

Comparison of analgesic efficacy of two different preparations of intravenous paracetamol for day care surgeries

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Abstract

Background: Paracetamol is a non-opioid analgesic drug which is widely used for treatment of pain and fever. Intravenous paracetamol (with excipients) given as infusion provide analgesia by the end of 15 minute infusion. Its relative high cost is one of the limiting factors. Inj Paracetamol available in ampoule (without excipients) can be suitably diluted and given as infusion. Its cost is comparatively less than ready to use infusion preparation. In this study we have compared postoperative analgesic efficacy of both preparations of paracetamol. **Methodology:** Patients in the age group 18 to 60 yrs ASA grade I and II of both sex for day care surgeries receiving general anesthesia were studied. One group of 40 patients received 15mg/kg of Inj. Paracetamol infusion (with excipients) 30 minute before induction and another group of 40 patients received 15mg/kg of Inj. Paracetamol infusion from ampoule diluted in 100 ml normal saline (without excipients) 30 minutes before induction in premedication room. Intraoperative hemodynamic parameters were recorded. Pain level was assessed by Visual Analog Scale at postoperative 30, 60, 90 and 120 minutes. **Result:** The patient characteristics, demographic data and surgical procedures were comparable in the two groups. VAS score in postoperative period in both groups of patients were comparable. **Conclusion:** Paracetamol infusion prepared from ampoule (without excipients) provides comparable and cost effective postoperative analgesia as with paracetamol 100 ml infusion (with excipients).

Key Word: excipients; paracetamol; postoperative analgesia

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INTRODUCTION

Postoperative analgesia is required for achieving patient satisfaction and enhanced recovery. It is seen that sufficient pain relief improves the surgical outcome, reduces morbidity and hospital stay. Thus optimal pain relief is a prerequisite for early postoperative recovery.¹

Pre-emptive analgesia has 'protective' effect on the nociceptive system, thus is more effective than a similar analgesic treatment initiated after surgery.² Immediate postoperative pain causes discomfort and is one of the main cause of delayed discharge. The ability to provide adequate pain relief by simple methods that are readily available is one of the major challenges for day care surgeries. Paracetamol is a non-opioid analgesic drug which is widely used for the treatment of pain and fever. It primarily acts on central nervous via cyclooxygenase pathway inhibition and probably through direct serotonergic pathways.³ It can be given via different routes namely oral, rectal, intramuscular and intravenous. Intravenous paracetamol available as ready to use infusion produces significant analgesia by end of 15 minute infusion. Its relative high cost is one of the limiting factors. Injection paracetamol available in ampoule is without excipients, it can be suitably diluted

and given as infusion. Its cost is comparatively less than ready to use infusion preparation.

MATERIAL AND METHODS

A hospital based prospective randomized study was designed with the objective to compare analgesic effect of ready to use 1gm/100ml intravenous paracetamol with excipients to intravenous paracetamol available in ampoule without excipients. After approval by the Institutional Review Board the study was conducted between march 2016 to September 2016. Eighty adult ASA I-II physical status patients (62 female and 18 male) with a mean age of 49.1 years (range; 18 to 60 years) for day care surgeries receiving general anesthesia were included in study in tertiary care hospital. Patients having severe hepatic or renal impairment, having addiction or any kind of communication problem were excluded from the study. Drugs for general anesthesia, 1g in 100 ml intravenous paracetamol ready to use for infusion and ampoules of 300 mg each of injection paracetamol, 100 ml normal saline were taken. Patients were randomly divided in two groups. One group(A) of 40 patients received 15mg/kg of Injection Paracetamol 1gm in 100ml ready to use infusion 30 minutes before induction and another group(B) of 40 patients received 15mg/kg of Injection Paracetamol infusion from ampoule diluted in 100 ml normal saline 30 minutes before induction in premedication room. In the operating room, electrocardiogram (ECG), non-invasive blood pressure (NIBP), heart rate (HR), end tidal co2 (ETCO2) and peripheral oxygen saturation (SpO2) were monitored. Anaesthetic technique was standardized using propofol (2 mg/kg), fentanyl (2 µg/kg), and atracurium (0.5 mg/kg) and maintained using N2O in oxygen and sevoflurane. Patients were extubated when fully awake. All the patients were transferred to post anaesthesia care unit (PACU). For postoperative pain assessment Visual analogue scale (VAS) was used (VAS: 0-10; 0: no pain, 10: worst pain imaginable). An anesthesiologist, not a part of anaesthesia team, assessed various parameters like VAS for pain scores at 30, 60, 90,120 minutes postoperatively. Also the side effects like nausea, vomiting, hypotension and respiratory depression were observed. Rescue analgesia was planned with intravenous tramadol 2mg/kg

RESULTS

Among eighty adult patients 62 were female and 18 male with a mean age of 49.1 years. The baseline patient parameters of each group are as shown in Table1 Demographic data and operation values of eighty patients were compared, no statistically significant

differences were found between the two groups. Mean operation time in both group were 42.5 minutes. Cardio respiratory variables such as systolic and diastolic blood pressure, heart rate and oxygen saturation in the intra operative as well as postoperative period were comparable in both groups. Respiratory depression, bradycardia and hypotension were not observed in any patient.

