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Comparison of First Analgesic Demand in Post-Operative Period Among Diclofenac Group Versus Paracetamol Group

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Abstract **Original Research Article**

Background: Pain after major surgery causes delays in patients' postoperative recovery, extended hospitalization periods, excessive use of analgesics, and is extremely stressful for both surgery and anesthesia. Preemptive analgesia is a treatment that begins before surgery to prevent the development of central sensitization caused by incisional and inflammatory damage that occur during surgery and in the early postoperative period. Opioids and nonsteroidal anti-inflammatory medications (NSAIDs) are commonly used for this purpose. Diclofenac sodium is a typical, inexpensive NSAIDS. Preemptive analgesia can reduce the severity and duration of pain while also delaying it. ***Objectives:*** The aim of the study was to evaluate the Comparison of first analgesic demand in post-operative period among Diclofenac group versus Paracetamol group. ***Methods:*** This randomized controlled trial study was carried out in the Department of Anaesthesiology & ICU Bangladesh Medical College Hospital Dhaka, Bangladesh during 18th January 2020 to 17th July 2020. A total of 50 patients were participated in the study. Sample was selected by random sampling in two groups distributed as- group A (Oral diclofenac sodium), group B (Oral paracetamol). Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24). ***Results:*** The majority of patients (63.0%) were between 40 and 59 years old, with a mean age of 48.3 ± 11.2 years. In groups A (58%) and B (56%), nearly two-thirds of the patients had an ASA grade of one. There was no statistically significant difference between the two groups ($p>0.05$). At baseline, no significant change in heart rate, SBP, or DBP was seen across groups. The postoperative heart rate and other haemodynamic state were assessed at two, six-, and twelve-hours following surgery. ***Conclusion:*** Preemptive oral Diclofenac sodium had significant effect on reducing postoperative pain and postoperative analgesic requirement in patients planned for abdominal surgery. Surgical pain results from traction of tissues during surgery, surgical wound and surgical drains. The intensity of pain is greatest during the first postoperative day and requires efficient pain control.

Keywords: Preemptive analgesia, Non-steroidal anti-inflammatory drugs (NSAID), Diclofenac sodium.

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INTRODUCTION

Pain from surgical treatments results from tissue trauma and can cause physical, cognitive, and emotional distress. Almost a century ago, researchers first proposed a link between intraoperative tissue injury and an increase in acute and long-term postoperative pain, a phenomenon known as central sensitization. Chemicals released in reaction to cellular or tissue injury activate nociceptor receptors. Pre-emptive analgesia is a key concept in understanding postoperative analgesia treatment options. Pre-emptive analgesia aims to reduce postoperative pain and avoid central sensitization and persistent neuropathic pain by administering analgesia prior to surgery but not afterward [1]. The anaesthesiologist's involvement in the immediate postoperative period has always included pain treatment, and the establishment of acute postoperative pain services has expanded this focus beyond the post-anaesthesia care unit. The goal of postoperative pain treatment is to provide optimal analgesia, allowing for a rapid return to normal physiological function.

Preemptive analgesia, a developing clinical concept, is initiating an analgesic regimen prior to the

commencement of noxious stimuli in order to prevent the nervous system from becoming sensitized to later stimuli that may exacerbate pain [2]. Preemptive analgesia is an antinociceptive medication that prevents the development of altered afferent input processing. The concept was proposed in the early 1980s, when experimental research revealed that methods to block nociceptive signals before damage reduced central hypersensitization, lowering the degree of pain after injury [3].

Some animal experiments have shown that anesthetic procedures that significantly lower the quantity of pain information that enters the spinal cord and brain can avoid central sensitization and subsequent pain-related behavior when used prior to the painful stimulation [4]. However, other animal trials did not yield the same results. Several preemptive analgesic regimens have been tested in humans. These include opioids administered intravenously, nonsteroidal anti-inflammatory medications, peripheral nerve blocks, and multimodal combinations. Preventive treatment has included systemic administration of nonsteroidal anti-inflammatory medications and NMDA receptor antagonists [5].

