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Original research article

A study to evaluate the efficacy of preemptive intravenous paracetamol on reducing postoperative opioid requirement in laparoscopic cholecystectomy

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Abstract

Background: The purpose of the present study was to determine the postoperative analgesic effects of preemptive intravenous (iv) paracetamol and the amount of reduction in opioid consumption.

Materials and Methods: After obtaining Ethics committee approval, ninety patients were randomly allocated to one of three groups for ASA I-II: Group I was given IV paracetamol 1 g/100 mL ten minutes before skin incision, and they also received 100 mL of normal saline solution after the procedure. Group II was given 100 mL of normal saline solution ten minutes before the skin incision, and they also received 100 mL of IV Paracetamol after the procedure. Group III was given a placebo, who also received 100 mL of normal saline solution ten minutes before the skin incision and 100 mL of normal saline solution at the end of the procedure. The first need for analgesics and the total amount of analgesics consumed in 24 hours were noted. Every patient had their pain scores measured using the Visual Analog Scale (VAS) at the end of the operation.

Results: Group I and Group II experienced a substantially longer time to first analgesic demand than Group III (p<0.05). Group I experienced a substantially longer time to first analgesic demand than Group II (p<0.05). Compared to Group III, Group I and II recorded considerably reduced total analgesic intake and postoperative VAS pain score. Group I recorded considerably lower postoperative VAS pain scores and used fewer analgesics overall than Group II (p<0.05).

Conclusion: In conclusion, preemptive intravenous paracetamol lowered post-operative pain scores, the requirement for and usage of supplemental opioids, and the time to first request analgesics after laparoscopic cholecystectomy procedures. It also offered effective and reliable postoperative pain control.

Keywords: Preemptive paracetamol, opioids, cholecystectomy, pain

1. Introduction

The advent of minimally invasive surgery has not only transformed surgical techniques in recent times, but it has also impacted anesthesiology practice.

While the discomfort following laparoscopic surgery is significantly less severe and less prolonged discomfort than following an open procedure, postoperative pain is still significant and requires effective management with minimal side effects to minimize complications and hospital stays.

Pre-emptive pain control aims to minimize the need for analgesics by applying systemic or localized analgesics before to the commencement of the surgical operation, hence minimizing central sensitization of pain pathways [1].

Using anti-nociceptive measures before administration of nociceptive stimulation can lessen the quantity of analgesic that is required, which was shown by experimentation [2, 3]. Data from several clinical trials, however, have revealed variations that may not always corroborate this theory [4].

Numerous medications, including opioids, non-steroidal anti-inflammatory medicines (NSAIDs), paracetamol, local anesthetics, ketamine and adjuvants-which have also been utilized as preemptive analgesics recently-can be used to treat post-operative pain.

Paracetamol is a centrally-acting drug, that inhibits prostaglandin synthesis and cyclooxygenase (COX) of the nervous system. Paths based on the spinal serotonergic mechanism of action of other central mechanisms may be involved in the acting mechanism of paracetamol. In clinical practice, paracetamol does not cause the side effects that seem typically with other nonsteroid anti-inflammatory drugs (NSAID), which are thought to occur due to inhibition of peripheral COX-1 (gastric toxicity, and

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antiplatelet activity.
Paracetamol is considered to be a safe drug, and it does not have such gastrointestinal problems or central side effects according to other NSAID drugs and opioids.
With an excellent safety record, the intravenous form of paracetamol is utilized to effectively relieve acute post-operative pain. Preventive intravenous paracetamol administration can result in a remission of pain and a reduction in the need for analgesic medication throughout the recovery phase [5].
Therefore, using a placebo-controlled experiment, we tried to assess the impact of prophylactic intravenous paracetamol on the need for post-operative opioid analgesics in patients having laparoscopic cholecystectomy under general anesthesia.

2. Materials and Methods
The present study is a prospective randomized controlled study conducted in the Department of Anaesthesiology, in Mamata General Hospital during the period of October 2023 to June 2024.
Ninety ASA I and II adult patients, aged 18 to 60 years, who underwent laparoscopic cholecystectomy under general anesthesia for a duration of less than or equal to ninety minutes, were included in the study after receiving clearance from the ethics committee and gaining informed consent.

Inclusion Criteria
1. American Society of Anesthesiologists (ASA) I and II patients.
2. **Age:** 18-60 years.
3. **Weight:** 50-70 kg.
4. Patients posted for Laparoscopic Cholecystectomy.
5. **Surgery Duration:** Less than or equal to Ninety minutes.

