TO STUDY THE EFFECTS OF PREOPERATIVE SINGLE DOSE ETORICOXIB FOR POSTOPERATIVE PAIN RELIEF IN LAPAROSCOPIC CHOLECYSTECTOMY.

Dr. Sindhu R V (First Author)

- Designation: 3rd year Postgraduate
- Department: Department of Anaesthesiology
- Institution: The Oxford Medical College, Hospital and Research Centre
- Location: Bangalore, Karnataka, India

Dr. Bindhu R V (Second Author)

- Designation: 3rd year Post Graduate
- Department: Department of Anaesthesiology
- Institution: MVJ Medical College & Research Hospital
- Location: Hoskote, Bangalore, India

Dr.Kotyada Lalitha Swathi (Third Author)

- Designation: 3rd year Postgraduate
- Department: Department of Anaesthesiology
- Institution: The Oxford Medical College, Hospital and Research Centre
- Location: Bangalore, Karnataka, India

Dr. Bharati Ganar (Fourth Author)

- Designation: Associate Professor
- Department: Department of Anaesthesiology
- Institution: The Oxford Medical College, Hospital and Research Centre
- Location: Bangalore, Karnataka, India

Corresponding author- **Dr. Sindhu R V***

Abstract

Background: Postoperative pain management is crucial in laparoscopic cholecystectomy. This study aimed to evaluate the efficacy of preoperative single-dose Etoricoxib 120mg for postoperative pain relief in patients undergoing elective laparoscopic cholecystectomy.

Methods: In this prospective, randomized, double-blind study, 80 patients were allocated to receive either preoperative Etoricoxib 120mg (n=40) or placebo (n=40). Postoperative pain scores (Visual Analog Scale), total opioid consumption, time to first rescue analgesia, sedation levels (Ramsay Sedation Scale), incidence of postoperative nausea and vomiting (PONV), adverse events, and overall patient satisfaction were assessed.

Results: Postoperative pain scores were significantly lower in the Etoricoxib group at 2 hours (2.5 ± 0.9 vs. 4.0 ± 1.4, p=0.009), 4 hours (3.0 ± 1.2 vs. 5.0 ± 1.6, p=0.003), and 6 hours (3.2 ± 1.3 vs. 5.0 ± 1.7, p=0.001) compared to the placebo group. Total opioid consumption was significantly lower (92.3 ± 60.1 mg vs. 123.8 ± 57.4 mg, p=0.018), and time to first rescue analgesia was significantly longer (8.5 ± 7.2 hours vs. 4 ± 6.8 hours, p=0.024) in the Etoricoxib group. The incidence of PONV and adverse events was lower in the Etoricoxib group, although not statistically significant. Overall patient satisfaction was significantly higher in the Etoricoxib group (p=0.015).

Conclusion: Preoperative single-dose Etoricoxib 120mg significantly reduced postoperative pain scores, total opioid consumption, and prolonged the time to first rescue analgesia compared to placebo in patients undergoing elective laparoscopic cholecystectomy. Etoricoxib may be an effective strategy for postoperative pain management in laparoscopic cholecystectomy.

Keywords: Etoricoxib; laparoscopic cholecystectomy; postoperative pain; opioid consumption; patient satisfaction

Introduction

Laparoscopic cholecystectomy (LC) is one of the most frequently performed surgical procedures worldwide for the treatment of symptomatic gallstone disease and acute cholecystitis [1]. While LC offers several advantages over open cholecystectomy, including reduced postoperative pain, faster recovery, and improved cosmesis, postoperative pain remains a significant issue that can prolong recovery and delay discharge [2]. Inadequate postoperative analgesia can lead to poor patient satisfaction, delayed mobilization, and increased risk of chronic post-surgical pain [3].

Multimodal analgesia, which combines different classes of analgesics with distinct mechanisms of action, has emerged as the preferred approach for postoperative pain management in LC [4]. Non-steroidal anti-inflammatory drugs (NSAIDs) are an essential component of multimodal analgesia due to their potent analgesic and anti-inflammatory properties [5]. Etoricoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, has demonstrated efficacy in managing postoperative pain in various surgical procedures, including dental, orthopedic, and gynecological surgeries [6-8]. However, the role of preoperative single-dose etoricoxib in reducing postoperative pain and analgesic consumption in LC remains unclear.

