Original Article

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Effect of Preemptive Intravenous Paracetamol on Post-operative Analgesic Requirements in Patients Undergoing Laparoscopic Surgeries

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Abstract

Introduction: Preemptive analgesia has been defined as the treatment which starts before surgery to prevent the establishment of central sensitization of pain. Paracetamol is a safe, the well-tolerated drug with proven efficacy as the preemptive analgesic for moderate post-operative pain in laparoscopic surgeries.

Aim: To determine the effect of preemptive use of 1 g intravenous (IV) paracetamol on post-operative pain scores and analgesic requirements in patients undergoing laparoscopic surgeries under general anesthesia.

Materials and Methods: A total of 60 patients undergoing laparoscopic surgeries were randomized into two groups, who were given either an IV placebo or an IV injection of 1 g paracetamol, 15 min before induction. The post-operative pain relief was evaluated by a visual analog scale and consumption of tramadol as rescue analgesic in the post-operative period. The incidence of post-operative nausea and vomiting (PONV) and any other complications were also measured in the post-operative period.

Results: At 15 min and 30 min, mean pain scores of "Group NS" were significantly more than those of "Group P" ($P < 0.05$). At 1, 2, and 6 h, mean pain scores of the two groups were comparable and statistically not significant ($P < 0.05$). The requirement of tramadol as rescue analgesia in "Group NS" was significantly more than "Group P" ($P < 0.05$). The incidence of PONV in the "Group NS" was more than "Group P."

Conclusion: Preemptive administration of 1 g of IV paracetamol in patients undergoing laparoscopic surgeries provided satisfactory analgesia and decreased post-operative tramadol consumption.

Key words: Intravenous paracetamol, Intravenous tramadol, Pain after laparoscopic surgeries, Post-operative analgesia, Preemptive analgesia

INTRODUCTION

Pain is a public health issue throughout the world, and it is the major clinical, social, and economic problem.[1] Although laparoscopic surgery results in substantially less severe, and prolonged discomfort compared with the corresponding open procedure, post-operative pain is still considerable and needs to be treated to reduce post-operative complications and hospital stay.[2]

The most common using drugs in the treatment of post-operative pain are opioid and non-opioid analgesics. Drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, cyclooxygenase-2 (COX-2) inhibitors, local anesthetics, and steroids are often used for their opioid-sparing action to reduce the opioid-related side effects and hasten recovery.[3,4]

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The primary mechanism of these analgesic drugs is to inhibit the COX and prostaglandin synthesis.[5] Paracetamol (acetaminophen; *N*-acetyl-p-aminophenol) is an acetanilide derivative, safe, the well-tolerated drug with proven efficacy the analgesic. Its clinical effects arise most likely from the central action, and intravenous (IV) administration provides rapid and predictable therapeutic plasma concentration. Paracetamol was introduced for IV administration in a unit-dose form, ready for infusion solution in 2002. The mechanism of action of paracetamol is through the inhibition of prostaglandins and activation of descending serotonergic inhibitory pathways.[6,7]

The aim of this study was to evaluate the analgesic efficacy of preemptive IV paracetamol for post-operative pain relief after laparoscopic surgeries.

MATERIALS AND METHODS

After Ethical Committee approval and written informed consent of all the patients, this study was conducted. Patients aged 18-60 years scheduled for laparoscopic surgeries and classified as American Association of Anesthetists (ASA) physical Status I or II were included. Patients those having contraindications to paracetamol (allergy, liver disease) or to NSAIDs (esophagogastroduodenal disease, renal insufficiency, and abnormal coagulation) and patients those on treatment by steroids, NSAIDs, or opioids before surgery were excluded. The patients were divided into two groups of 30 in each. After shifting into the operation theater, all standard monitoring equipment was connected, and the crystalloid infusion was started. The study drugs were given IV as slow infusion 30 min before induction in the pre-anesthetic room. In "Group P," patients received 1 g of IV paracetamol and in "Group NS," patients received 100 ml IV normal saline over 15 min.

All the patients were pre-oxygenated with 100% oxygen using Bain's circuit for 3 min. All the patients were induced with injection thiopentone 5 mg/kg IV, injection fentanyl 2 μg/kg IV, injection vecuronium 0.1 mg/kg IV, and trachea was intubated with appropriate size ETT. Following intubation, maintenance of general anesthesia was accomplished by providing isoflurane in 40/60 oxygen/nitrous oxide and, if required, 0.01 mg/kg vecuronium was administered. If the duration of surgery was more than 90 min, the cases were excluded from the study. Heart rate, noninvasive blood pressure, SpO_2 and end-tidal CO_2 were monitored throughout the procedure. Patients were extubated after reversal with glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg) and thorough suctioning.

