

## Original Article

# A comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies

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## Abstract


**Background:** Pain in the perioperative setting or thereafter plays a significant role in delaying an otherwise successful recovery. Hence, mitigation of such postoperative pain assumes importance. Among the various agents employed for such mitigation, opioids and non-steroidal anti-inflammatory drugs have for some time taken center stage. However, alas they are not without their share of adverse effects. This study was undertaken with the purpose of elucidating the efficacy of intravenous (IV) paracetamol as compared to IV tramadol in mitigating postoperative pain while observing its effect on hemodynamic stability and the presence of adverse drug reactions, if any.

**Materials and Methods:** A total of 60 randomized cases aged ranges from 20 to 60 years of both sexes divided into two groups (each for paracetamol and tramadol) scheduled for laparotomies were administered IV paracetamol and tramadol for postoperative pain relief and assessed with visual analog scale (VAS) score and variations in vital parameters to ascertain extent of pain relief and post-operative nausea vomiting (PONV).

**Results:** Data so collected was statistically interpreted, and observations extrapolated. Save for a perceptible decline in PONV with paracetamol group compared with tramadol group with a statistically significant  $P < 0.001$ , nothing statistically significant was observed in any other parameter, including VAS scores between either group.

**Conclusion:** IV paracetamol is a safer alternative to tramadol with lesser PONV in the postoperative period translates into the lesser duration of hospitalization and hence earlier discharge.

**Key words:** Paracetamol, postoperative pain, tramadol

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## INTRODUCTION

Pain is a predictable component of any surgical procedure, and postsurgical pain is commonly treated ineffectively. Inadequately treated postoperative pain may result in pain and suffering, as well as multiple physiological and psychological consequences (e.g., splinting, impaired gastrointestinal motility, and impaired wound healing)

which may adversely affect perioperative outcomes and contribute to increased length of stay. Successful recovery from surgery includes comprehensive management of post-operative pain.<sup>[1]</sup> Postoperative pain paves the way for a host of complications in major surgeries like laparotomy, which can deleteriously impact convalescence.<sup>[2]</sup> For decades now, opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) have been used and have not been entirely devoid of undesirable effects like postoperative nausea and vomiting (PONV), respiratory depression, sedation, gastrointestinal bleeding and renal injury among others.<sup>[3]</sup> With the advent of intravenous (IV) paracetamol, interest is now being shown as to its efficacy in mitigating pain especially against the backdrop of commonly used analgesics.<sup>[4]</sup> IV paracetamol was approved and made available in United States in 2010. IV paracetamol is an analgesic and antipyretic agent, recommended worldwide as a first-line agent for the treatment of pain and fever in adults and children. Paracetamol (acetaminophen), now also available for IV use, is not an NSAID and interferes neither with platelet nor kidney functions nor does it present the unwanted side effects of NSAIDs. Adverse reactions emerging from the use of the IV formulation of paracetamol are extremely rare (<1/10,000).<sup>[5]</sup> Tramadol has been shown to provide effective analgesia after both intramuscular and IV administration for the treatment of postoperative pain. While it is not recommended as a supplement to general anesthesia because of its insufficient sedative activity, tramadol has been successful in the treatment of postoperative pain. A randomized double-blind study reported acceptable analgesia with postoperative IV tramadol 50 mg, repeated once if required after 30 min. It produced an effect similar to that of morphine 5 mg or the alpha 2 agonist, clonidine 150 µg. Tramadol, a synthetic opioid of the aminocyclohexanol group, is a centrally acting analgesic with weak opioid agonist properties, and effects on noradrenergic and serotonergic neurotransmission. In addition, these opioids and nonopioids modes of action appear to act synergistically.<sup>[6]</sup> Tramadol is an isomeric drug, of which the (+) enantiomer is a weak mu-opioid agonist with an analgesic potency about 1/10<sup>th</sup> that of morphine.<sup>[7]</sup> Therefore this prospective, randomized double-blinded study was designed to compare IV paracetamol and tramadol for postoperative analgesia in laparotomies. Our outcomes of study is to assess statistically for difference in visual analog scale (VAS) score and vital parameters as reflective of extent of pain relief in the post-operative period and PONV in two groups of patients receiving paracetamol and tramadol.

## MATERIALS AND METHODS

After obtaining approval from Ethical Committee and Written informed consent from the patients, the prospective randomized clinical study was carried out

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on 60 patients admitted to a tertiary health care center to undergo laparotomies from November 2010 to April 2012.