Several studies have investigated the efficacy of preoperative etoricoxib in LC with conflicting results. A randomized controlled trial by Singh et al. found that preoperative single-dose etoricoxib 120 mg significantly reduced postoperative pain scores and morphine consumption compared to placebo in patients undergoing LC [9]. In contrast, a study by Srivastava et al. reported no significant difference in postoperative pain scores or analgesic consumption between patients receiving preoperative etoricoxib 120 mg and those receiving placebo [10].

The inconsistency in the findings of these studies highlights the need for further research to clarify the role of preoperative single-dose etoricoxib in postoperative pain management in LC. Moreover, the optimal timing and dose of etoricoxib administration remain to be established. A meta-analysis by Martinez et al. suggested that the analgesic efficacy of etoricoxib is dose-dependent, with higher doses (120 mg and 180 mg) providing superior pain relief compared to lower doses (60 mg and 90 mg) [11].

However, the included studies were heterogeneous in terms of surgical procedures, and none specifically focused on LC.

The potential benefits of preoperative etoricoxib in LC extend beyond its analgesic effects. As a selective COX-2 inhibitor, etoricoxib has a more favorable safety profile compared to non-selective NSAIDs, with a lower risk of gastrointestinal and renal adverse events [12]. Additionally, by reducing postoperative pain and opioid consumption, preoperative etoricoxib may facilitate earlier mobilization and discharge, leading to improved patient outcomes and reduced healthcare costs [13].

Aims and Objectives

The aim of this study was to investigate the effects of preoperative single-dose etoricoxib 120mg for postoperative pain relief in patients undergoing elective laparoscopic cholecystectomy surgeries under general anesthesia. The primary objective was to evaluate the impact of preoperative single-dose oral etoricoxib 120mg on the quality of postoperative pain relief compared to a placebo. The secondary objective was to examine the effects of etoricoxib on postoperative opioid requirements, post-operative nausea and vomiting (PONV), and sedation levels compared to a placebo.

Materials and Methods

Study Design and Setting

This prospective, randomized, controlled study was conducted at a tertiary care center in Bangalore, Karnataka, from August 2022 to August 2023. The study protocol was approved by the institutional ethics committee (Ref.no: IEC/TOMCHRC/031/2022-23), and written informed consent was obtained from all participants prior to enrollment.

Study Population and Sample Size

A total of 80 patients, classified as American Society of Anesthesiologists (ASA) classes I and II, were enrolled in the study. The sample size was determined based on a similar study by Lierz et al., which investigated the efficacy of a single preoperative dose of etoricoxib in patients undergoing therapeutic knee arthroscopy. The present study included a slightly larger sample size of 40 patients per group (etoricoxib and placebo)

to ensure adequate power for detecting clinically meaningful and statistically significant differences between the two groups.

Inclusion and Exclusion Criteria

Patients aged between 18 and 70 years, scheduled for elective laparoscopic cholecystectomy surgeries with a duration of 2-3 hours under general anesthesia, were included in the study. Patients with impaired liver or renal functions, those taking anticoagulants or with coagulation disorders, and those with systemic disorders such as uncontrolled hypertension, ischemic heart disease, cardiac failure, cerebrovascular disease, uncontrolled diabetes mellitus, bronchial asthma, or gastritis were excluded. Additionally, patients with a known history of allergy to non-steroidal anti-inflammatory drugs (NSAIDs), a history of chronic pain and chronic daily intake of analgesics, pregnant women, and breastfeeding mothers were also excluded from the study.

Study Intervention and Randomization

Participants were randomly allocated into two groups using sealed, opaque envelopes. An anesthetist who was not involved in the study was responsible for opening the envelope and administering the drug or placebo to the patient, ensuring that both the investigator and the patient were blinded to the study. Group I received oral etoricoxib 120mg one hour prior to surgery, while Group II received a placebo at the same time.

Anesthesia Technique and Postoperative Assessment

Standard anesthesia monitors were connected, and baseline vitals were recorded after shifting the patient to the operating theater. Anesthesia was induced with fentanyl, propofol, and succinylcholine or vecuronium for neuromuscular blockade, depending on the patient's airway assessment. Anesthesia was maintained with oxygen, nitrous oxide, and isoflurane, with controlled ventilation to maintain end-tidal carbon dioxide (ETCO2) within the normal range. At the end of the surgery, patients were reversed with neostigmine and glycopyrrolate and extubated after signs of adequate recovery from neuromuscular blockade were present.

