Paracetamol versus Diclofenac as Intravenous Post-Operative Analgesia in Patients after Laparoscopic Surgeries

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ABSTRACT

BACKGROUND

Laparoscopic surgery is becoming a widely used procedure in recent days due to its minimal invasive nature and faster recovery. Pain is a stressful stimulus in post-operative period. Pain is a subjective experience. Poor pain management may hinder better postoperative outcome, leading to patient suffering and lengthened recovery period. We wanted to compare the efficacy of intravenous paracetamol and intravenous diclofenac for post-operative analgesia following laparoscopic surgeries.

METHODS

This randomised controlled double-blind prospective study was conducted between October 2017 and May 2019 among 48 participants posted for laparoscopic abdominal surgeries, block randomised into 24 participants each in 2 groups. All patients were given general anaesthesia and 30 minutes prior to extubation patients were given the test drug according to the groups assigned using closed envelop technique. The test drugs were continued post operatively at prescribed intervals. Visual analogue score (VAS) score, systolic and diastolic blood pressure (BP) and heart rate were monitored at 2, 4, 6, 12 and 24 hours postoperatively. Furthermore, need for rescue analgesia with inj. tramadol 50 mg intramuscular (IM) and post-operative nausea and vomiting (PONV) were noted.

RESULTS

The study results showed increased pain scores in diclofenac group up to 12 hours but were statistically insignificant. High pain score was seen in diclofenac group at 24 hours with statically significant P-value of 0.022 and PONV occurring in 3 patients. Paracetamol group had better haemodynamic stability.

CONCLUSIONS

Intravenous paracetamol and intravenous diclofenac were found to be equally effective in post-operative analgesia in patients undergoing laparoscopic surgeries; however, paracetamol has an advantage of providing better analgesia for longer duration with better haemodynamic stability.

KEYWORDS

Intravenous Paracetamol, Intravenous Diclofenac, Laparoscopic Surgeries, Post-Operative Analgesia

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BACKGROUND

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] Pain is a subjective experience; only patients know the location of the pain and its degree of intensity. Pain is an important symptom in medical and surgical conditions, interfering with a person's quality of life and general functioning. Insufficient pain relief in the postoperative phase is a familiar problem worldwide. Apart from the suffering caused by inadequate pain relief, there is a matter of probable physiological and psychological concerns for patients, as well as financial disadvantages for patient attenders.[2,3]

The major objective in the management of postoperative pain is adjusting the dose of medications to reduce side effects while still providing sufficient analgesia. This objective is best achieved with multimodal and pre-emptive analgesia.[4] Opioids remained the superior choice for severe pain; but their adverse effects demerit their wide use.[5,6] Opioids, like morphine, have associated respiratory depression, sedation, biliary spasm, decreased gastrointestinal motility, post-operative nausea and vomiting with confusion, in older patients.[7]

Paracetamol and diclofenac, the two non-opioid drugs selected in this study are preferred in post-operative pain reduction where the use of opioids are limited by their adverse effect.[8] Paracetamol is freely available as analgesic in hospital and community settings. In spite of extensive use, its efficacy as postoperative analgesic is still not fully elucidated. With the recent availability of intravenous solution of paracetamol there is increased interest in its use in the peri-operative setting. Paracetamol has been an effective analgesic in the management of post-operative pain, unaided or as a combination with other analgesics.[9,10] Paracetamol is not linked with higher incidence of gastrointestinal, haematological, renal or the cardiovascular effects associated with non-steroidal anti-inflammatory drugs (NSAIDs), comprising that of selective cyclo-oxygenase-2 (COX-2) inhibitors.[11]

Diclofenac a non-steroidal anti-inflammatory drug is administered to reduce inflammation and pain in postoperative period. It may be supplied as either the sodium or potassium salt.[12]

This study was conducted to compare the efficacy of paracetamol and diclofenac as intravenous post-operative analgesic after laparoscopic surgeries. We intended to assess post-operative pain by visual analogue pain scores and the total analgesic requirement in the first 24 hours, with or without the need for additional analgesic despite administration of either paracetamol or diclofenac in postoperative period. Data was also collected to study the side effects and haemodynamic parameters after paracetamol and diclofenac in the patients. The study strived to provide scope for an alternative non opioid analgesia regime in post-operative period following laparoscopic surgeries.