Sample size was selected on the basis of cross-over pilot study of 10 patients in both groups to detect a projected difference of 35% between the two groups for analgesia for type I error ( $\alpha$ ) of 0.05 and power of the study 0.8. At the end of the study, all data were compiled systematically and analyzed using mean, the standard deviation was estimated, cross tabulations were done. ANOVA and paired sample *t*-test. All the statistical calculations were done through SPSS 16.0 (SPSS Inc. 233 South Wacker Drive, 11<sup>th</sup> Floor, Chicago, IL 60606-6412) for windows. Value of  $P < 0.05$  is considered significant and  $P < 0.0001$  as highly significant.

Sixty cases are randomized into two equal groups of 30 each who fulfill the inclusion-exclusion criteria.

### Inclusion criteria

All patients of American Society of Anesthesiologists-I, II, III both elective and emergency cases between 20 and 60 years of both sex undergoing laparotomies.

### Exclusion criteria

Age <18 years and >80 years, patients whose liver function tests are abnormal. (Serum bilirubin >2 mg%), recent myocardial infarction history (<3 months), a known case of allergy to study drug, recent cerebrovascular accident within 6 months, angina pectoris, congestive heart failure (left ventricular ejection fraction <30%), severe pulmonary diseases, pregnancy or lactation, patients taking monoamine oxidase inhibitors, patients with a history of seizures, serum creatinine >2 mg%, coagulopathy.

Patients were divided into two groups:

- Group I: Received IV paracetamol 1 g in 100 ml vial infused over 15 min before 30 min completion of surgery
- Group II: Received IV tramadol 2 mg/kg slow IV before 30 min completion of surgery.

The dose is repeated 6<sup>th</sup> hourly. The maximum total dose for paracetamol and tramadol were 4 g/day and 400 mg/day respectively.

Anesthetic protocol was similar for all patients. Postoperatively hemodynamic parameters, pain score using VAS scale and PONV was evaluated at frequent interval. Pain intensity was measured based on VAS pain grading that included scores: 0 (no pain), 10 (worst pain).

Visual analog scale was obtained at 30 min, 1, 2, 4, 6, 8, 10, 12, 15, 18, 21, and 24 h.

Postoperative hemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and side-effects like PONV using PONV scoring: No nausea (0) to severe nausea and vomiting (10),

was evaluated at regular intervals at 0 min, 30 min, 1 h, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h, 15 h, 18 h, 21 h and 24 h.

## RESULTS

The demographic parameters of the patients included in the study were comparable between the groups [Table 1]. The majority of the patients (53.3% in group I and 60.0% in group II) were diagnosed as hollow viscous perforation. The two groups showed no statistical significant difference with respect to types of surgeries [Table 2].

The mean VAS scores at 30 min in group I was 5.76 and in group II was 6.23. The mean VAS scores at 24 h in group I was 1.83 and in group II was 2.10. As per above graph, the gradual fall of the VAS scores are comparable, and the decrease in VAS scores showed no statistical significance between two groups with a  $P$  - 0.653 [Graph 1].

When hemodynamics is compared between two groups:

- There was no statistical significance difference of HRs between two groups with a  $P$  - 0.536 [Graph 2]
- There was no statistical significance in the difference of SBP between two groups with a  $P$  - 0.0682 [Graph 3]
- There was no statistical significance in the difference of DBPs between two groups with  $P$  - 0.584 [Graph 4].

In group I, 3.33% of patients had PONV scores more than 5, but in group II 43.33% patients had PONV scores more than 5, suggesting group II has significant PONV compared to group I. As per the above graphs [Graph 5] on comparison of the mean PONV scores, statistically significant difference between the groups with a  $P$  - 0.001 was observed. We did not observe any other side effects like respiratory depression, pruritus, icterus, or urinary retention in both the groups.

## DISCUSSION

Effective postoperative pain management has been demonstrated to improve clinical outcome. Opioids are widely used to relieve postoperative pain due to their efficacy and effectiveness. However, their adverse effects such as nausea, vomiting, itching, and respiratory depression are of concern. Physicians are either worried about the cost of paracetamol or unaware of its efficacy due to lack of supportive clinical data. IV paracetamol was evaluated in hysterectomy, general surgical, coronary bypass, and orthopedic surgeries. During the review of recent 14 randomized controlled trials 12 have supported the use of IV paracetamol for better postoperative analgesia.<sup>[8]</sup> Paracetamol, an active metabolite of phenacetin affords a central analgesic action secondary to a raised pain threshold and can be administered orally, rectally, intramuscularly and of late IV. Excretion occurs following conjugation in the liver. Action tends to peak by 1 h and lasts till 4–6 h. Hepatic toxicity can occur only

