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Original Research Article

# A Randomized Control Study on Effect of Preemptive Paracetamol on Postoperative Analgesic Requirement Inpatients Undergoing Laparoscopic Cholecystectomy

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**Abstract:**

**Background**: In several patient populations, preemptive Paracetamol has been demonstrated to reduce the need for postoperative analgesia; however, there is insufficient data to support its use in laparoscopic cholecystectomy. Our goal was to ascertain how preemptive Paracetamol affected the need for postoperative analgesia in individuals having laparoscopic cholecystectomy.

**Methods**: Three groups of 90 patients with physical status I or II, according to the American Society of Anesthesiologists, were chosen at random. One gram of Paracetamol was injected intravenously into Group I half an hour before surgery, one gram was injected into Group II during skin closure, and Group III was the control group and did not receive any Paracetamol. Up to six hours after surgery, the three groups' postoperative pain scores, by VAS and analgesia required, were compared.

**Results**: For the majority of the trial, the three groups' postoperative pain levels were similar. Compared to Group III, Groups I and II consumed much less Fentanyl after surgery. The incidence of PONV and the sedation scores did not differ between the two groups.

**Conclusion**: Postoperative discomfort following laparoscopic cholecystectomy can be effectively managed with preemptive intravenous paracetamol.

**Keywords**: Pain, Paracetamol.



## Introduction

Preemptive pain management aims to decrease the need for analgesics by using systemic or localized analgesics before the surgical operation, which prevents central sensitization of pain pathways.[1] Experimental evidence has shown that it can lessen the quantity of analgesia required by acting as an anti-nociceptive agent prior to the delivery of a nociceptive stimulus.[2,3] Data from a number of clinical investigations, however, have revealed discrepancies and may not always corroborate this theory.[4] Numerous medications, including opioids, non-steroidal anti-inflammatory medicines (NSAIDs), Paracetamol, local anesthetics, Ketamine, and adjuvants, can be used to treat post-operative pain. In recent years, these medications have also been utilized as preventative analgesics. Effective analgesia for immediate post-operative pain is provided by the intravenous preparation of Paracetamol, which has an excellent safety profile. Preventive intravenous Paracetamol use may result in a pattern of pain that subsides and a reduction in the need for analgesics during the recovery phase. [5]

## Materials and Methods

This prospective randomized controlled study was conducted in the Department of Anaesthesia, Madhubani Medical College and Hospital, Madhubani, Bihar from February 2023 to September 2023. 90 ASA I and II adult patients, aged 18 to 60, who were undergoing laparoscopic cholecystectomy under general anesthesia for less than or equal to ninety minutes, were included in the study after obtaining their informed consent. To detect a significant difference of 20% or more in opioid intake with a power of 80% and a significance threshold of 5%, a sample size of 30 patients per group was determined. ASA grade III

or higher, patient refusal, history of study drug allergic reactions, chronic alcoholism, obesity, pregnancy, gastro-oesophageal reflux disease, neurological or bleeding disorders, and history of Paracetamol, opioids, or non-steroidal anti-inflammatory drug use 48 hours prior to surgery were among the exclusion criteria.

Following the pre-anesthesia examination, all patients were given tablet Alprazolam 0.25 mg the night before the procedure. Ringer lactate infusion was initiated and an IV line was established following the acquisition of baseline data.

During the pre-anesthesia examination, all patients received an explanation of the visual analogue scale (VAS) for pain.

Using computer-generated randomization, patients were divided into three groups at random:

1. Group I (n=30, pre-emptive group): Received IV Paracetamol 1 g (100 ml) 30 min prior to induction, and 100 ml of IV normal saline prior to skin closure.
2. Group II (n=30, intra-operative group): Received 100ml IV normal saline 30 min before induction, and IV paracetamol 1 g (100 ml) prior to skin closure.
3. Group III (n=30, control group): Receiving 100 ml IV normal saline 30 min before induction, and prior to skin closure.

Anaesthesia was induced with Propofol 2 mg/kg IV, fentanyl 2□g/kg IV, and Vecuronium 0.1 mg/kg IV. Anaesthesia was maintained by Sevoflurane in 40/60 Oxygen/Nitrous oxide ratio with top up doses of Vecuronium as required.