Table 1

Demographic parameter	Group A	GROUP B
NUMBER	40	40
AGE	28.65 +_8.08	28.07+_9.61
WEIGHT	49.17+_5.74	48.76+_5.57
SEX F/M	31/9	31/9

Postoperative visual analogue scale was compared in two groups, as shown in figure 1. Though significantly less VAS score is observed in control group initially i.e. at 30 and 60 minute the difference in VAS score of the two group were not statically significant at 90 and 120 minutes. Overall VAS scores were compared by taking average VAS scores at different point of time and there was no statistically significant difference. Mean value of VAS scores at 30,60,90 and 120 minutes postoperatively were 0.36875 in ready to use paracetamol infusion and 0.743001 in prepared paracetamol infusion and these values were not statistically different among groups (p<0.69). Only one patient required rescue analgesia in group A.

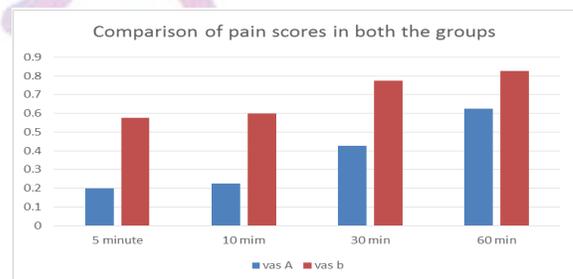


Figure 1

DISCUSSION

In the present study, the effect of two different preparations of IV paracetamol administration was investigated in patients undergoing day care surgeries. Paracetamol is most commonly prescribed analgesic for treatment of acute pain. Cochrane based meta-analysis did not demonstrate statistical differences in analgesia by IV paracetamol/propacetamol and active comparators,³ Despite its wide use, the mechanism of action of acetaminophen has not been fully understood. It inhibits prostaglandin (PG) synthesis weakly and has little anti-inflammatory activity. It causes weak in- vitro inhibition of both cyclooxygenase (COX)-1 and COX-2 by acetaminophen, so existence of unidentified form of

COX was thought and it was named COX-3. Brain COX is more sensitive to inhibition by acetaminophen. Because of its potent analgesic and antipyretic actions; it is generally regarded as an NSAID. However, it lacks the other typical actions of NSAIDs, such as antiplatelet activity and gastrotoxicity.⁴ Paracetamol also has an interaction with the serotonergic system.⁵ In addition, its weak effect on the peripheral system has also been demonstrated.⁶ In one of the retrospective cohort study of the patients undergoing total hip replacement or knee replacement surgery, iv acetaminophen was shown to have better outcome as it was associated with less adverse effect, short hospital stay and economical as compared to patients done without acetaminophen.⁷ There are studies associated with intravenous ready to use infusion which were given preoperatively and found to be effective. As in one of the study intravenous acetaminophen was given preoperatively for patients for abdominal hysterectomy and they found it to reduce opioid side effects as well as opioid dose, but found no difference in pain.⁸ But another study done with intravenous acetaminophen given preemptively for abdominal hysterectomy itself showed better analgesia and decreased use of opioid and lesser side effects.⁹ In another study where patients undergoing open nephrectomy it was found that preemptive or postoperative paracetamol reduces fentanyl consumption in the first postoperative day, while it decreased fentanyl associated nausea and vomiting in early postoperative period.¹⁰ New 1 gm. paracetamol available in market contains many excipients namely cysteine hydrochloride monohydrate, disodium phosphate dehydrate, hydrochloric acid 1M (for ph adjustment) mannitol, sodium hydroxide (for ph adjustment). One particular study in vitro it showed that without added cofactors, COX-2 activity was very low, but it increased to the same levels as those produced with cofactors when acetaminophen was added in higher concentration. In concentrations above 1 mM, acetaminophen again reduced PG synthesis.¹² In the present study we found that preemptively given single dose of paracetamol without excipients to be as effective as paracetamol with excipients for analgesia in immediate postoperative period for day care surgeries. Visual analogue scale scores at rest and postoperative 2hrs were comparable among groups in this current study. There is emphasis on cost containment along with efficiency and safety in the health system. So we have to quantify and justify the costs and benefits related to specific therapies. It is the need of the time that rational therapeutic decisions should be made with the use of cost-effective techniques for the comparison of different treatment alternatives. Single dose of Paracetamol

without excipients is a good cost-effective option for immediate postoperative analgesia and is comparable with 1 gm. paracetamol with excipients. It should be remembered that despite the fact that paracetamol has a wide clinical application it is not a drug devoid of side effects. Not more than 4 gm. to be given in a day. Therefore, before administering paracetamol, each time a balance of benefits and losses should be made so as to get desired outcome.⁹

CONCLUSION

Paracetamol without excipients given preemptively can be effective for analgesia in the immediate postoperative period in day care surgeries. Furthermore this can be achieved at lesser cost. Thus even use of IV paracetamol without excipients can provide significant contribution to the multimodal methods of postoperative pain control for short term if used judiciously keeping in mind cost benefit and safety.

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