**Table 1: Demographic data**

Parameters	Paracetamol (n=30)	Tramadol (n=30)
Age (years)		
Mean	33.14	37.60
SD	5.22	7.12
Range	22-58	20-60
Height (cm)		
Mean	158	159.43
SD	4.6	3.49
Range	150-170	150-170
Weight		
Mean	50-70	58.24
SD	4.6	5.28
Range	44-64	40-70

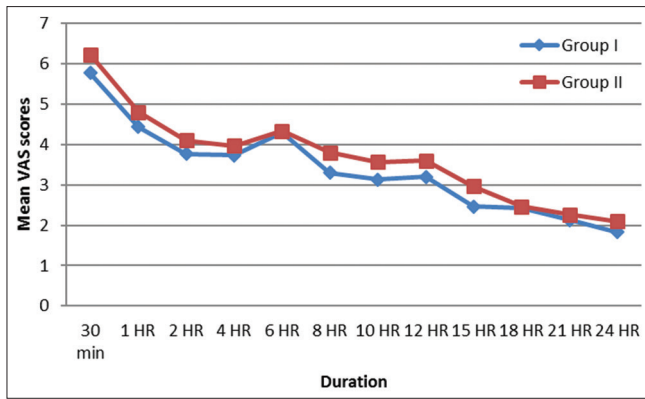
$P > 0.078$ . SD=Standard deviation

**Table 2: Types of surgeries**

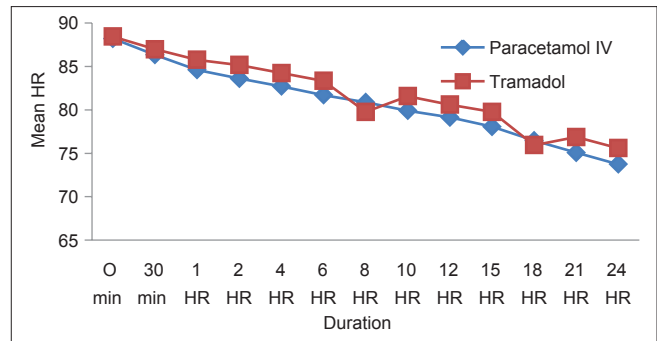
Surgeries	Group I		Group II	
	Number of cases	Percentage	Number of cases	Percentage
Acute intestinal obstruction	2	6.7	0	0.0
Appendicular mass	2	6.7	0	0.0
Bleeding duodenal ulcer	0	0.0	1	3.3
Stab injury	2	6.7	0	0.0
Blunt injury	0	0.0	1	3.3
Colostomy	0	0.0	1	3.3
Duodenal perforation	1	3.3	2	6.7
Fecal fistula	0	0.0	1	3.3
Gall bladder perforation	1	3.3	0	0.0
Hollow viscous perforation	16	53.3	18	60.0
Intestinal obstruction (volvulus)	0	0.0	1	3.3
Malignancy	0	0.0	1	3.3
Mesentric infarction	2	6.7	0	0.0
Pain abdomen	1	3.3	0	0.0
Sigmoid	1	3.3	0	0.0
Splenic infarction	0	0.0	1	3.3
Subacute intestinal obstruction	2	6.7	3	10.0
Total	30	100.0	30	100.0

$P = 0.287$

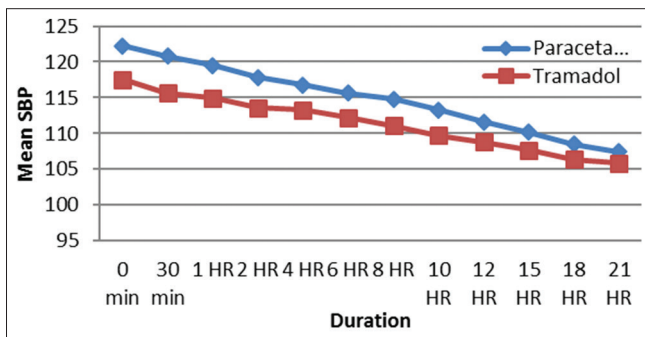
if therapeutic doses are exceeded (for patients weighing 50 kg or more, the total daily dose of paracetamol should not exceed 4 g).<sup>[9]</sup> Paracetamol, a centrally acting inhibitor of cyclooxygenases, has weak peripheral effects recently demonstrated. Paracetamol is nevertheless devoid of side effects commonly observed with the use of NSAIDs. The analgesic efficacy of a 2 g starting dose of IV paracetamol was superior over the recommended dose