A meta-analysis examined different odontologic, abdominal, and orthopedic surgeries. As a preventive measure, NSAIDs such as diclofenac, naproxen, flurbiprofen, ketorolac, ketoprofen, diflunisal, and ibuprofen were administered at clinically relevant doses. All trials included intraoperative coadministration of fentanyl, alfentanil, local anesthetics, or nitrous oxide as part of the anesthesia. Preemptive treatment dramatically improved pain levels immediately after surgery when compared to postoperative treatment. A quantitative analysis indicated that there is no indication that preventive treatment with NSAIDs, intravenous opioids, intravenous ketamine, peripheral local anesthetics, and caudal analgesia is any better at relieving postoperative pain than a similar postincisional treatment [6].

Diclofenac sodium is an efficient NSAID that reduces peripheral sensitization and is also a powerful inhibitor of the cyclooxygenase pathway, resulting in prostaglandin synthesis. A previous trial found that diclofenac sodium taken prior to induction had a significant and definitive opiate sparing effect. Diclofenac alone and in combination with other medications reduced post-operative pain scores and opioid intake in the first 24 hours. Additionally, the time to the first rescue analgesia was extended. As a result, diclofenac as a preventative treatment had superior analgesic efficacy [7].

Surgery is the most promising scenario for preemptive analgesia because the timing of unpleasant stimuli is predictable. When suitable medication doses are given to carefully selected patients before to surgery, intravenous opiates, local anesthetic infiltration, nerve block, subarachnoid block, and epidural block provide benefits that can last up to a year after surgery. The most effective preemptive analgesic regimens are those that may limit nervous system sensitization during the perioperative period.

METHODOLOGY

This randomized controlled trial study was carried out in the Department of Anaesthesiology & ICU Bangladesh Medical College Hospital Dhaka, Bangladesh during 18th January 2020 to 17th July 2020. The study included a total of 50 patients. Random sampling was used to divide the sample into two groups: group A (oral diclofenac sodium) and group B (oral paracetamol). All patients underwent a full pre-anaesthetic evaluation, which included a history, clinical examination, and all pertinent investigations. All patients were informed preoperatively to use the pain visual analogue scale (VAS) to measure their pain. Pantoprazole (20 mg) tablets were administered the night before surgery and on the morning of surgery. The first group (group A) of patients received Tab. Diclofenac-sodium (50 mg) two hours before surgery, while the second group (group B) received Oral paracetamol (500mg) two hours before to surgery. After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation. Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24). Patients undergoing abdominal operation under general anaesthesia with American Society of Anaesthesiogist's (ASA) physical status I, II along with normal renal, hepatic function, no allergic history or chronic disease were included in the study. Patient with ASA II, IV, hypersensitivity to test drug, patients with chronic pain, patients with cardiovascular, psychiatric diseases, patients using psychotropic drugs, pregnant patients, geriatric patients, patients with alcohol abuse, patients with abnormal liver function were excluded from the study. Tablet. Diclofenac sodium 50 mg was given to Group A patients and Tablet Paracetamol 500mg given to Group B patients 2 hours before surgery. First dose of inj. Tramadol 50mg was given intravenously when patient complained of pain in both group A and group B.

RESULTS

Table-1: Age distribution of the study population

Age (years)	Group-A n(%)	Group-B n(%)	P value
20-39	6(24.0)	5(20.0)	0.685^{ns}
40-59	15(62.0)	16(64.0)	
≥60	4(14.0)	4(16.0)	

Mean ±SD	48.3±11.2	

ns= not significant, P value reached from chi square test

Table-1 shows age distribution of the study population, it was observed that the majority of the patients i.e. 62.0% were between 40-59 years, 24.0% of patients were age 20-39 years. Mean age was found to 48.3±11.2 years. The difference was not statistically significant (p>0.05) between two groups.

