Original Article

Comparative evaluation of preemptive use of intravenous Paracetamol and intramuscular Diclofenac on postoperative analgesia in lower abdominal surgeries done under spinal anesthesia

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Abstract

Background: Preemptive analgesia is the treatment that is initiated before occurrence of a painful event (surgical procedure); in order to reduce the physiological consequences of nociceptive transmission provoked by the procedure. **Aim and objective**: To study and compare the effects of intravenous Paracetamol and intramuscular Diclofenac when used for preemptive analgesia; on postoperative pain, postdural puncture headache (PDPH) and development of chronic pain thereafter. **Material and Method:** 60 adult patients of either sex of ASA grade Iand II posted for surgery under spinal anesthesia in a stipulated period of 1 year in a tertiary care hospital were enrolled for this study. The patients were divided randomly into 2 groups. The patients from Group A received IV Inj. Paracetamol 1 gm while the patients from Group B received IM Inj. Diclofenac sodium 75 mg;30 minutes prior to spinal anesthesia with injection Bupivacaine 0.5% (Hyperbaric). A questionnaire was responded by all the patients and a chart was maintained for pain score in visual analogue scale and for side effects. **Observations and Results**: Paracetamol and Diclofenac both the study drugs produced satisfactory postoperative pain relief and there was no incidence of PDPH in either group. Mean duration of analgesia was longer and the difference was statistically highly significant in Group A.($p < 0.005$).We found the significant reduction ($p < 0.001$ at 1,2,4,6 hr postoperatively) in VAS pain score in intergroup comparison at different time intervals. Group A had shown better outcome with less requirement of rescue analgesia and side effects. The incidence of adverse events was less with group A (20% Vs 43.5%) **Conclusion:** Compared to intramuscular Diclofenac, intravenous Paracetamol is safer and more effective analgesic when used preemptively for the treatment of postoperative pain after spinal anesthesia.

Key Words: Postoperative analgesia, Preemptive analgesia, Visual analog scale.

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INTRODUCTION

Pain has been a major concern of mankind since the very beginning and it has been the object of ubiquitous efforts to understand and treat it.[1] According to International Association for the Study of Pain, pain is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.'[1] Pain is inevitable after every surgery; hence management of post-operative pain is of utmost importance for early ambulation and discharge reducing

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days of hospital stay.[2] The different classes of analgesics used, exert their effect through different mechanisms. Non-opioid analgesics are favored world-wide as they are devoid of opioid induced side effects like respiratory depression and nausea – vomiting, which require intense postoperative monitoring.[3] Paracetamol and diclofenac are the two non opioid drugs that are being used for postoperative pain where use of opioids is contraindicated. Non-steroidal anti-inflammatory drugs (NSAIDS) like diclofenac exert their action via inhibition of prostaglandin synthesis by inhibiting COX-1 and COX-2 enzymes with relative equipotency[4] while *in vivo* effects of paracetamol are similar to those of the selective COX 2 inibitors. Intramuscular (IM) injection of diclofenac has established its role as an effective post-operative analgesic for major surgeries causing moderate intensity pain.[5,6,7] Intravenous (IV) paracetamol (acetaminophen) is a newer agent gaining worldwide popularity in acute post-operative pain relief.[8] There has been a recent trend of combining different NSAIDs with paracetamol for the management of acute post-operative pain[9,10] but the therapeutic superiority between intramuscular diclofenac and intravenous paracetamol remains understudied.[11,12] Preemptive analgesia is an evolving concept and is defined as a treatment that is started before surgery in order to prevent the establishment of central sensitization evoked by the incisional and inflammatory injuries occurring during surgery and in the early postoperative period. Owing to this 'protective' effect on the nociceptive system, preemptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery.[13] In an attempt to reduce immediate postoperative pain, incidence of postdural puncture headache (PDPH) and development of chronic pain therafter, we have decided to study and compare the efficacy and safety of intravenous Paracetamol and intramuscular Diclofenac when used as preemptive analgesics.