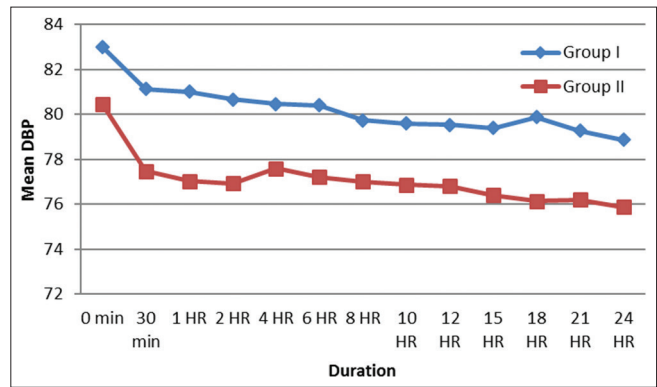
Graph 1: Distribution of visual analogue scale grades between groups



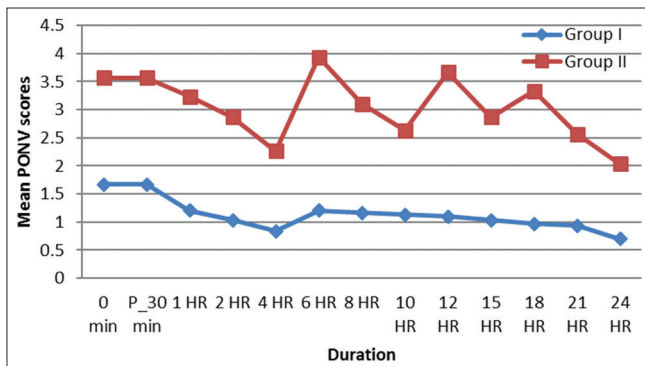
Graph 2: Comparison of heart rates between two groups



Graph 3: Comparison of systolic blood pressure between two groups



Graph 4: Comparison of diastolic blood pressure between two groups



Graph 5: Distribution of postoperative nausea vomiting scores between groups

of 1 g in terms of magnitude and duration of analgesic effect for postoperative pain.<sup>[10]</sup> The efficacy of tramadol for the management of moderate to severe postoperative pain has been demonstrated in both inpatients and day surgery patients. Unlike other opioids, tramadol has no clinically relevant effects on respiratory or cardiovascular parameters. Tramadol may prove particularly useful in patients with poor cardiopulmonary function, including the elderly, the obese, smokers, in patients with impaired hepatic or renal function, and in patients in whom NSAIDs are not recommended or need to be used with caution.<sup>[11]</sup>

Nikoda *et al.*,<sup>[12]</sup> showed postoperative analgesia based on the IV infusion of paracetamol in a single dose of

1 g (4 g/day) caused a reduction in the intensity and duration of pain and the IV formulation of paracetamol should be regarded as one of the essential nonopioid components of multimodality therapy for pain in patients in the early postoperative period.<sup>[12]</sup> Tramadol, a centrally acting synthetic opioid like analgesic seems to act by modifying the transmission of pain impulses via inhibition of noradrenaline and serotonin reuptake. The relative lack of respiratory depression, major organ toxicity or abuse potential affords credence to the drug.<sup>[13]</sup>

Many a trial have been conducted under different circumstance concerning the relative advantage of one drug over the other. Our study was done to assess the efficacy of IV paracetamol over IV tramadol for laparotomies. There are no studies comparing the efficacy of these drugs for postoperative analgesia for laparotomies and hence we decided to do one. We found IV paracetamol and tramadol tends to offer adequate postoperative analgesia and IV paracetamol is a safer alternative to tramadol with less PONV in the postoperative period.

Kela *et al.* compared the efficacy of either drug in the postoperative period in cardiothoracic surgery and found them to be on par. They found 10.0% of the subjects in paracetamol group and 13.3% out of total cases in tramadol group suffered nausea and vomiting which were comparable and difference was insignificant which is similar to our study.<sup>[3]</sup>

In urosurgery, Aghamir *et al.* compared proparacetamol and tramadol after urologic open surgeries and found proparacetamol useful, but inadequate in cases of severe pain.<sup>[13]</sup> whereas Akcali *et al.*,<sup>[14]</sup> compared the efficacy of paracetamol, tramadol and lornoxicam in extracorporeal shockwave lithotripsy and found similar efficacy among all three. Interestingly, Cattabriga *et al.*<sup>[15]</sup> compared paracetamol with tramadol and found paracetamol to be better especially when used against background tramadol analgesia in postoperative median sternotomies. Uysal *et al.*<sup>[16]</sup> compared either of the drugs in postadenotonsillectomy pediatric patients and found IV paracetamol to be superior in terms of early recovery, but associated with similar analgesic properties.