Exclusion Criteria
1. American Society of Anesthesiologists (ASA) III and IV.
2. History of allergic reactions to paracetamol.
3. History of usage of paracetamol, opioids, or NSAIDs in the 48 hours (h) before requiring chronic analgesic treatment.
4. Chronic alcoholism, deficiency of liver and kidney.
5. Cardiovascular system illness.
6. Bleeding diathesis.

After recording baseline parameters, an IV line was secured and ringer lactate infusion was started. The visual analog scale (VAS) for pain was explained to all the patients during the pre-anesthesia check-up.
Three groups of patients were randomly assigned which are as follows:
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 100 ml 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):** Received 100 ml IV normal saline 30 min before induction, and prior to skin closure.

Propofol (2 mg/kg IV), fentanyl (2 µg/kg IV), and vecuronium (0.1 mg/kg IV) were used to induce anesthesia. Isoflurane in a 40/60 oxygen/nitrous oxide ratio was used to maintain anesthesia, and vecuronium top-up doses were given as needed.
Heart rate (HR), noninvasive blood pressure (NIBP), pulse oxygen saturation (SpO2), and end-tidal carbon dioxide ($ETCO_2$) were all monitored in all patients during the process.
Following reversal, patients were extubated using a full suctioning technique along with 0.01 mg/kg of glycopyrrolate and 0.05 mg/kg of neostigmine.
Side effects, such as nausea, vomiting, respiratory depression, itching, rash, allergic reaction, stomach irritation, diarrhea, and constipation, headache, drowsiness, dry mouth, sweating, hypotension (noted as mild, moderate, severe) were recorded.

Statistical analysis
To detect a significant difference in opioid use of 20% or more with a power of 80% and a significance level of 5%, a sample size of 30 patients per group was determined. The unpaired t-test and ANOVA were utilized to compare the quantitative variables, which were represented as mean ± SD. The Chi-square test was used to analyze the qualitative variables once they were expressed as frequencies or percentages. The statistical analysis was conducted using SPSS version 15.0. It was determined that a p-value of less than or equal to 0.05 was statistically significant.

3. Results

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A total of ninety patients were involved in the study. There were no significant differences between the groups about demographic variables (age, gender, weight, and height) and ASA physical status or the mean duration of anesthesia and surgery time [Table 1].

Table 1: Demographic properties, and operation and anesthesia duration [Mean ± SD, n]

	Group I (n:30)	**Group II (n:30)**	**Group III (n:30)**
Gender(M/F)	14/16	12/18	19/11
Age(years)	42.7±9.8	41.2±7.7	44.5±6.5
Weight(kg)	70.8±10.2	70.5±8.1	69.2±7.1
Height(cm)	167.5±6.4	166.3±7.1	163.4±8.2
ASA(I/II)	12/18	16/14	13/17
Operation duration(min)	86.3±10.4	88.5±9.2	93.7±11.2
Anesthesia duration(min)	102.1±10.2	104.3±9.2	109.4±8.0

The changes in post-operative VAS pain scores are shown in Table 2. In Group I vs II, mean VAS scores were significantly higher in group II (2.90±0.92) at two hours as compared to Group I (2.50±0.51). At 15 min, 30 min, one, and six hours, the mean pain scores of group I and II were comparable and statistically not significant ($p>0.05$). In Group I vs III, mean pain scores were significantly higher in Group III (3.97±1.47 and 2.90±0.80) at 15 min and two hours as compared to Group I (3.03±0.76 and 2.50±0.51). At 30 min, one, and six hours, the mean pain scores of groups I and III were comparable and statistically not significant. In Group II vs III, mean VAS scores were significantly higher than in Group III (3.97±1.47) at 15 min as compared to Group II (2.87±1.11). At 30 min, one, two, and six hours, mean pain scores of groups II and III were comparable and statistically not significant ($p>0.05$).