MATERIAL AND METHOD

After obtaining institutional ethical committee approval and informed written consent from study subjects, a comparative study was conducted on a predetermined sample size in a tertiary care hospital. Sixty adult patients between 18-65 years of age with the American Society of Anesthesiologists (ASA) I and II admitted for elective lower abdominal surgery under spinal anesthesia with incision to closure time between 60-150 min were selected for the study. Paediatric age group, patients with ASA grade III and IV, those with known allergy to study drugs, renal dysfunction, liver dysfunction, unable to comprehend VAS score and bleeding disorders were excluded from the study. The enrolled patients were randomized into two groups by lottery method. Patients in group A received intravenous Paracetamol 15mg /kg (maximum 1g in 100 mL infusion) over 20 minutes whereas those in group B were given intramuscular Diclofenac sodium 2mg/kg (maximum75 mg). Both study drugs were given 30 minutes prior to the spinal anesthesia with injection hyperbaric bupivacaine 0.5%.

Study procedure

Prior to the day of surgery all patients underwent pre anaesthesia check up with routine and subjective investigations as per institutional protocol. After receiving the study subject in pre anesthesia room, the baseline parameters were noted. The patients were explained about 'visual analogue scale' and the procedure. After preoperative preparation, IV line was secured. The patients from Group A received IV Paracetamol 15mg/kg(maximum 1gm in 100 ml infusion) over 20 minutes,30 min prior to the spinal anaesthesia while patients from Group B received IM Diclofenac sodium 2mg/kg (maximum 75 mg), 30 min prior to spinal anaesthesia. All the patients were premedicated with Inj. Ondensetron 4 mg iv, Inj.Glycopyrrolate 0.2 mg iv. Under all aseptic conditions, lumbar puncture at L3-L4 interspace using 25G spinal needle with patient in sitting position was performed. Intra-operative monitoring of ECG, heart rate, mean arterial pressure, systolic and diastolic blood pressure, peripheral oxygen saturation (SpO2) of all patients were recorded as per standard protocols. No additional analgesic was given over the entire course of the surgery. Inraoperative and postoperative complications if any, were observed and managed according to standard protocols. Postoperative pain score was measured by using 'visual analogue scale'. Rescue analgesic in the form of injection Tramadol 50 mg intravenously was given if VAS score was > 7 at any point of time. All the patients were observed in post-anesthesia recovery room and later in high dependency ward as per institutional protocol. Duration and type of surgery was noted. A questionnaire prepared and chart was filled up as per response of patients. The changes in the pulse rate, mean blood pressure and respiratory rate at different time intervals were also recorded. Time interval and number of doses of rescue analgesic (Inj Tramadol 50 mg) given when VAS > 7 were also recorded. Post operative pain score was measured by using visual analogue scale (VAS) of 0 to 10, where 0 indicated no pain and 10 most severe pain. Postoperative pain was observed at the interval of 15 min, 1h, 2h, 4h, 6h. Side effects such as nausea, vomiting, respiratory depression, headache, itching, allergic reaction were cross examined and recorded.

Statistical Analysis

Data was compiled in MS-Excel. It was analysed and expressed as mean ± SD. Intergroup comparison was done using paired t test. Statistical analysis was done by using chi square test with a significant p- value of <0.05. Statistical package for social sciences (SPSS) version 22- (USA) was used for statistical analysis.

OBSERVATION AND RESULTS

Table 1: Comparison of demographic variables

	Group A	Group B	p value	Significance
Age (yrs) Mean ±SD	45.4±8.5	48.2 ±6.4	0.1549	NS
Wt (kgs) Mean ± SD	57.5±2.8	56.38± 2.6	0.1138	NS
ASA (I/II)	26/4	21/9	>0.05	NS
Sex (Male/Female)	10/20	18/12	>0.05	NS
Duration of surgery	71.32±9.2	68.63±6.52	0.1965	NS

(NS: not significant)

The data in table 1 suggests that both the groups are demographically comparable.

Table 2: Comparison of MAP at different time intervals

Time interval	Group A MAP (Mean ±SD)	Group B MAP (Mean ±SD)	p value	Significance
0 hr	91.55± 3.94	89.75±6.03	0.1180	NS
1 hr	83.9±13.14	83.63±4.41	0.9023	NS
2 hr	88.07±4.90	90.08±3.77	0.081	NS
4 hr	80.63±5.49	77.53±7.05	0.0312	NS
6 hr	79.08±6.17	75.92±6.16	0.0246	NS

*0 hr- at the end of surgery

While comparing MAP in both the groups, we observed that MAP gradually reduced up to 6 hrs in both the groups. Intergroup variation in MAP at different time intervals was comparable.

