

Prospective, double-blind randomized study of comparison of analgesic efficacy of parenteral paracetamol and diclofenac for postoperative pain relief

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Abstract

Background and Aims: Injectable paracetamol has analgesic and antipyretic activities, especially used in postoperative period. The aim of this study was to assess the analgesic efficacy and safety of IV paracetamol in comparison with IV diclofenac for postoperative pain relief.

Material and Methods: Randomly selected 120 patients who underwent elective surgery under general anesthesia were divided into two groups: group A (paracetamol group): patients received IV paracetamol (15 mg/kg)/100 mL, 30 min before completion of surgery over the period of 15 min (rounded of to 1 g), the selected cases were in range of 60-70 kg body weight. Group B (diclofenac group): patients received IV diclofenac (1 mg/kg) diluted in 100 mL NS, 30 min before completion of surgery over the period of 15 min (rounded of to 75 mg). Pain relief and side effects were observed in postoperative period. Statistical analysis of continuous data was done by unpaired *t*-test and Chi-square test was applied for discrete data.

Results: Both IV paracetamol and IV diclofenac were effective for postoperative pain relief. No significant differences were found between them for any measures of analgesic activity. Only minor and common adverse events were reported, with no overall differences between groups.

Conclusion: Both paracetamol and diclofenac drugs are safe to provide analgesia through IV route in postoperative period without any major significant side effects.

Keywords: Diclofenac, paracetamol, postoperative pain relief

Introduction

Effective, nonsedating pain relief in the postoperative period is essential to minimize the risk of delayed recovery and discharge from hospital.^[1-3] Commonly used painkillers, opioids, have sedating property.^[4,5] Nonsteroidal anti-inflammatory drugs (NSAIDs) are useful because of their lack of sedative properties and their opioids-sparing effects, but their efficacy is

limited due to its side effects such as nausea, vomiting, phlebitis at injection site,^[6] and relative contraindication like known hypersensitivity to drugs, allergic asthma, kidney disorders, and acid peptic disorder.^[7] Diclofenac is the most commonly used drug among NSAIDs. Diclofenac was available in intramuscular oily preparation and aqua preparation which can be given intravenous (IV) in diluted form. Both preparations have the above-mentioned side effects. Paracetamol, a centrally acting inhibitor of cyclo-oxygenase, is emerging as a safe and quite effective drug, also having lesser side effects than diclofenac

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especially the IV preparation. In addition, IV paracetamol has quick onset of action, reasonable durability, good analgesic efficacy, and practically no side effect in the dose that we have used.^[8-10] Hence, this clinical study of comparative evaluation of paracetamol and diclofenac is undertaken to evaluate their feasibility as effective analgesics for postoperative pain relief.

Material and Methods

Following institutional approval by the ethical committee of our institute, written informed consent to participate this study was obtained from 120 patients. The study population consisted of 120 randomly selected American Society of Anaesthesiologists (ASA) I and II adult (within 18–60 years) patients of either sex, weighing within 60–70 kg who underwent elective surgical procedure under general anesthesia lasting <2 h. Patients having preexisting severe liver and renal dysfunction and allergy to either drug were excluded in our study. Patients were divided by computer-generated random number into two study groups A and B; each consists of 60 patients as follows: group A (paracetamol group): patients received IV paracetamol (15 mg/kg)/100 mL, 30 min before completion of surgery over a period of 15 min (rounded off to 1 g). Group B (diclofenac group): patients received IV diclofenac (1 mg/kg) diluted in 100 mL NS, 30 min before completion of surgery over a period of 15 min (rounded off to 75 mg). This was a randomized, controlled double-blind prospective study. Postoperative data collection was in the form of visual analogue scale (VAS) score. Assessments of side effects were done clinically. Strict double-blind technique was maintained at all time. Data were collected and tabulation was formed, and statistical analysis of continuous data was done by unpaired *t*-test and Chi-square test was applied for discrete data. The results were considered statistically significant with *P* value <0.05 and highly significant with *P* value <0.001.

Results

Demographic data (age, gender, weight, ASA grade, type of surgery) were noted for groups A and B. Data were comparable and statistically not significant. The observed difference between types of surgeries in two groups was not significant (Chi-square = 1.1; DF = 2, *P* = 0.6) [Table 1].