Table-2: Distribution of study subjects according to BMI (n=50)

Body mass index (kg/m^2)	Group A n(%)		Group B n(%)		P value
	n	%	n	%	
23.1-25.0	10	38.0	11	44.0	0.101^{ns}
25.1-30.0	10	38.0	10	40.0	
>30.0	5	24.0	4	16.0	
Total	50	100.0	50	100.0	

In this series we found that body mass index (kg/m^2) was almost similar in both groups, the difference was not statistically significant (p>0.05) between two groups. Maximum patients (44.0%) had observed normal weight.

Table- 3: Distribution of the study patients according to types of ASA status (n=50)

ASA status	Group A n(%)		Group B n(%)		P value
	n	%	n	%	
I	14	58.0	14	56.0	0.790^{ns}
II	11	42.0	11	44.0	

Table shows ASA status of the study patients, it was observed that almost two third (58.0% & 56.0%) patients had ASA grade I in group A and group B respectively. The difference was not statistically significant (p>0.05) between two groups.

Table- 4: Evaluation of heart rate amongst the study subjects (n=50)

Heart rate (beat/min)	Group A n(%)	Group B n(%)	P value
	Mean±SD	Mean±SD	
Baseline	86.7±9.4	85.9±7.1	0.258^{ns}
Range (min-max)	80-110	81-105	
2 hr after	87.7±11.2	92.0±11.9	0.074^{ns}
Range (min-max)	75-110	85-110	
6 hr after	90.7±8.2	98.5±7.7	0.001^{s}
Range (min-max)	80-105	90-110	
12 hr after	94.2±7.8	96.9±7.4	0.206^{ns}
Range (min-max)	80-110	86-110	

At baseline no significant difference of heart rate alteration was detected in between groups; mean heart rate was found 86.7±9.4 beat/min in group A and 85.9±7.1 beat/min in group B. Postoperative heart rate and other haemodynamic status were evaluated at 2h, 6h, 12h after surgery. Present study shows that, at 2 hr after mean heart rate was 87.7±11.2 beat/min and 92.0±11.9 beat/min in group A and group B respectively. At 6 hr after, mean heart rate was 90.7±8.2 beat/min in group A and 98.5±7.7 beat/min in group B. At 12 hr after surgery, mean heart rate was 94.2±7.8 beat/min and 96.9±7.4 beat/min in group A and group B respectively. At after 6 hr difference was statistically significant (p<0.05) between two groups.

Table- 5: Evaluation of systolic blood pressure (SBP) amongst the study subjects (n=50)

Systolic BP (mmHg)	Group A n(%)	Group B n(%)	P value
	Mean±SD	Mean±SD	
Baseline	108.3±5.8	109.6±6.3	1.246^{ns}

Systolic BP (mmHg)	Group A n(%)	Group B n(%)	P value
	Mean±SD	Mean±SD	
Range (min-max)	100-125	100-125	
2 hr after	102.3±4.8	113.6±11.2	0.001[s]
Range (min-max)	100-125	100-125	
6 hr after	107.4±6.2	109.5±6.8	0.083[ns]
Range (min-max)	100-125	100-125	
12 hr after	108.2±5.1	109.6±5.6	0.467[ns]
Range (min-max)	100-125	100-125	

Table shows systolic blood pressure during follow up it was observed that at baseline, mean systolic BP was found 108.3±5.8 mmHg in group A and 109.6±6.3 mmHg in group B. 2 hr after surgery blood pressure was more stabilize in group-A than group-B; mean systolic blood pressure was 102.3±4.8 mmHg and 113.6±11.2 mmHg in group A and group B respectively. At 6 hr after, mean systolic blood pressure was 107.4±6.2 mmHg in group A and 109.5±6.8 mmHg in group B. At 12 hr after, mean systolic blood pressure was 108.2±5.1 mmHg and 109.6±5.6 mmHg in group A and group B respectively. At 6 hr and 12 hr after surgery difference was statistically non-significant (p>0.05) between two groups.