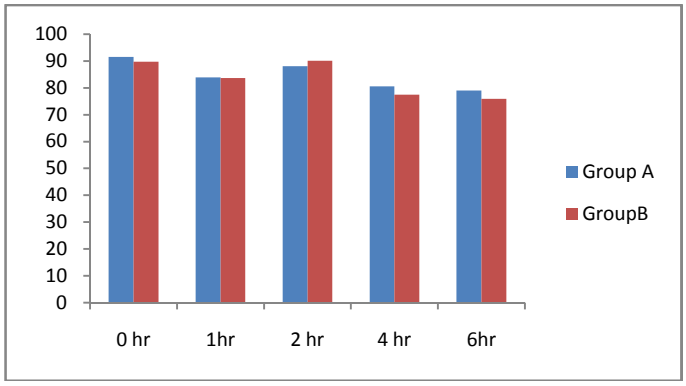

Figure 1: Comparison of Mean Arterial Pressure (mm Hg)

As indirect parameters of analgesia and other systemic effects of both the drugs, the changes in the heart rate, blood pressure (systolic, diastolic and mean arterial pressure) and changes in respiratory rate were studied and compared between 2 study groups at different time intervals. We observed that the difference between two groups was statistically not significant for all the parameters studied.

Table 3: Comparison of VAS score

Time	Group A	Group B	p value	Significance
0 hr	0.40±0.80	1.08±0.99	0.010	Significant
1 hr	1.68±0.65	1.01.±0.85	0.001	Significant
2 hr	1.9±0.59	2.21±0.32	0.0142	Significant
4 hr	2.67±0.89	3.09±2.3	0.3548	Non Significant
6 hr	4.41±1.71	4.99±0.93	0.1081	Non Significant

It is evident from the Table 3 that, VAS scores in both the groups was < 3 till 4 hrs in postoperative period indicating effective analgesia produced by both the study drugs. While on intergroup comparison, we found that Mean VAS score was higher in Group B compared to Group A, and the difference was statistically highly significant at 0, 1,2 hr postoperatively. It indicated that onset, duration and quality of postoperative analgesia was better in group A. 6 patients in group B and one patient in group A needed rescue analgesia with Inj. Tramadol (50 mg iv) due to higher VAS score at 4 hrs.

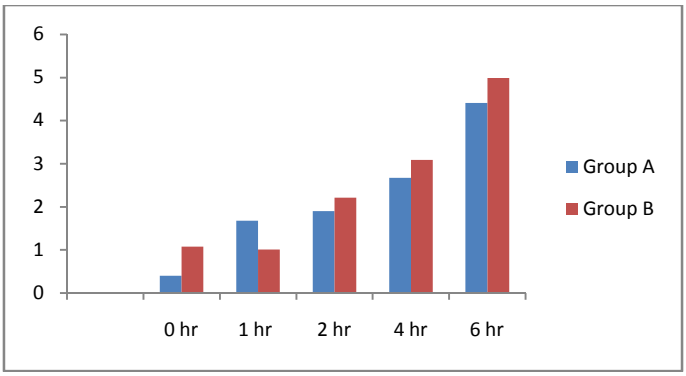

Figure 2: Visual Analogue Score

Table 4: No. of patients requiring rescue analgesia

Time interval	Group A (n=30)	Group B(n=30)
0-2 hr	0	0
2-4 hr	0	1
4- 6 hr	1	5

One patient in group A and 6 patients in group B (20%) received rescue analgesia when recorded pain score was > 7 in the early postoperative period.

Table 5: Incidence of side effects

Complications	Group A (N=30)	Group B (N=30)
Nausea	(4/30) 13.33%	(7/30) 23.5%
Vomiting	(2/30) 6%	(6/30) 20%
Itching	-	-
Respiratory depression	-	-
Allergic reaction	-	-
PDPH	-	-

Side effects noted were in the form of post operative nausea- vomiting (PONV). The incidence of nausea and

vomiting was higher (43.5%) in Group B than Group A (20%)