At immediate postoperative period, VAS was 0 in 30%, 1 in 40%, 2 in 18.3%, 3 in 10%, and 4 in 1.7% for group A, and for group B it was 0 in 36.7%, 1 in 45%, 2 in 16.7%, and 3 in 1.6% which was not statistically significant. VAS values at the end of 1st, 2nd, 3rd, 4th, 5th & 6th hour postoperatively were comparable and statistically insignificant [Table 2].

The mean pain score for ENT surgeries in group A was 1.0 at 0 h, 1.1 at 1 h, 1.7 at 2 h, 2.4 at 3 h, 2.6 at 4 h, 2.7 at 5 h, and 3.3 at 6 h, and in group B it was 0.6 at 0 h, 1.0 at 1 h, 1.7 at 2 h, 2.1 at 3 h, 3.2 at 4 h, 2.8 at 5 h, and 2.9 at 6 h. *P* value was statistically significant only at 4 h; in all other time intervals, *P* value was not significant. The mean pain score for general surgeries in group A was 1.1 at 0 h, 0.9 at 1 h, 1.7 at 2 h, 2.1 at 3 h, 2.7 at 4 h, 2.8 at 5 h, and 2.9 at 6 h, and in group B it was 0.9 at 0 h, 1.2 at 1 h, 1.7 at 2 h, 2.3 at 3 h, 2.7 at 4 h, 3.3 at 5 h, and 3.4 at 6 h. *P* value was statistically significant at 5 and 6 h; in all other time intervals, *P* value was not significant. The mean pain score for other (orthopedic and gynecological) surgeries in group A was 1.6 at 0 h, 0.9 at 1 h, 2.0 at 2 h, 2.6 at 3 h, 3.1 at 4 h, 3.2 at 5 h, and 3.2 at 6 h, and in group B it was 1.2 at 0 h, 1.0 at 1 h, 1.8 at 2 h, 2.3 at 3 h, 2.7 at 4 h, 2.7 at 5 h, and 3.2 at 6 h. *P* value was statistically nonsignificant at all the time intervals.

In group A, 14 patients required rescue analgesia; among them, 2 required in 3 h postoperatively and 12 required in 4–6 h post operatively. In group B, 12 patients required rescue analgesia; among them, 2 required in 3 h postoperatively and 10 required in 4–6 h postoperatively. Use of rescue analgesia in both the groups was statistically nonsignificant for ENT surgeries, general surgeries, and others (0.7).

About six patients in group A and five patients in group B had nausea/vomiting and required antiemetics in the form of Inj. ondansetron 0.08 mg/kg. Reported side effects in both groups for ENT surgeries, general surgeries, and

Table 1: Types of surgery

Type of surgery	Group A		Group B	
	n	%	n	%
ENT	22	36.7	20	33.3
General surgery	29	48.3	34	56.7
Others	9	15	6	10
Total	60	100	60	100

Table 2: Postoperative VAS score

Group	Group A		Group B		t-test <i>P</i>	Significance
	Mean	SD	Mean	SD		
VAS_0 h	1.1	1.0	0.8	0.8	0.1	Nonsignificant
VAS_1 h	1.0	0.7	1.1	0.8	0.2	Nonsignificant
VAS_2 h	1.8	0.8	1.8	0.7	1.0	Nonsignificant
VAS_3 h	2.3	0.8	2.2	0.9	0.7	Nonsignificant
VAS_4 h	2.7	0.8	2.9	0.8	0.4	Nonsignificant
VAS_5 h	2.9	0.8	3.1	0.9	0.2	Nonsignificant
VAS_6 h	3.1	1.0	3.2	0.9	0.3	Nonsignificant

SD=Standard deviation; VAS=Visual analogue scale

others (orthopedic and gynecological) surgeries were not statistically significant (0.995).