Table- 6: Evaluation of diastolic blood pressure (DBP) amongst the study subjects (n=50)

Diastolic BP (mmHg)	Group A n(%)	Group B n(%)	P value
	Mean±SD	Mean±SD	
Baseline	60.7±7.4	58.6±6.5	0.856[ns]
Range (min-max)	60-80	60-80	
2 hr after	64.5±8.2	65.4±5.6	1.023[ns]
Range (min-max)	55-80	50-75	
6 hr after	62.1±6.5	64.3±5.9	0.895[ns]
Range (min-max)	50-75	50-75	
12 hr after	61.5±7.3	63.5±7.1	0.901[ns]
Range (min-max)	60-80	60-80	

Regarding diastolic blood pressure during follow up, after 2 hr, mean diastolic blood pressure was found 64.5±8.2 mmHg in group A and 65.4±5.6 mmHg in group B. After 6 hr, mean diastolic blood pressure was 62.1±6.5 mmHg in group A and 64.3±5.9 mmHg in group B. After 12 hr, mean diastolic blood pressure was 61.5±7.3 mmHg in group A and 63.5±7.1 mmHg in group B.

Table- 7: Assessment of pain sensation using Visual Analogue Score (VAS) (n=50)

Diastolic BP (mmHg)	Group A n (%)		Group B n (%)		P value
	n	%	n	%	
2 hr After surgery					
0-2	5	16.6	2	3.3	
3-6	13	53.3	12	46.7	
7-10	7	30.0	11	50.0	
Mean±SD	5.2±0.47		7.4±0.68		0.001[s]
6 hr After surgery					
0-2	13	54.0	7	26.0	
3-6	10	40.0	13	50.0	
7-10	2	6.0	5	24.0	
Mean±SD	31±0.32		5.2±0.51		0.001[s]
12 hr After surgery					
0-2	17	68.0	15	58.0	
3-6	8	32.0	10	42.0	
7-10	0	0	0	0	
Mean±SD	2.1±0.23		2.8±0.27		0.091[s]

The day before surgery patients were instructed about the Visual Analog Scale (VAS) in which 0=no pain and 10=worst pain imaginable. Patients in the group-B had higher VAS, during the second hours (P = 0.0001), compared with the group-A. Mean verbal pain score was 5.2±0.47 and 7.4±0.68 in group A & group B respectively. Six hours after the surgery, both groups showed downward trends of the pain VAS, but significantly in group A. Mean score was 3.1±0.32 and 5.2±0.51 in group A & group B respectively.

Table- 8: Distribution of the study patients according to Analgesic requirement (n=50)

Post-operative analgesic requirement	Group A n(%) Mean±SD	Group B n(%) Mean±SD	P value
Time of 1st demand of analgesic (min)	229.7±24.2	103.8±39.2	0.0001[s]
Total analgesic requirement in 24 hrs (mg)	68.6±8.3	112.5±12.8	0.0001[s]

Table shows the Distribution of the study patients according to post-operative analgesic requirement. Post operatively1st demand of analgesia was earlier in Group-B. The difference was statistically significant (p=< 0.0001). Total analgesic requirement was higher in Group-B, which was statistically significant (p=< 0.0001).

Table- 9: Evaluation of any adverse events (n=50)

Complication	Number of Patient		P value
	Group A n (%)	Group B n (%)	
Hypersensitivity or rash	0	0	0.402
Hypotension	2	0	
Nausea, vomiting	7	4	
Cardiovascular collapse	0	0	
Myoclonus	0	0	

Nausea and vomiting were lower for the group-B, compared with the groups-A; however, this difference was not statistically significant (P = 0.402). In both groups, nausea and vomiting scores decreased after the 6th hour, reaching even zero after 12 hours.

DISCUSSION

This prospective randomized trial was carried out over a six-month period at the Department of Anaesthesiology and ICU at Bangladesh Medical College Hospital in Dhaka. A total of 50 patients who met the inclusion/exclusion criteria were evaluated to determine the efficacy of preemptive diclofenac on postoperative pain control following abdominal surgery. The majority of patients (63.0%) were between the ages of 40 and 59, with a mean age of 48.3±11.2 years. There was no statistically significant difference between the two groups (p>0.05).