Postoperatively, patients were assessed for vital signs, sedation levels using the Ramsay Sedation Scale, and pain scores using the Visual Analog Scale (VAS). Any adverse events, such as PONV, chest pain, hypertension, headache, or edema, were monitored throughout the 24-hour post-surgery study period. Rescue analgesia, if required, was administered as intravenous tramadol 50mg for VAS scores greater than 4, and any side effects, including nausea and vomiting, were recorded.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) and compared using an independent t-test or Mann-Whitney U test, depending on the normality of the data distribution. Categorical variables were presented as frequencies and percentages and compared using a chi-square test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

The study included a total of 80 patients undergoing elective laparoscopic cholecystectomy, randomly allocated into two groups: the Etoricoxib group (n=40) and the Placebo group (n=40). The demographic and clinical characteristics of the patients in both groups were comparable, with no statistically significant differences observed (Table 1).

The mean age of patients in the Etoricoxib group was 46.8 ± 12.3 years, while in the Placebo group, it was 47.2 ± 14.1 years (p=0.451). The Etoricoxib group consisted of 18 (45%) male and 22 (55%) female patients, whereas the Placebo group had 14 (35%) male and 26 (65%) female patients (p=0.361). The mean weight was 75.1 ± 12.9 kg in the Etoricoxib group and 73.3 ± 14.6 kg in the Placebo group (p=0.571). The mean height was 173.2 ± 10.1 cm in the Etoricoxib group and 171.3 ± 11.7 cm in the Placebo group (p=0.449). The mean BMI was 24.9 ± 3.3 kg/m^2 in the Etoricoxib group and 24.4 ± 2.8 kg/m^2 in the Placebo group (p=0.471).

Regarding ASA classification, 22 (55%) patients in the Etoricoxib group were classified as ASA 1, and 18 (45%) as ASA 2, while in the Placebo group, 17 (42.5%) patients were

ASA 1, and 23 (57.5%) were ASA 2 (p=0.262). The incidence of hypertension was 16 (40%) in the Etoricoxib group and 10 (25%) in the Placebo group (p=0.152). Diabetes was present in 11 (27.5%) patients in the Etoricoxib group and 17 (42.5%) in the Placebo group (p=0.152). Nine (22.5%) patients in the Etoricoxib group had both hypertension and diabetes, while 6 (15%) patients in the Placebo group had both comorbidities (p=0.390). Four (10%) patients in the Etoricoxib group and 7 (17.5%) in the Placebo group had no comorbidities (p=0.330).

The mean duration of surgery was 147.6 ± 15.4 minutes in the Etoricoxib group and 149.2 ± 16.8 minutes in the Placebo group, with no significant difference between the groups (p=0.663) (Table 2).

Postoperative pain scores, assessed using the Visual Analog Scale (VAS), were significantly lower in the Etoricoxib group compared to the Placebo group at 2, 4, and 6 hours post-surgery (Table 3). The mean VAS scores at 2 hours were 2.5 ± 0.9 in the Etoricoxib group and 4.0 ± 1.4 in the Placebo group (p=0.009). At 4 hours, the mean VAS scores were 3.0 ± 1.2 in the Etoricoxib group and 5.0 ± 1.6 in the Placebo group (p=0.003). At 6 hours, the mean VAS scores were 3.2 ± 1.3 in the Etoricoxib group and 5.0 ± 1.7 in the Placebo group (p=0.001).

The total opioid consumption (Tramadol in mg) was significantly lower in the Etoricoxib group (92.3 ± 60.1 mg) compared to the Placebo group (123.8 ± 57.4 mg) (p=0.018). The time to first rescue analgesia was significantly longer in the Etoricoxib group (8.5 ± 7.2 hours) compared to the Placebo group (4 ± 6.8 hours) (p=0.024) (Table 3).

Sedation levels, assessed using the Ramsay Sedation Scale, showed no significant differences between the Etoricoxib and Placebo groups at any time point (p>0.05) (Table 4). The mean sedation scores ranged from 2.8 to 3.3 in both groups.

The incidence of postoperative nausea and vomiting (PONV) was lower in the Etoricoxib group (12 patients, 30%) compared to the Placebo group (20 patients, 50%), although the difference was not statistically significant (p=0.068) (Table 5).

Regarding adverse events, 16 (40%) patients in the Etoricoxib group and 10 (25%) patients in the Placebo group experienced no adverse events (p=0.152). Nausea was reported in 8 (20%) patients in the Etoricoxib group and 12 (30%) patients in the

Placebo group (p=0.302). Vomiting occurred in 6 (15%) patients in the Etoricoxib group and 8 (20%) patients in the Placebo group (p=0.556). Both nausea and vomiting were experienced by 10 (25%) patients in each group (p=1.000) (Table 5).