Intravenous paracetamol cross blood brain barrier easily and its analgesic action starts within 15–20 min. Sinatra *et al.* found the efficacy of IV paracetamol in orthopedic surgeries to be superior to tramadol in terms of rapid onset of analgesia. Sinatra *et al.* showed IV paracetamol 1 g, administered in patients with moderate to severe pain after orthopedic surgery provided rapid and effective analgesia. They found IV propacetamol significantly reduced morphine consumption over the 24-h period and safe in terms of clinical and laboratory examinations.<sup>[17]</sup>

Paracetamol stands out among nonopioid analgesics due its effective analgesia and reduced side effect profile. Dejonckheere *et al.*,<sup>[18]</sup> compared IV tramadol to propacetamol for postoperative analgesia following thyroidectomy. They found more patients complained of nausea and vomiting ( $P = 0.01$ ) in the tramadol group during first 2 h of the study, but PONV is comparable between the group during the entire study period.<sup>[18]</sup> Paracetamol is a viable alternative to nonsteroidal anti-inflammatory agents, because of its less adverse effects.

Lee *et al.*,<sup>[19]</sup> found paracetamol may represent an alternative to ketorolac for pain prevention after mild to moderate painful surgery in situations where the use of NSAIDs is unsuitable. Since morphine is considered as a gold standard drug for treating pain, Van Aken *et al.*,<sup>[20]</sup> observed IV propacetamol in repeated doses has a significant analgesic effect that is indistinguishable from that of morphine administration after dental surgeries with better tolerability.

Pendeville *et al.*<sup>[21]</sup> compared the postoperative analgesia between paracetamol and tramadol for day care tonsillectomies in children and showed postoperative pain scores (Children's Hospital of Eastern Ontario Pain Scale) in recovery, numerical pain scale in the ward and at home, and rescue analgesic use were significantly lower in the tramadol group.

One concern regarding the use of opioids is respiratory depression. Tramadol is safe and less respiratory depressant when compared to other strong opioids. In

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the Hoogewijs' study, patients had considerably higher PaCO<sub>2</sub> in the tramadol compared to the propacetamol group ( $48 \pm 6$  mmHg vs.  $42.2 \pm 3.4$  mmHg).<sup>[22]</sup>

There are studies which do not support the use of IV paracetamol like Cakan *et al.*,<sup>[23]</sup> showed repeated IV paracetamol usage after lumbar laminectomy and discectomy did not demonstrate a significant opioid-sparing effect, it did decrease VAS scores at certain evaluation times and incidence of vomiting and increase patient satisfaction. Hiller *et al.*,<sup>[24]</sup> observed that IV acetaminophen 90 mg/kg/day, as adjuvant to oxycodone, did improve analgesia, but did not diminish oxycodone consumption during 24 h after major spine surgery in children and adolescents.

In terms of comparison of analgesia our study results are similar to, Kela *et al.*, Uysal *et al.* Hoogewijs *et al.*<sup>[3,16,22]</sup> These varying references listed here serve to illustrate in different surgeries the efficacy of paracetamol to be better either in terms of rapid onset, fewer side effects and earlier recovery as compared to tramadol and other analgesics. Very few studies surfaced in terms of a comparison in terms of hemodynamics, PONV between the two. This prompted our study, and the results it bore are as listed graphically above.

From first glance, no difference comes to light in terms of hemodynamics and VAS scores. However, on closer inspection, there is a clear perceptible difference in terms of reduced PONV in the paracetamol group compared to tramadol group.

## CONCLUSION

Postoperative analgesia is the cornerstone of successful recovery from any surgery. Among the various agents tried so far, each have brought with it specific advantages and disadvantages to the fore. From the different parameters compared and outlined in our study, following inferences could be drawn IV paracetamol and tramadol tends to offer adequate post-operative analgesia. IV paracetamol is a safer alternative to tramadol with less PONV in the postoperative period, which translates into the lesser duration of hospitalization and hence earlier discharge.

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