Discussion

This study was undertaken to evaluate the effects of single dose of IV paracetamol and IV diclofenac for postoperative analgesia. Groups A and B were comparable and there was no statistically significant difference seen with regard to mean age, weight, ASA grade, gender distribution, duration of surgery, and type of surgeries. The selected doses, time, and route of administration in our study were similar as in the studies conducted by Hyllested M *et al.*,^[11] Hiller A *et al.*,^[12] Hynes D *et al.*,^[13] Ahmed F *et al.*,^[14] Inal M *et al.*,^[15] Durak P *et al.*,^[16] Yoganarimha N *et al.*,^[17] and Pratyush G *et al.*^[18] Bijur PE *et al.*^[19] have described VAS score as the simple, effective, and easiest way to measure the intensity of pain. In our study, we observed VAS score to decide the time to give the dose of the analgesic postoperatively and also to compare the quality and duration of analgesia between both the study groups. We decided to give the dose of rescue analgesia when VAS score was more than 4 as it correlates with moderate to severe intensity of pain which may be associated with hemodynamic changes and patients' discomfort. In the recovery room, patients were evaluated on VAS in the immediate postoperative period, 1, 2, 3, 4, 5, and 6 h postoperatively after administration of analgesic drug as it correlates with pharmacokinetic properties of the selected study drugs.

The mean VAS score in groups A and B was nonsignificant at all the time intervals. This showed that paracetamol and diclofenac provide equal analgesia. On comparing the mean VAS in groups A and B for ENT surgeries, *P* value was significant only at 4 h; For general surgeries, *P* value was significant at 5 and 6 h; in all other time intervals, *P* value was not significant. The results in ENT surgeries at 4 h and in general surgeries at 5 and 6 h were similar to the study conducted by Yoganarimha N *et al.*^[17] For other surgeries (LAVH, shoulder arthroscopy), *P* value was nonsignificant at all time intervals. Our study results were comparable with the results of studies done by Hiller A *et al.*,^[12] Hynes D *et al.*,^[13] Hugo V *et al.*,^[20] and Inal M *et al.*^[15]

Fourteen patients in group A and 12 patients in group B required rescue analgesia within 6 h of postoperative period when VAS score was >4 in the form of IV tramadol (1 mg/kg) given slowly. However, the requirement of rescue analgesia was not significant between the groups. In our study, 5 patients of 22 in group A and 3 patients of 20 in group B posted for ENT surgeries, 6 patients of 29 in group A and 7 patients of 34 in group B posted for general surgeries, and 3 patients

of 9 in group A and 2 patients of 6 in group B posted for other surgeries required rescue analgesia within 6 h of postoperative period. Use of rescue analgesia in both the groups was statistically nonsignificant for ENT surgeries, general surgeries, and others. We have selected mainly laparoscopic surgeries and surface surgeries in general surgery types, whereas in gynecological surgery group we have selected laparoscopic gynecological surgeries and in orthopedic surgeries we have selected arthroscopic surgery cases, so rescue analgesia requirement was not statistically significant. The results from the studies by Durak P *et al.*,^[16] Hugo V *et al.*,^[20] Hiller A *et al.*,^[12] and Hynes D *et al.*^[13] were in concurrence with our study. In group A, 14 patients required rescue analgesia; among them, 2 required in 3 h postoperatively and 12 required in 4–6 h postoperatively. This result is in concurrence with the study of Luthy *et al.*^[21] which has shown that the duration of analgesic effect of paracetamol was approximately 4–6 h. In group B, 12 patients required rescue analgesia; among them, 2 required in 3 h postoperatively and 10 required in 4–6 h postoperatively. This result is in concurrence with the study of Willis JV *et al.*^[22] which has shown that after IV injection, plasma levels of diclofenac fell rapidly and were below the limits of detection at 5.5 h post dosing. There were many factors playing role in the requirement of rescue analgesia which was not the aim of our study. Hence, we have not considered the factors affecting requirement of rescue analgesia in this study.

In our study, nausea or vomiting was reported in 10% of cases in group A and 8.33% of cases in group B which was not statistically significant. It was treated with antiemetics in the form of Inj. ondansetron 0.08 mg/kg. This result was similar to the studies conducted by Hiller A *et al.*,^[12] Hynes D *et al.*,^[13] Durak P *et al.*,^[16] and Yoganarimha N *et al.*^[17] IV diclofenac is supposed to have significant side effect when compared with IV paracetamol, but generally it is seen with repeated and multiple usage of IV diclofenac. Hyllested M *et al.*^[11] concluded that paracetamol was a viable alternative to NSAIDs because of low incidence of adverse effects and should be preferred choice in high-risk patients. As we have taken single dose of IV diclofenac and we have used this drug in ASA grade I and II patients, it justifies the minimal side effects that we have observed with the use of IV diclofenac. Thus, both IV paracetamol and IV diclofenac provided similar postoperative analgesia with only minor side effects reported with no overall differences.