In the post anesthesia care unit, post-operative pain score was measured by using visual analog scale (VAS) of "0" to "10" where "0" indicated no pain and "10" is the worst imaginable pain. Post-operative pain was observed at the intervals of 15 min, 30 min, 1 h, 2 h and 6 h. Injection tramadol 50 mg IV used as rescue analgesic was given if the VAS score was more than three.[4]

Statistical Analysis

The comparison between the two groups was done by student's unpaired *t*-test and Mann–Whitney test. A probability value ($P \leq 0.05$ was considered as statistically significant.

RESULTS

The demographic data reveals that both groups are comparable in age, weight, sex, and ASA grade (Table 1). There was no statistically significant difference in the duration of surgery (74.35 ± 13.34 in "Group P," whereas in "Group NS" was 71.61 ± 14.34) (Table 1). At 15 min and 30 min mean pain scores of "Group NS" were significantly more than those of "Group P" ($P < 0.05$) (Table 2 and Figure 1). At 1, 2, and 6 h, mean pain scores of the two groups were comparable and statistically not significant ($P < 0.05$) (Table 2 and Figure 1). The requirement of tramadol as a rescue analgesia in "Group NS" was significantly more than "Group P" ($P < 0.05$) (Table 3 and Figure 2). Post-operative nausea and vomiting (PONV) was shown in Table 4 and Figure 3.

DISCUSSION

In the present study, pain management was started prior to pain initiation on the basis of preemptive analgesia. The

Table 1: Comparison of demographic parameters between two groups

Parameters	*n*=30		*P* value
	Group P	Group NS	
Age (years)	32.54±11.01	34±10.67	0.60
Sex (female/male)	16/15	17/14	0.79
Weight (kg)	59.19±7.91	56.84±6.87	0.215
ASA (I/II)	28/3	28/3	1.00
Duration of surgery (min)	74.35±13.34	71.61±14.34	0.438

ASA: American association of anesthetists

Table 2: Comparison of mean pain scores (VAS) between two groups

Intervals	Group P	Group NS	*P* value
15 min	2.06±0.63	2.61±0.56	0.0006
30 min	2.35±1.17	3.84±1.55	0.0001
1st h	2.42±1.12	2.87±0.99	0.0989
2nd h	2.13±1.06	2.52±0.89	0.1219
6th h	2±0.52	2.52±0.89	0.0549

VAS: Visual analog scale

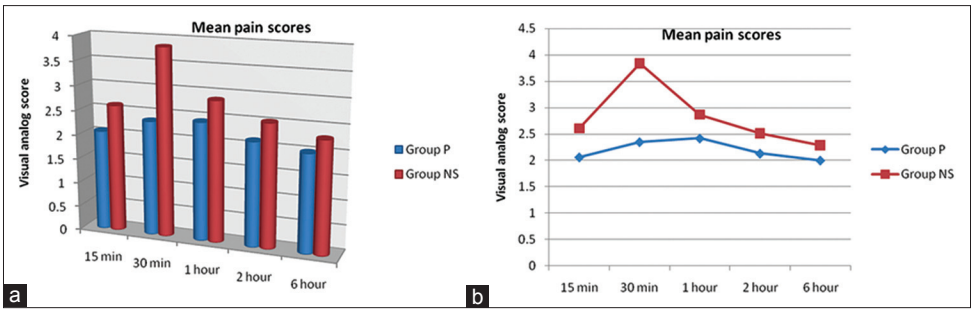

Figure 1: (a and b) Comparison of mean pain scores (visual analog scale) between two groups

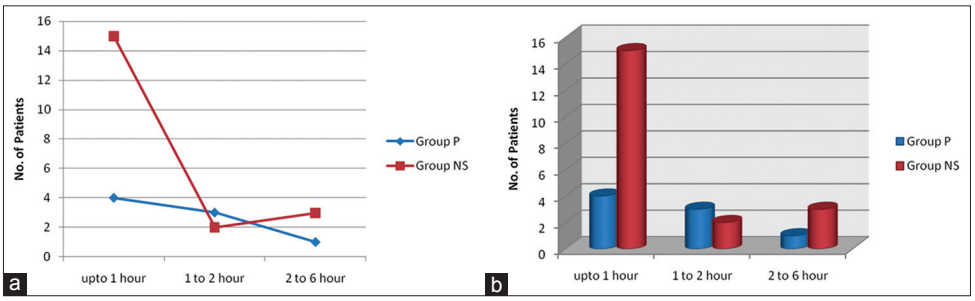

Figure 2: (a and b) Comparison of tramadol requirement between two groups

Table 3: Comparison of tramadol requirement between two groups

Duration	Number of patients (%) (*n*=30)		*P* value
	Group P	Group NS	
Up to 1 h	4 (12.90)	15 (48.39)	0.0002
1-2 h	3 (9.68)	2 (6.45)	0.64
2-6 h	1 (3.23)	3 (9.68)	0.301
Total	8 (25.81)	20 (64.52)	0.002