Table 2: Post-operative VAS values [Mean ± SD, (min-max)]

VAS	**15 min**	**30 min**	**1 hr**	**2 hr**	**4 hr**	**6 hr**
Group I (N=30)	3.0±1.8	2.8±1.5	2.9±1.2	3.7±2.1	3.1±1.7	2.4±1.2
Group II (N=30)	3.2±1.3	3.9±1.9	3.9±2.3	3.7±1.9	3.3±1.7	2.5±1.3
Group III (N=30)	4.5±2.0	5.4±2.5	3.8±1.7	3.5±1.3	3.1±1.5	3.1±0.8

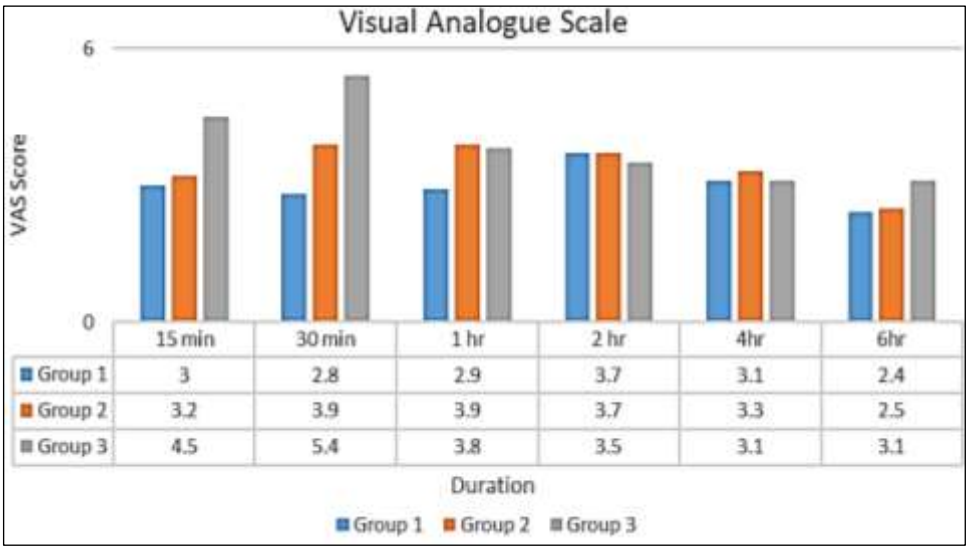

Fig 1: Visual Analogue Scale

The time to first request analgesic was considerably longer in Group I compared to Group II ($P = 0.08$), and in Group I compared to Group III ($P < 0.001$, $P = 0.03$, respectively).

According to Table 3, patients in Group I took longer (153.0 min) than patients in Group II (91.9 min) and Group III (33.7 min) to take post-operative analgesics ($p<0.05$). The total amount of opioids consumed during the post-operative 24-hour period was considerably lower in Group I ($P < 0.001$), Group II ($P < 0.001$), and Group III than in Group I ($P = 0.018$) [Table 3]. Of the patients in Group III, 91% used supplemental analgesics. 43 percent of patients in Group I and 66 percent of patients in Group II. Group I and Group II had a considerably smaller number of patients requiring additional analgesics at 0-6, 6-12, and 12-24 hours than Group III ($p<0.05$). When comparing Group I to Group II, the proportion of patients needing additional analgesics at 0-6 and 6-12 hours was significantly reduced ($p<0.05$). [Table 3].

Table 3: First analgesic requirement time and post-operative analgesic requirements [Mean ± SD, n]

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	Group I	Group II	Group III
First analgesic requirement time(min)	153.0±110.9	99.1±55.1	30.3±18.1
Analgesic consumption in mg	50.0±80.5	101.3±86.8	182.3±92.6
No. of patients requiring supplemental analgesia in the first 6 hr	14/30	18/30	27/30
No. of patients requiring supplemental analgesia in 6-12 hr	8/30	12/30	18/30
No. of patients requiring supplemental analgesia in 12-24 hr	0/30	0/30	8/30
No. of patients requiring supplemental analgesic >24hr	15/30	18/30	27/30

4. Discussion

One of the most significant issues is providing adequate care for post-operative pain, which makes the patient comfortable makes early mobilization easier, and shortens hospital stays. Three distinct types of pain are felt during laparoscopic procedures: visceral pain, also known as deep intra-abdominal pain, incisional pain (also known as somatic pain), and shoulder pain (also known as visceral pain). In addition, the pain frequently varies in strength and duration from person to person. [6] Numerous recent research has looked into different ways to manage pain following laparoscopic cholecystectomies. [7–9]. Treatment that does one of the following three things:

1. Begins before surgery.
2. Prevents the development of central sensitization brought on by incisional damage (covering only the period of surgery).
3. (Covers the surgical and early postoperative periods) inhibits the development of central sensitization brought on by incisional and inflammatory damage.