Patients in this study were taught the Visual Analog Scale (VAS) on the day before surgery, with 0 representing no discomfort and 10 being the worst pain possible. Patients in group B exhibited a higher VAS during the second hour (P = 0.0001) compared to group A. The mean verbal pain score was 5.2±0.47 and 7.4±0.68 in groups A and B, respectively. The difference was statistically significant. Six hours after surgery, both groups had lower pain VAS scores, although group A had a considerable decrease. The mean scores for groups A and B were 3.1±0.32 and 5.2±0.51, respectively. At the 12th hour, practically all patients were pain-free. Overall, the findings revealed that preemptive usage of oral Diclofenac sodium greatly reduced post-operative discomfort. The first postoperative urge for analgesia occurred in Group B. The difference was statistically significant (p<0.0001). Group-B had a significantly higher total analgesic demand (p-value < 0.0001).

A similar study was conducted among four groups. Paracetamol (group one), diclofenac (group two), a combination of paracetamol and diclofenac (group three), and a placebo (group fore) were administered one hour before surgery. Morphine was used as a rescue analgesic in the first 24 hours after surgery. The intensity of pain, time and dose of first rescue analgesia, and total analgesic requirement were all documented. The combination group had the lowest dose of the initial rescue analgesic, mean VAS, mean morphine, and total morphine needs. The time to first rescue analgesic was longer in the diclofenac and combination groups compared to paracetamol and placebo. Global satisfaction scores for postoperative pain at 12 and 24 hours were considerably higher in the combination and diclofenac groups compared to paracetamol and placebo. As a result, diclofenac is more effective than paracetamol as a pre-emptive analgesic.

Diclofenac inhibits thromboxane-prostanoid receptors, arachidonic acid production and uptake,

lipoxygenase enzymes, and activates the nitric oxide-cyclic guanosine monophosphate anti-nociceptive pathway, in addition to COX inhibition. Paracetamol works by inhibiting slow-moving COX-2-dependent processes. Paracetamol has a central analgesic effect that is caused by activation of descending serotonergic pathways, but its primary activity may be to limit PG production.

Tuzuner *et al.,* investigated the effects of 1 g intravenous paracetamol, 75 mg intramascular diclofenac, and 8 mg intravenous lornoxicam in 60 patients undergoing third molar surgery and discovered that pain scores were comparable in all groups [8]. In our study of individuals following abdominal surgery, we discovered that diclofenac sodium appears to be a superior post-operative analgesic compared to paracetamol in terms of rescue analgesic requirements.

Diclofenac sodium may be a preferable analgesic alternative if there are no relative or absolute contraindications to its use, while paracetamol may be recommended in cases where the relative safety profile is important. Combination is not recommended because it may increase side effects, costs, and provide no additional benefit. Further research with a bigger sample size is recommended to develop clear conclusions and influence post-operative pain management strategies [9].

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

CONCLUSION

Preemptive oral Diclofenac sodium had a substantial effect in reducing postoperative pain and analgesic requirements in patients scheduled for abdominal surgery. Surgical pain is caused by tissue traction during surgery, as well as surgical wounds and drainage. The severity of discomfort is highest on the first postoperative day and requires effective pain management. Different analgesic medicines have been employed for this purpose, and the combination of opioid and non-opioid analgesic drugs has resulted in good postoperative pain control. Excessive opioid use may result in adverse effects such as respiratory depression, however prophylactic use of Diclofenac sodium has been proven to reduce the total dose of Tramadol required in surgical patients, lowering the likelihood of side effects. The study's null hypothesis was that there would be no difference in the preemptive analgesic efficacy of Diclofenac sodium and paracetamol in lowering opioid requirements in individuals undergoing abdominal surgery. The results contradicted our null hypothesis, demonstrating that a single dose of 50 mg of Diclofenac sodium administered before surgery considerably reduced postoperative opioid demand during the first 24 hours. However, haemodynamic parameters (HR, SBP, and DBP) were practically same in both groups.

RECOMMENDATION

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for future use and emphasize points to ensure better management and adherence.

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