Conclusion

Both paracetamol and diclofenac drugs are safe to provide analgesia through IV route in postoperative period without any major significant side effects. The duration and quality of analgesia in both groups were similar in postoperative period.

IV paracetamol provides effective non-sedating pain relief in postoperative period. IV paracetamol and/or IV diclofenac can be a part of multimodal analgesia.

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Conflicts of interest

There are no conflicts of interest.

References

- Miller RD, editor. Anaesthesia 7th ed. New York: Churchill Livingstone; 2009. p. 1799-800.
- Healy TJ, Knight PR, editors. Wylie and Churchill-Davidson's a Practice of Anesthesia. London: Arnold Press; 2003. p. 1213-34.
- Pain pathophysiology and management. In: Rathmell JP, Fields HL, editors. Harrison's Principles of Internal Medicine. 16th ed. New York: The McGraw Hill; 2012. p. 71-3.
- Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sengal N, et al. Opioid complication and side effects. Pain Physician 2008;11:105-20.
- Furlan AD, Sandoval JA, Mailis-Gangnon A, Tunks E. Opioids for chronic noncancer pain: A metaanalysis of effectiveness and side-effects. Can Med Assoc J 2006;174:1589-94.
- Gopinath R. Suggesting the value of diluted Diclofenac infused over a longer period of time as a method for reducing venous sequelae of IV diclofenac. Br J Anaesth. 1991;67:803.
- Strumer T, Erb A, Keller F, Gunther KP, Brenner H. Determinants of impaired renal functions with non-steroidal anti-inflammatory drugs. Am J Med 2001;111:521-7.
- Jahr JS, Lee VK. IV Acetaminophen. Anaesthesiol Clin 2010;28:619-45.
- Duggan ST, Scott LJ. Intravenous paracetamol (acetaminophen). Drugs 2009;69:101-3.
- Luthy CS, Collart L, Dayer P. The rate of administration influences the analgesic effects of Paracetamol. Clin Pharmacol Ther 1993;2:171.
- Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management. Br J Anaesth 2002;88:199-214.
- Hiller A, Silvanto M, Sawolainen S, Tarkkila P. Paracetamol and Diclofenac alone and in combination for analgesia after elective tonsillectomy. Acta Anaesthesiol Scand 2004;48:1185-9.
- Hynes D, McCarroll M, Hiesse-provost O. Analgesic efficacy of parenteral Paracetamol (Propacetamol) and Diclofenac in post operative orthopaedic pain. Acta Anaesthesiol Scand 2006;50:374-81.
- Ahmed F, Ahmed A, Ibrahim G. Intravenous Paracetamol, Morphine and their combination for post-operative pain after release of post burn neck contracture. Bas J Surg 2006;101.
- Inal M, Celik N, Tuncay F. Efficacy of IV Paracetamol infusion versus IV Meperidine infusion for analgesia in post caesarian section patients. Internet J Anaesthesiol 2007;15:5.
- Durak P, Yagar S, Uzuner A, Kilic M, Dilber E, Ozgok A. Post operative pain therapy after laparoscopic cholecystectomy: Paracetamol vs Diclofenac. AGRI 2010;22:117-20.
- Yoganarasimha N, Raghavendra TR, Radha MK, Amitha S, Sridhar K. Comparison of Paracetamol infusion with Diclofenac infusion for perioperative analgesia. RRJMHS 2012;1:18-22.
- Pratyush G, Samir K, Neha G, Amit K, Shashikala C. Pre emptive analgesia with IV Paracetamol and IV Diclofenac sodium in patients undergoing various surgical procedures. Int J Biol Med Res 2013;4:3294-300.
- Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Acad Emerg Med 2001;8:1153-7.
- Hugo V, Thys L, Veekman L, Buerkle H. Assessing analgesia in single and repeated administration of Paracetamol for post-operative pain comparison with Morphine after dental surgery. Anaesth Analg 2004;98:159-65.
- Luthy CS, Collart L, Dayer P. The rate of administration influences the analgesic effects of Paracetamol. Clin Pharmacol Ther 1993;2:171.
- Willis JV, Kendell MJ, Flinn RM, Thornhill DP, Welling PG. The pharmacokinetics of Diclofenac sodium following intravenous and oral administration. Eur J Clin Pharmacol 1979;16:405-10.

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