METHODS

This randomised controlled double-blind prospective study was conducted in a multispecialty teaching hospital from October 2017 to May 2019 after obtaining the institute ethics committee clearance.

Selection of Patients

With the help of Open Epi version 3.03, mean pain score using visual analogue score between two groups of paracetamol and diclofenac, 1.13 (SD of 1.31) and 2.2 (SD of 2.01) respectively, was taken from previous study. Study sample comprised of 24 patients in both paracetamol as well as diclofenac group, identified with 95 % confidence interval and 90 % power and 1:1 allocation, a sample size of 24 in each group was derived, making a total of 48 participants. Written informed consent was obtained from all patients.

Criteria for Inclusion

- Age, 18 - 60 years
- American Society of Anesthesiologists (ASA) I and ASA II
- Both genders
- Laparoscopic surgeries (with incision to closure time > 30 mins)

Criteria for Exclusion

- Patients with known allergy to drugs to be used in the study.
- Decreased renal function.
- Patients who are unable to comprehend visual analog score.
- Bleeding diathesis or patients on anticoagulation.
- Patients with decreased liver function.

Randomisation

The samples of 48 patients were randomised using block randomization technique. Randomization sequence were generated by an external person (epidemiology unit, DCM) and handed over to the investigator in sealed opaque sequentially numbered envelope.

Block randomisation was used to ensure that the number of participants in the study groups was nearly equal. It was done with varying block sizes to prevent prediction of the treatment. Block randomisation of two treatment groups: A and B, number of blocks = 9, size of blocks = 4 / 6 / 8, and variable size blocks.

Sequentially numbered, opaque, sealed envelope technique: the randomisation group was written on a paper and was kept in an opaque sealed envelope. The envelope was labelled with a serial number. The investigator opened the sealed envelope once the patient had consented to participate and then assigned the treatment group accordingly.

Drugs Used in Each Group

Group A

Intravenous paracetamol at 15 mg / kg (maximum 1 g in 100 mL infusion) administered over 15 - 20 minutes, 30 minutes before the end of laparoscopic surgery, as the first dose of analgesic with subsequent doses at 8 hourly intervals after shifting the patient to the ward.

Group B

Intravenous diclofenac at 2 mg / kg (max 75 mg) in 100 mL of normal saline administered over 15 - 20 minutes, 30 minutes before the end of laparoscopic surgery, as the first dose of analgesic with subsequent doses at 12 hourly intervals after shifting the patient to the ward.

Procedure

All patients were given tablet alprazolam 0.25 mg and tablet ranitidine 150 mg on the night before surgery. On the day of surgery, the patients received tab ranitidine 150 mg and tab metoclopramide 10 mg at 7 am. The patients were shifted to pre-operative holding area and again re-assessed. After checking the anaesthesia machine and breathing apparatus, the patient was shifted to the operating room and then standard monitors as per American Society for Testing and Materials-ASTM (ECG-electrocardiogram, HR-heart rate, SPO2-oxygen saturation, NIBP-non-invasive blood pressure) were connected and baseline parameters were monitored.

An intravenous line was started using an 18G or 20G intravenous cannula. Conventional general anaesthetic technique was followed as per protocol. Throughout the surgery intra-abdominal pressure was maintained within 12 - 15 mm Hg in both the groups.

All the patients were given their "study drug" 30 minutes prior to completion of surgery. Intra-operative complications if any were noted. At the end of surgery, the oropharynx was cautiously suctioned using a soft suction catheter and patient was extubated after standard reversal of muscle relaxation with neostigmine and glycopyrrolate. Following which the patients were shifted to recovery room and vitals were monitored. In recovery room, the patients were monitored for vital parameters (SBP-systolic blood pressure, DPB-diastolic blood pressure, MAP-mean arterial pressure, HR) at 2 hr., 4 hr., 6 hr., 12 hr. and 24 hr. VAS score were also recorded at the above-mentioned intervals and noted down.