All the patients were monitored for heart-rate (HR), non-invasive blood pressure (NIBP), pulse oxygen saturation (SpO2) and end tidal carbon dioxide (ETCO2) throughout the procedure. Patients were extubated after reversal with Inj Glycopyrrolate (0.01 mg/kg) and Inj Neostigmine (0.05mg/kg) and thorough suctioning was done.

In the post anaesthesia care unit, postoperative pain score was measured by using VAS of 0-10 (0 indicated no pain and 10 indicated worst imaginable pain). Postoperative pain was observed postoperatively at 15minutes, 30 minutes, one hour, two hours and six hours after shifting the patient to the post-anaesthesia care unit.

Injection Fentanyl 1 □g/kg IV was used as rescue analgesic, if the VAS >3.

The pain score assessment was done by a trained nursing professional who was blinded to the study drugs administered.

To detect a significant difference of 20% or more in opioid intake with a power of 80% and a significance threshold of 5%, a sample size of 30 patients per group was determined. Mean±SD was used to express the quantitative variables, and the unpaired t-test and ANOVA were used for comparison. Using the Chi-square test, the qualitative variables were analyzed and presented as frequencies or percentages. The statistical analysis was conducted using SPSS version 20.0.

A p value of $\leq 0.05$ was considered as statistically significant.

## Results

95 patients in all had their eligibility to take part in the study evaluated. Four patients were disqualified for having a history of liver disease, and one patient was disqualified for refusing to take part in the trial.

Age, sex, weight, ASA physical status score, and length of operation did not differ among the three groups at baseline. (Table 1)

**Table 1: Baseline Characteristics**

| Variables | Group I | Group II | Group III | P-value |
|---|---|---|---|---|
| Age (Mean±SD in years) | 45.07±11.10 | 43.83±12.39 | 43.27±9.58 | 0.814 |
| Weight (Mean±SD in kgs) | 62.8±6.27 | 60.27±6.14 | 60.57±6.43 | 0.238 |
| Gender (M/F) | 10/20 | 12/18 | 7/23 | 0.38 |
| ASA (I/II) | 20/10 | 17/13 | 17/13 | 0.659 |
| Duration of surgery (Mean±SD in min.) | 70.40±9.00 | 72.07±7.44 | 71.07±7.08 | 0.713 |

The mean VAS ratings at two hours were considerably higher in Group II (2.90±0.92) than in Group I (2.50±0.51). Group I and II's mean pain scores at 15 and 30 minutes, as well as at one and six hours, were similar and not statistically significant ($p>0.05$). The mean pain scores at 15 minutes and two hours were substantially greater in Group III (3.97±1.47 and 2.90±0.80) than in Group I (3.03±0.76 and 2.50±0.51). The mean pain scores for groups I and III were similar and not statistically significant at 30 minutes, 1 hour, and 6 hours.

The mean VAS scores at 15 minutes were substantially higher in Group III (3.97±1.47) than in Group II (2.87±1.11). Group II and III's mean pain scores at 30 minutes, 1 hour, 2 hours, and 6 hours were similar and not statistically significant ($p>0.05$).

**Table 2: Post-operative VAS Score**

| VAS Score | 15 min. | 30 min. | 1 hour | 2 hours | 6 hours |
|---|---|---|---|---|---|
| Group I (Mean±SD) | 3.03±0.76 | 3.17±1.21 | 2.80±0.89 | 2.50±0.51 | 2.67±0.92 |
| Group II (Mean±SD) | 2.87±1.11 | 3.37±152 | 2.97±0.96 | 2.90±0.92 | 2.77±0.77 |
| Group III (Mean±SD) | 3.97±1.47 | 3.00±0.59 | 3.10±0.88 | 2.90±0.80 | 2.67±0.84 |
| p-value (Overall) | <0.001 | 0.692 | 0.134 | 0.108 | 0.440 |
| I versus II | 0.500 | 0.574 | 0.489 | 0.042 | 0.651 |
| I versus III | 0.003 | 0.499 | 0.195 | 0.025 | 1.000 |
| II versus III | 0.002 | 0.223 | 0.579 | 1.000 | 0.634 |

Overall, post-operative fentanyl consumption was24.87±34.32 mcg in Group I, 43.87±32.17 □g in GroupII, and 60.67±44.98 □g in Group III. The requirement of fentanyl as a rescue analgesic in group III was significantly more than in group I, and requirement in group II was significantly more than in group I ($p<0.05$). In Group II vs III, fentanyl consumption was found to be more in Group III as compared to Group II but this difference failed to reach statistical significance with P value > 0.05.