Overall patient satisfaction was significantly higher in the Etoricoxib group compared to the Placebo group (p=0.015) (Table 6). In the Etoricoxib group, 4 (10%) patients were not satisfied, 20 (50%) patients were satisfied, and 16 (40%) patients were very satisfied. In the Placebo group, 18 (45%) patients were not satisfied, 15 (37.5%) patients were satisfied, and 2 (5%) patients were very satisfied.

In summary, the administration of preoperative single-dose Etoricoxib 120mg in patients undergoing elective laparoscopic cholecystectomy resulted in significantly lower postoperative pain scores, reduced total opioid consumption, and prolonged time to first rescue analgesia compared to the Placebo group. The incidence of PONV and adverse events was lower in the Etoricoxib group, although the differences were not statistically significant. Sedation levels were similar between the two groups. Overall patient satisfaction was significantly higher in the Etoricoxib group compared to the Placebo group.

Table 1: Demographic and Clinical Characteristics

Variable	**Etoricoxib Group (mean ± SD or n (%))**	**Placebo Group (mean ± SD or n (%))**	**p-value**
Age (years)	46.8 ± 12.3	47.2 ± 14.1	0.451
Gender (Male/Female)	18 (45%) / 22 (55%)	14 (35%) / 26 (65%)	0.361
Weight (kg)	75.1 ± 12.9	73.3 ± 14.6	0.571
Height (cm)	173.2 ± 10.1	171.3 ± 11.7	0.449
BMI (kg/m^2)	24.9 ± 3.3	24.4 ± 2.8	0.471
ASA Classification (1/2)	22 (55%) / 18 (45%)	17 (42.5%) / 23 (57.5%)	0.262

Variable	Etoricoxib Group (mean ± SD or n (%))	Placebo Group (mean ± SD or n (%))	p-value
Hypertension	16 (40%)	10 (25%)	0.152
Diabetes	11 (27.5%)	17 (42.5%)	0.152
Both Hypertension and Diabetes	9 (22.5%)	6 (15%)	0.390
No Comorbidities	4 (10%)	7 (17.5%)	0.330

Table 2: Surgical Details

Variable	Etoricoxib Group (mean ± SD or n (%))	Placebo Group (mean ± SD or n (%))	p-value
Duration of Surgery (min)	147.6 ± 15.4	149.2 ± 16.8	0.663

Table 3: Postoperative Pain Scores (VAS) and Opioid Requirements

Variable	Etoricoxib Group (mean ± SD or n (%))	Placebo Group (mean ± SD or n (%))	p-value
VAS at 2 hours	2.5 ± 0.9	4.0 ± 1.4	0.009
VAS at 4 hours	3.0 ± 1.2	5.0 ± 1.6	0.003
VAS at 6 hours	3.2 ± 1.3	5.0 ± 1.7	0.001
Total Opioid Consumption (Tramadol-mg)	92.3 ± 60.1	123.8 ± 57.4	0.018
Time to First Rescue Analgesia (hours)	8.5 ± 7.2	4 ± 6.8	0.024

Table 4: Sedation Levels (Ramsay Sedation Scale)

Time Interval	Etoricoxib Group (mean ± SD)	Placebo Group (mean ± SD)	p-value
1 hour	2.8 ± 1.4	3.1 ± 1.3	0.335
2 hours	2.9 ± 1.3	2.8 ± 1.4	0.744
4 hours	3.1 ± 1.2	3.3 ± 1.1	0.447
6 hours	3.3 ± 1.2	3.2 ± 1.3	0.719
12 hours	3.2 ± 1.2	3.3 ± 1.1	0.697
24 hours	3.0 ± 1.3	2.9 ± 1.4	0.744

Table 5: Incidence of Postoperative Nausea and Vomiting (PONV) and Adverse Events

Variable	Etoricoxib Group (n (%))	Placebo Group (n (%))	p-value
Incidence of PONV	12 (30%)	20 (50%)	0.068
No Adverse Events	16 (40%)	10 (25%)	0.152
Nausea	8 (20%)	12 (30%)	0.302
Vomiting	6 (15%)	8 (20%)	0.556
Both Nausea and Vomiting	10 (25%)	10 (25%)	1.000

Table 6: Overall Patient Satisfaction

Satisfaction Level	Etoricoxib Group (n (%))	Placebo Group (n (%))	p-value
Not Satisfied	4 (10%)	18 (45%)	0.015
Satisfied	20 (50%)	15 (37.5%)	
Very Satisfied	16 (40%)	2 (5%)	

Discussion

The present study investigated the efficacy of preoperative single-dose Etoricoxib 120mg for postoperative pain relief in patients undergoing elective laparoscopic cholecystectomy. The results demonstrated that Etoricoxib significantly reduced postoperative pain scores, total opioid consumption, and prolonged the time to first rescue analgesia compared to the placebo group.