Reading were taken by visual analog scale: A 10 cm line anchored at one end by a label as "no pain" and at the other end by a label as "the worst pain imaginable" or "pain as bad as can be". The patients were asked to mark on the line to indicate the pain intensity in relation to 0 being no pain and 10 being worst possible pain. The result was interpreted as distance in centimetre (cm) between 0 to the point marked by the patient.

Pain scored as mild, moderate or severe pain when VAS score is between 1 and 3; 4 and 6 or more than 7 respectively. First dose of postoperative rescue analgesic was given when VAS score was 7 - 10 or on demand made by the patient for analgesic (whichever was earlier) and repeated if required. Rescue analgesia was injection tramadol 50 mg IM. Any complication or complaint like nausea and vomiting, pruritus, sedation, respiratory rate (RR) < 10 per minute or any other abnormal findings were recorded.

Statistical Analysis

Data entry was carried out using MS Excel 2013 and data analysis was carried out using SPSS version 23.0. Test for normality were carried out for continuous variables. Difference in means for non-parametric data was tested using Mann Whitney U test. Differences in proportions were tested using chi-square test. P value < 0.05 was considered statistically significant.

RESULTS

Demographical variables in both groups showed no statistically significant variation and were comparable in age, gender, ASA criteria and MMS classification in the two groups with 54.2 % males and 45.8 % females [Table 1].

Gender	Study Group: Group A N (%)	Study Group: Group B N (%)	Total N (%)	P Value*
Male	15 (62.5)	11 (45.8)	26 (54.2)	0.247
Female	9 (37.5)	13 (54.2)	22 (45.8)	
Total	**24 (100.0)**	**24 (100.0)**	**48 (100.0)**	

Table 1. Distribution of Study Groups Based on Gender (N = 48)

Chi Square test was applied to test statistical difference in proportions

The pain scores (VAS) at 2, 4, 6, and 12 were considerably low in paracetamol group than with diclofenac but they were statistically insignificant. However, at 24th hour diclofenac group had higher VAS score and were significant with a P-value of 0.022 [Table 2]. Also 2 patients in group B required rescue analgesic with inj. tramadol.

Pain Score at 24 Hours	Study Group: Group A N (%)	Study Group: Group B N (%)	Total N (%)	P Value*
3	4 (16.7)	1 (4.2)	5 (10.4)	
4	16 (66.7)	8 (33.3)	24 (50.0)	
5	4 (16.7)	12 (50.0)	16 (33.3)	0.022
6	0 (0.0)	1 (4.2)	1 (2.1)	
7	0 (0.0)	2 (8.3)	2 (4.2)	
Total	**24 (100.0)**	**24 (100.0)**	**48 (100.0)**	

Table 2. Distribution of Study Groups Based on Score at 24 Hours (N = 48)

Chi square test was applied to test statistical difference in proportions

DBP at 24 Hours	Group A (N = 24) Median	Group A (N = 24) IQR	Group B (N = 24) Median	Group B (N = 24) IQR	P-Value*
	74.5	71.25 - 77.75	79	75.25 - 83	0.006

Table 3. Distribution of Study Groups Based on DBP at 24 Hours (N = 48)

*Mann Whitney U test was applied for comparison of means

While comparing the HR, SBP, DBP and MAP in both the groups, we have observed that there was no significant variation in both the groups in different intervals, except the mean values for DBP at 24 hr. of post-operative period

where it was found that DBP was higher in the diclofenac group. The differences in their median values were statistically significant. The median DBP in group A was 74.5 and in group B was 79 with P-value 0.006 [Table 3, Figure 1].

We observed that in patients of group-A, there is no case of post-operative complication; whereas in patients of group-B, 3 patients showed signs of post-operative nausea and vomiting [Table 4].