DISCUSSION

Paracetamol is a well established analgesic for postoperative pain management. A systematic review and meta-analysis by McNicol *et al*[8] has confirmed the efficacy and safety of single dose of intravenous paracetamol in preventing acute postoperative pain. Intravenous paracetamol is also used as preemptive analgesic for prevention of postoperative pain. Arici and colleagues [5] demonstrated efficacy and safety of preemptive use of intravenous paracetamol in patients undergoing total abdominal hysterectomy. In this study they observed that 1 gm iv paracetamol ensures an effective postoperative analgesia and improvement in patient satisfaction by reducing postoperative opioid consumption and side effects. These results are in line with our study where incidence of side effects observed was much less (20%) in patients receiving IV paracetamol compared to 43.5% in patients receiving IM diclofenac. Goel *et al*[2] in their comparative study for preemptive analgesia with IV paracetamol and IV diclofenac sodium in patients undergoing various surgical procedures found that mean VAS score was higher in diclofenac group for initial period followed by insignificant difference in pain score for 4 hrs. In our study, comparative analysis of mean VAS score showed significantly better pain relief with intravenous paracetamol compared to intramuscular diclofenac group immediately after surgery and two hours postoperatively. Better pain relief with paracetamol immediately after procedure suggests faster onset of action compared to diclofenac. Though there was no significant difference in the VAS score between two groups at four and six hours in the postoperative period, higher number of patients (6/30) requiring rescue analgesic during early postoperative period in diclofenac group suggests that intravenous paracetamol provides better quality and longer duration of pain relief. In our study, it was noted that the pain relief with intramuscular diclofenac was significantly better than intravenous paracetamol at one hour after surgery. This discrepancy in analgesic effect may be explained by the subjective responses about pain relief by the patients. M Inal *et al*[14] conducted randomized double blinded study between intravenous paracetamol and intravenous meperidine for postoperative analgesia after caesarean section. They found that 1gm intravenous paracetamol administration results in lesser requirement of rescue analgesics than 100 mg intravenous meperidine, a synthetic opioid agonist when used for postoperative pain management. In our study, rescue analgesia was required in only one patient receiving intravenous paracetamol as opposed to 20% patients in intramuscular diclofenac group. In a prospective double blind, randomized placebo controlled study conducted on 40 patients undergoing lumbar laminectomy and discectomy by Cakan *et al*[15] they demonstrated that IV paracetamol decreased VAS scores and incidence of vomiting and patient satisfaction. Mohammed Jalili *et al*[16] compared the analgesic efficacy of iv paracetamol 1gm and iv morphine 0.1mg/kg in acute limb trauma. Interestingly, they found that single dose 1 gm intravenous paracetamol provided a better postoperative analgesia than intravenous morphine. Diclofenac, a commonly used non-steroidal anti-inflammatory drug (NSAID) acts by inhibiting cyclo-oxygenase enzymes. Dose dependent gastrointestinal adverse events are known with diclofenac use.[17] Inhibition of prostaglandin synthesis is the underlying mechanism for the gastrointestinal adverse events with NSAIDs. The patients enrolled in present study, reported only gastrointestinal adverse effects in the form of nausea and vomiting. Incidence of vomiting was much higher with intramuscular diclofenac compared to intravenous paracetamol (20% vs 6%). Tramadol, the rescue analgesic used in the study can also cause nausea and vomiting. More patients in diclofenac group received tramadol, so its contribution in causing these gastrointestinal adverse events cannot be ruled out. Paracetamol is centrally acting cyclo-oxygenase inhibitor without causing effect on prostaglandin synthesis in the gastrointestinal tract[16] Better gastrointestinal tolerability is an advantage of paracetamol over NSAID.[18] No other serious adverse events were reported in this study. With the above mentioned literature review, we confirmed our findings that inj Paracetamol is a better analgesic than inj Diclofenac. However, Pal *et al*[3] when compared 1gm IV paracetamol, 75 mg IM diclofenac with a combination of both after 8 hrly administration of study drugs, found that Paracetamol alone is an inferior analgesic compared to diclofenac and diclofenac+ paracetamol combination when used preemptively, but all the three groups were comparable with respect to safety (side effects).

LIMITATION AND SCOPE

With the inclusion of control group, efficacy of study drugs in alleviating post-dural puncture headache could have been definitively commented upon. To draw definitive inference about alleviation of postdural puncture headache, sample size should have been larger, since incidence of PDPH quoted in the literature is 0.1-36%.[19]

CONCLUSION

From the above study it can be concluded that Intravenous paracetamol and intramuscular diclofenac, both provide satisfactory post operative analgesia. Intravenous paracetamol causes lesser gastrointestinal adverse events and provide better quality and longer duration of postoperative analgesia than intramuscular diclofenac when used as preemptive analgesic in lower abdominal surgeries performed under spinal anesthesia.

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