Table 4: Comparison of PONV between two groups

PONV	
Group P	Group NS
0	4

PONV: Post-operative nausea and vomiting

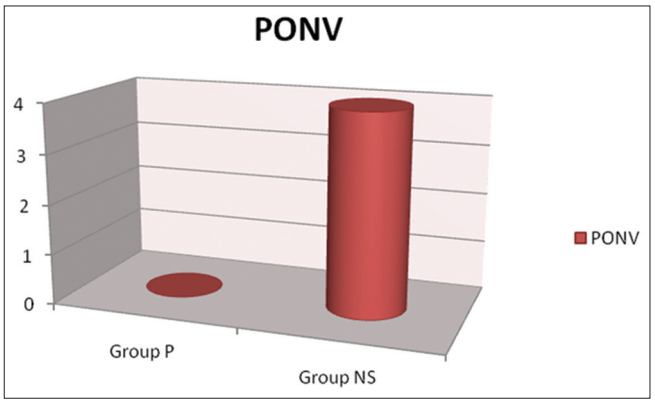

Figure 3: Comparison of post-operative nausea and vomiting between two groups

aim of preemptive analgesia, which has been investigated in recent years, is to provide analgesia prior to a painful stimulus to prevent central sensitization caused by the painful stimulus and, consequently, to decrease the need for post-operative analgesia.

Preemptive analgesia has been defined as treatment that: (1) Starts before surgery; (2) prevents the establishment of central sensitization caused by incisional injury and inflammatory injuries.

Paracetamol rapidly passes the blood-brain barrier, reaches a high concentration in the cerebrospinal fluid and has an anti-nociceptive effect mediated by the central nervous system (CNS).[8] This central effect has been regarded primarily as an indirect and reciprocal influence through COX enzyme inhibition, and probably through the serotoninergic system as well. Besides this central effect, it is accepted that paracetamol has a peripheral anti-inflammatory influence, although this effect is somewhat limited.[9]

Pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery. Consequently, immediate post-operative pain may be reduced, and the development of chronic pain may be prevented.[10]

In our study significant high mean pain scores were observed during post-operative period at 15 min and

30 min in "Group NS" (2.61 ± 0.56 and 3.84 ± 1.55, respectively) compared to "Group P" (2.06 ± 0.63 and 2.35 ± 1.17, respectively) (*P* - value 0.0006 and 0.0001, respectively). There was no significant difference in mean pain scores at 1, 2 and 6 h in both groups (*P*>0.05).

Choudhuri and Uppal *et al.*[11] Administered IV paracetamol 1 g as a pre-emptive analgesic in laparoscopic cholecystectomy and assessed its effects on intraoperative analgesic requirement, post-operative analgesic effectiveness, showed that IV paracetamol when used as pre-emptive analgesic just before induction as part of multimodal analgesic regime has significant opioid sparing effect, concluded that, no differences were observed between the two groups in the adequacy of analgesia as assessed by VAS scores. However, the median pain scores were significantly lower in the paracetamol group (Group P) at two intervals which are comparable with our study. This may be because of the initial loading dose of paracetamol providing a higher plasma concentration.

In a related study by Salihoglu *et al.*, preemptive use of 1 g IV paracetamol caused similar decrease in post-operative pain scores and requirement of rescue analgesia.[12] The similarly in another study Arici *et al.*, demonstrated significantly lower post-operative pain scores and consumption of rescue analgesia in patients who received 1 g IV preemptive paracetamol compared to patients who received normal saline.[13]

Clinical studies have also found that 1 g IV paracetamol employed alone is just as effective as 30 mg ketorolac, 75 mg diclofenac or 10 mg morphine.[14,15]

The requirement for rescue tramadol analgesia was in 25.8% of patients in the "Group P" compared to 64.5% of patients in "Group NS," which suggests that preemptive paracetamol group had less pain, high pain threshold or both. These results indicate that sufficient analgesic effectiveness was ensured in the post-operative period in Group I. In addition, the less values of the pain scores in the Group I may be explained by decreases in excitability in the CNS through blockade of nociceptive stimuli before damaging tissue architecture. We believe that since the preemptively delivered paracetamol prevents central sensitization; its analgesic effect continues longer than its effect period.

It is also demonstrated that the analgesic effect of IV paracetamol starts within 5 min, peaks at 1 h and lasts 4-6 h.[16]

Piguet *et al.*,[17] had demonstrated the close correlation between plasma concentration and analgesic effect of paracetamol with IV doses of up to 2 g in healthy volunteers.

Juhl *et al.*,[18] had demonstrated that the extent and duration of pain relief following third molar surgery was significantly improved after 2 g over 1 g of the initial IV dose of paracetamol.

In our study, we observed that four patients had PONV in Group NS, none of the patient had developed PONV in Group P, the related study done by Apfel *et al.*[19] concluded prophylactically administered IV Acetaminophen reduced PONV, mainly mediated through superior pain control.

CONCLUSION

To conclude, preemptive administration of 1 g of IV paracetamol in patients undergoing laparoscopic surgeries provided satisfactory analgesia and decreased post-operative tramadol consumption. Hence, 1 g of IV paracetamol can be safely administered preemptively for post-operative analgesia for laparoscopic surgeries.

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