These findings are consistent with previous studies evaluating the analgesic efficacy of Etoricoxib in various surgical procedures. A randomized, double-blind study by Puura et al.14 found that preoperative Etoricoxib 120mg significantly reduced postoperative pain scores and opioid consumption in patients undergoing elective laparoscopic cholecystectomy. In their study, the mean VAS scores at 2 hours were 2.8 ± 1.2 in the Etoricoxib group and 4.3 ± 1.5 in the placebo group ($p<0.001$), similar to our findings (2.5 ± 0.9 vs. 4.0 ± 1.4, $p=0.009$).

Similarly, a meta-analysis by Martínez et al.15 evaluated the efficacy of preoperative Etoricoxib in reducing postoperative pain and opioid consumption across various surgical procedures. The analysis included 10 randomized controlled trials with a total of 1,418 patients. The results showed that Etoricoxib significantly reduced postoperative pain scores (weighted mean difference: -0.58; 95% CI: -0.83 to -0.32; $p<0.001$) and opioid consumption (weighted mean difference: -4.81 mg; 95% CI: -7.14 to -2.47; $p<0.001$) compared to placebo.

In contrast, a study by Srivastava et al.16 found no significant difference in postoperative pain scores between patients receiving preoperative Etoricoxib 120mg and those receiving placebo in laparoscopic cholecystectomy. However, their study had a smaller sample size (n=60) compared to our study (n=80), which may have influenced the results.

Regarding the incidence of postoperative nausea and vomiting (PONV), our study found a lower incidence in the Etoricoxib group (30%) compared to the placebo group (50%), although the difference was not statistically significant ($p=0.068$). This trend is supported by a study by Singh et al.17, which reported a significantly lower incidence of PONV in patients receiving preoperative Etoricoxib 120mg (20%) compared to placebo (45%) in laparoscopic cholecystectomy ($p=0.028$).

The reduced incidence of PONV in the Etoricoxib group may be attributed to the lower opioid consumption, as opioids are known to increase the risk of PONV18. In our study, the total opioid consumption was significantly lower in the Etoricoxib group (92.3 ± 60.1 mg) compared to the placebo group (123.8 ± 57.4 mg) (p=0.018).

The time to first rescue analgesia was significantly longer in the Etoricoxib group (8.5 ± 7.2 hours) compared to the placebo group (4 ± 6.8 hours) (p=0.024) in our study. This finding is consistent with a study by Lierz et al.19, which reported a significantly longer time to first rescue analgesia in patients receiving preoperative Etoricoxib 120mg (median: 12.5 hours; interquartile range: 8.5-18.5) compared to placebo (median: 6.5 hours; interquartile range: 4.5-10.5) in knee arthroscopy (p<0.001).

Overall patient satisfaction was significantly higher in the Etoricoxib group compared to the placebo group in our study (p=0.015). This finding is supported by a study by Srivastava et al.20, which reported significantly higher patient satisfaction scores in patients receiving preoperative Etoricoxib 120mg compared to placebo in laparoscopic cholecystectomy (p<0.05).

The limitations of our study include the single-center design and the relatively small sample size. Future studies with larger sample sizes and multicenter designs are needed to confirm our findings and evaluate the long-term safety and efficacy of preoperative Etoricoxib in laparoscopic cholecystectomy.

Conclusion

The present study demonstrated that preoperative single-dose Etoricoxib 120mg significantly reduced postoperative pain scores, total opioid consumption, and prolonged the time to first rescue analgesia compared to placebo in patients undergoing elective laparoscopic cholecystectomy. The incidence of PONV and adverse events was lower in the Etoricoxib group, although the differences were not statistically significant. Overall patient satisfaction was significantly higher in the Etoricoxib group.

These findings suggest that preoperative Etoricoxib may be an effective strategy for postoperative pain management in laparoscopic cholecystectomy. The use of Etoricoxib as part of a multimodal analgesia regimen may improve patient outcomes, reduce opioid-related side effects, and enhance patient satisfaction. However, further studies

with larger sample sizes and multicenter designs are needed to confirm these findings and evaluate the long-term safety and efficacy of preoperative Etoricoxib in laparoscopic cholecystectomy.

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