyperalgesia. This agrees with meta-analysis on preemptive analgesia by Ong et al, where they showed that preventive analgesia reduces pain and painkiller use if given before the injury.

The results of this study are consistent with previous randomized controlled trials on intravenous ibuprofen. Southworth et al. showed that intravenous ibuprofen significantly reduced postoperative pain scores and opioid consumption.[9] Gago-Martinez et al. also observed improved analgesia and decreased occurrence of rescue analgesia.[10] Singla et al. also documented reduced morphine consumption and improved pain control for various surgical procedures.

This study's opioid-sparing effect is significant. It helps avoid the complications associated with high levels of opioid use, such as respiratory depression, nausea, vomiting, and slow return of gut function.[8]

The ibuprofen group also had improved hemodynamic stability. They had lower postoperative blood pressure and heart rate. Pain from surgery increases stimulation of the sympathetic nervous system and release of catecholamines, causing tachycardia and hypertension.[4] Ibuprofen reduces both nociceptive and inflammatory responses, which may help mitigate the response.

This is in line with Sezen et al, who noted improved intraoperative blood pressure and heart rate, and increased analgesia with preemptive intravenous ibuprofen.[11] Kroll also found that intravenous ibuprofen provides hemodynamic stability by reducing inflammatory responses. This could be a result of different anesthetic practices, drug administration timing, or patient profiles.[12] Therefore, although the analgesic effects are dependable, the hemodynamic effects may be more variable.

Ibuprofen works by blocking cyclooxygenase (COX-1 and COX-2) enzymes. This inhibits prostaglandin synthesis and decreases inflammation and pain.[7] Rainsford described ibuprofen as safe and fast acting.[7] the intravenous formulation of ibuprofen is rapidly and consistently available when needed.

Intravenous ibuprofen provides more effective pain relief with a lower incidence of side effects than other analgesics. Derry et al.'s systematic review demonstrated the efficacy and safety of this agent in clinical practice.[18] White also added NSAIDs are important for multimodal pain relief.

But the efficacy of preemptive analgesia can be affected by the type of surgery and the overall pain relief strategy. Multimodal approaches are more effective than single-component analgesia as emphasized by Kehlet and Wilmore.[13] as such, intravenous ibuprofen should be combined with other analgesic strategies.

In summary, our results confirm previous studies. Preemptive intravenous ibuprofen is effective and safe. It is beneficial for postoperative pain, provides greater hemodynamic stability and decreases the need for opioids in laparoscopic cholecystectomy,

Conclusion

Preemptive intravenous ibuprofen significantly improves postoperative analgesia and hemodynamic stability in laparoscopic cholecystectomy, while reducing opioid requirement. It is a safe and effective component of multimodal perioperative pain management

REFERENCES

Keus F, de Jong JA, Gooszen HG, van Laarhoven CJ. Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis. Cochrane Database Syst Rev. 2006;(4):CD006231. doi:10.1002/14651858.CD006231

Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment. Surg Endosc. 2006;20(9):1392–1401. doi:10.1007/s00464-005-0561-1

Woolf CJ, Chong MS. Preemptive analgesia—treating postoperative pain by preventing central sensitization. Anesth Analg. 1993;77(2):362–379. doi:10.1213/00000539-199308000-00026

Kehlet H, Dahl JB. Anesthesia, surgery, and challenges in postoperative recovery. Lancet. 2003;362(9399):1921–1928. doi:10.1016/S0140-6736(03)14966-5

Kissin I. Preemptive analgesia: problems with assessment of clinical significance. Methods Mol Biol. 2010;617:475–482. doi:10.1007/978-1-60327-323-7_35

Ong CK, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg. 2005;100(3):757–773. doi:10.1213/01.ANE.0000144428.98767.0E

Rainsford KD. Ibuprofen: pharmacology, efficacy, and safety. Inflammopharmacology. 2009;17(6):275–342. doi:10.1007/s10787-009-0016-x

Sinatra R. Role of COX-2 inhibitors in the evolution of acute pain management. J Pain Symptom Manage. 2002;24(1 Suppl):S18–S27. doi:10.1016/S0885-3924(02)00422-0

Southworth S, Peters J, Rock A, Pavliv L. A multicenter, randomized, double-blind, placebo-controlled trial of intravenous ibuprofen for postoperative pain. Clin Ther. 2009;31(9):1922–1935. doi:10.1016/j.clinthera.2009.09.008

Gago-Martinez A, Escontrela Rodriguez B, Planas Roca A, et al. Intravenous ibuprofen for treatment of postoperative pain: a multicenter, double-blind, placebo-controlled randomized trial. PLoS One. 2016;11(5):e0154004. doi:10.1371/journal.pone.0154004

Sezen O, Cevik B, Saracoglu KT. The effect of single-dose preemptive intravenous ibuprofen on intraoperative hemodynamic parameters, recovery characteristics, and postoperative pain. Int J Anesth Anesthesiol. 2020;7:118. doi:10.23937/2377-4630/1410118

McNicol ED, Ferguson MC, Hudcova J. Patient controlled opioid analgesia versus non-patient controlled opioid analgesia for postoperative pain. Cochrane Database Syst Rev. 2015;(6):CD003348. doi:10.1002/14651858.CD003348.pub3

Dahl JB, Kehlet H. Preventive analgesia. Br J Anaesth. 2011;106(1):7–9. doi:10.1093/bja/aeq304

Singla N, Rock A, Pavliv L. A multicenter, randomized, double-blind placebo-controlled trial of intravenous ibuprofen for postoperative pain management. Pain Med. 2010;11(8):1284–1293. doi:10.1111/j.1526-4637.2010.00911.x

Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg. 2017;152(3):292–298. doi:10.1001/jamasurg.2016.4952

Kroll HR. Intravenous ibuprofen for treatment of pain. Ann Pharmacother. 2009;43(12):2029–2037. doi:10.1345/aph.1M332

Jahr JS, Lee VK. Intravenous ibuprofen for the management of postoperative pain. Expert Rev Clin Pharmacol. 2010;3(5):597–604. doi:10.1586/ecp.10.46

Derry CJ, Derry S, Moore RA. Single-dose oral ibuprofen for acute postoperative pain in adults. Cochrane Database Syst Rev. 2009;(3):CD001548. doi:10.1002/14651858.CD001548.pub2

White PF. Multimodal analgesia: its role in preventing postoperative pain. Curr Opin Investig Drugs. 2008;9(1):76–82

Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. Am J Surg. 2002;183(6):630–641.doi:10.1016/S0002-9610(02)00866