**Table 3: Fentanyl consumption (mcg)**

| | Upto 1 hour | 1 to 2 hours | 2 to 6 hours | Total |
|---|---|---|---|---|
| Group I (Mean±SD) | 14.20±26.37 | 4.30±16.41 | 6.37±19.55 | 24.87±34.32 |
| Group II (Mean±SD) | 26.03±30.56 | 16.17±27.41 | 3.33±12.69 | 43.87±32.17 |
| Group III (Mean±SD) | 38.40±30.17 | 15.93±27.04 | 6.33±19.50 | 60.67±44.98 |
| p-value (Overall) | <0.001 | 0.032 | 0.887 | 0.001 |
| I versus II | 0.114 | 0.046 | 0.479 | 0.031 |
| I versus III | 0.002 | 0.049 | 0.995 | 0.001 |
| II versus III | 0.120 | 0.974 | 0.483 | 0.102 |

There was no difference in the length of stay in PACU, incidence of PONV and in the incidence of sedation.

The sedation scores were similar in both the groups. No postoperative complications were reported from any of the groups.

**Discussion**

One of the most crucial issues is effectively managing post-operative pain, which not only makes the patient more comfortable but also makes early mobilization easier and shortens hospital stays. Incisional pain (also known as somatic pain), visceral pain (also known as deep intra-abdominal pain), and shoulder pain (also known as visceral pain) are the three main types of pain that patients suffer during laparoscopic procedures. In addition, the pain is frequently unpredictable, exhibiting individual variance in intensity and duration. [6] Numerous recent research have looked into different approaches to managing pain following laparoscopic cholecystectomies.[7–9]

Preemptive analgesia is defined as such: (a) beginning prior to surgery; (b) preventing the development of central sensitization due to incisional injury (covering only the surgical period); and (c) preventing the development of central sensitization due to incisional and inflammatory injuries (covering both the surgical period and the first postoperative period). In recent years, preemptive analgesia has been studied with the goal of reducing the need for postoperative analgesia by providing analgesia before a painful stimuli to avoid central sensitization. The need for postoperative analgesia has been shown to decrease with preemptive analgesia. [10]

In this study, we evaluated the effects of 1g IV Paracetamol as a preventative analgesic during laparoscopic procedures on post-operative pain scores and the need for Fentanyl during the recovery phase.

When 1 gm IV Paracetamol was given 30 minutes before to the start of surgery, we observed a substantial decrease in pain scores compared to when 1 gm IV Paracetamol was given intraoperatively prior to skin closure.

A randomized clinical trial with 80 patients who were candidates for laparoscopic cystectomy was carried out in 2011 by Choudhuri et al. [6] They evaluated the analgesic impact of Acetaminophen in comparison to a placebo and demonstrated that the Acetaminophen group had a lower mean VAS score for pain reduction than the placebo group.

Furthermore, they stated that the intervention group consumed fewer opioids (Fentanyl) overall than the control group (50 mg vs. 150 mg, respectively). Similar studies evaluating the analgesic impact of Acetaminophen on pain following cholecystectomy were carried out by Cakan et al. in 2008 and Salihoglu et al. in 2009, and the findings were comparable. [11,12] A systematic evaluation of 36 trials with 3896 patients was conducted in 2011 by Tzortzopoulou et al., who evaluated the

postoperative analgesic impact of Acetaminophen in comparison to a placebo in both adults and children. They found that the Acetaminophen group experienced 50% pain alleviation, whereas the placebo group experienced 16%. Additionally, compared to the control group, the intervention group used 30% fewer opioids overall during the first four hours following surgery.[13]

These findings suggest that in Group I, adequate analgesic efficacy was maintained during the postoperative phase. Furthermore, the reduced pain levels in group I could be explained by a reduction in central nervous system excitability brought on by blocking nociceptive stimuli before tissue architecture is harmed. Its analgesic effect lasts longer than its impact duration, in our opinion, because the pre-emptively administered Paracetamol avoids central sensitization.

## Conclusion

In conclusion, giving patients1g of IV Paracetamol beforehand, undergoing laparoscopic cholecystectomy, produced high-quality analgesia, resulting in lower pain levels during the postoperative phase, higher patient satisfaction, lower post-operative pain scores& less use of Fentanyl. Therefore, it is safe to provide 1g of IV paracetamol in advance for laparoscopic cholecystectomy for better post-operative analgesia.

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