Occurrence of PONV	Study Group Group A N (%)	Group B N (%)	Total N (%)	P Value*
Yes	0 (0.0)	3 (12.5)	3 (6.3)	0.074
No	24 (100.0)	21 (87.5)	45 (93.8)	
Total	**24 (100.0)**	**24 (100.0)**	**48 (100.0)**	

Table 4. Distribution of Study Groups Based on Occurrence of PONV (N = 48)

* Chi Square test was applied to test statistical difference in proportions

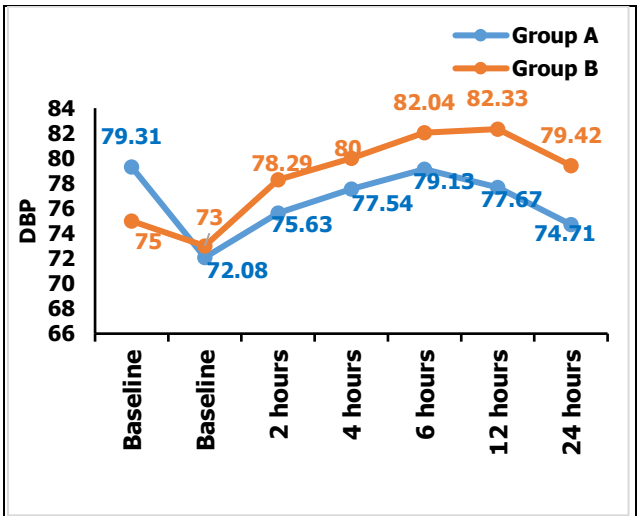

Figure 1. Mean DBP at Various Time Intervals

DISCUSSION

Pain in the post-operative period is an unpleasant sensory experience with emotional and mental trauma. It is precipitated by surgery with associated autonomic, endocrine-metabolic, physiological and behavioural response.[5] Pain after laparoscopic surgery has three different components: incision pain (somatic pain), visceral pain (deep intra-abdominal pain) and referred pain (referred by the visceral innervations). Pain if not adequately relieved may lead to complications like atelectasis / pneumonitis / hypoxemia, deep vein thrombosis, delayed recovery of bowel function, myocardial ischemia and infarction, urinary retention or residual psychological trauma.[13] The present study was carried out with an aim to compare the effects of intravenous paracetamol with that of intravenous diclofenac as post-operative analgesics in elective laparoscopic surgeries. The study groups were similar and comparable in terms of baseline characteristics like age, gender, MMS, ASA, body mass index (BMI) classification and duration of surgery. Higher pain scores were noted in diclofenac group till 12 hours as compared to that of paracetamol group, however, these differences were not statistically significant. Significantly higher pain scores were noted in diclofenac group at 24 hours. Hemodynamic parameters like HR, SBP, DBP and MAP were similar between the study groups at most different time intervals. Higher mean BP was noted in diclofenac group after 12 hours as compared to paracetamol group.

Paul D et al.[14] evaluated the efficacy of intravenous paracetamol and intravenous diclofenac as post-operative analgesia in laparoscopic cholecystectomy among 68 patients. The study reported that the significant outcome (P-values are 0.0005 at 0 hrs, 0.003 at 2 hrs, 0.001 at 6 hrs, 0.0005 at 12 hrs) in VAS pain score in between the two groups at different intervals. Patients who were administered intravenous paracetamol had shown better outcome with decreased requirement for rescue analgesia and its related side effects. Unlike this study, our study has shown significant difference in pain score at 24 hours interval only while on other occasion, though there was difference in pain scores it was not statistically significant.

Kharbuja K et al.[15] compared the efficacy of intravenous paracetamol and intravenous diclofenac as postoperative analgesia in laparoscopic cholecystectomy among 120 patients. Study data revealed that the profiles of hemodynamic changes were almost similar in both groups. It was observed statistically significant differences in visual analogue scale between the two groups. Most of the patients in paracetamol group had low mean pain scores in post-operative period and had extended analgesia compared to diclofenac group. All the findings in the above study were noted in similar lines in the present study also.

Shah UD et al.[16] assessed the analgesic efficacy and safety of IV paracetamol in comparison with IV diclofenac for postoperative pain relief among 120 patients. It was noted in their study findings that 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. These reports were identical to that of the findings demonstrated by the present study.

CONCLUSIONS

Intravenous paracetamol and intravenous diclofenac were found to be equally effective in post-operative analgesia in patients undergoing laparoscopic surgeries; however, paracetamol has an advantage of providing better analgesia for longer duration with better hemodynamic stability. Intravenous paracetamol has lesser requirement for rescue opioid analgesia in comparison to intravenous diclofenac thereby avoiding associated complication of opiates. No immediate adverse effects were observed in patients using intravenous paracetamol as postoperative analgesia in laparoscopic surgeries.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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