Pre-emptive analgesia, which has been studied recently, aims to reduce the need for postoperative analgesia by giving analgesia before a painful stimulus to avoid central sensitization. It has been demonstrated that preemptive analgesia can lessen the need for postoperative analgesia [10].

In this study, we administered 1 g of IV paracetamol as a preemptive analgesic before laparoscopic procedures and evaluated its impact on postoperative pain levels and the need for Opioids during the recovery phase.

When 1 gm iv paracetamol was given prophylactically, 30 minutes before surgery started, pain scores were significantly lower than when 1 gm iv paracetamol was given intraoperatively, before skin closure.

A randomized clinical trial was carried out in 2011 by Choudhuri *et al*. on eighty patients who were ineligible for laparoscopic cystectomy [6]. They evaluated the analgesic impact of acetaminophen in comparison to a placebo and found 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). Analogous research was done in 2008 by Cakan *et al*. and in 2009 by Salihoglu *et al*. to evaluate the analgesic impact of acetaminophen on pain following cholecystectomy. The findings were comparable [11, 12].

Tzortzopoulou *et al*. conducted a systematic analysis in 2011 that included 36 studies with 3896 participants. The review evaluated the analgesic impact of acetaminophen in comparison to placebo after surgery for both adults and children.

Compared to the placebo group, which experienced 16% pain relief, the acetaminophen group experienced 50% pain relief. Moreover, the intervention group used 30% less opioids overall in the first four hours following surgery than the control group [13].

These findings suggest that Group I had adequate analgesic efficacy during the postoperative phase. Furthermore, by blocking nociceptive stimuli before causing damage to tissue architecture, a decrease in excitability in the central nervous system may account for the low pain scores in group I.

Remy *et al*. [14] evaluated the effects of paracetamol on morphine consumption after major surgery in a meta-analysis and concluded that paracetamol reduces post-operative morphine usage.

Fijalkowska *et al*. [15] investigated the effectiveness of IV paracetamol on 92 patients scheduled for laparotomy or laparoscopy. Laparoscopic group, 16.3% of patients, needed additional morphine, while in the laparotomy group, 71.4% of patients had additional morphine requirements. In conclusion, they reported that paracetamol reduces the need for opioid analgesics but in major surgeries, a multimodal approach must be needed.

Guner *et al*. [16] study that compared paracetamol and tramadol, they reported paracetamol and tramadol reduce opioid requirements after major abdominal surgeries, but alone could not provide adequate analgesia, therefore in major surgeries a multimodal approach has to be needed.

We think that the analgesic effect of the preemptively administered paracetamol lasts longer than its effect time because it prevents central sensitization. For patients undergoing surgery, we advise using intravenous paracetamol as a preemptive analgesic.

We recommend the use of intravenous paracetamol as a pre-emptive analgesic in patients undergoing laparoscopic cholecystectomy with the following advantages: Paracetamol is an effective non-narcotic based analgesic that is easily available,

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With an effective dose of 15mg/kg.

1. For patients, the intravenous method is preferred above the intramuscular and oral routes.
2. Having surgery because of the higher bioavailability.
3. Reduction of opioid use after surgery.
4. A shorter hospital stay and less discomfort following surgery.
5. Financially advantageous.

One of the minor drawbacks of our trial was that all patients received a single dosage of 1g of IV paracetamol rather than doses every other day or every three days. The participants in our study were between the ages of 18 and 60yr, therefore the findings cannot be extrapolated to the juvenile and geriatric age groups. Additionally, patients weighing between 50 and 70 kg were included in our study and received 1g of IV paracetamol, which is an effective dose of 15-20 mg/kg. Thus, the results of our study can't be generalized for patients in the extreme weight range since a single bolus dose of 1g of paracetamol might cause under-dosing (weight > 70 kgs) or over-dosing (weight < 50kgs).

5. Conclusion

In conclusion, giving 1g of IV paracetamol ahead of time to patients having laparoscopic cholecystectomy resulted in good analgesia with lower pain scores during the postoperative period, more patient satisfaction, and lower post-operative discomfort.
Usage of opioids. Therefore, it is safe to provide 1g of IV paracetamol as a preventative measure. Help relieve pain after a laparoscopic cholecystectomy.

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Conflict of Interest: None declared.

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