 DOI: 10.18231/2394-4994.2017.0047

A study of injectable aceclofenac for acute postoperative pain in laparoscopic abdominal surgeries

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Abstract

Background and Objectives: Postoperative pain management is always a challenging task even though many modalities have been studied. The present study would like to compare the effects of two Nonsteroidal anti-inflammatory agents by Intramuscular route. The present study is undertaken to evaluate and compare the efficacy and duration of action of intramuscular injectable aceclofenac 150mg/3ml with intramuscular injectable diclofenac 75mg/3ml.

Material and Methods: The present study was undertaken compare the relative efficacy of aceclofenac and diclofenac by intramuscular route for postoperative analgesia in patients undergoing laparoscopic abdominal surgeries. A randomized study was conducted on 50 patients, planned for laparoscopic abdominal surgeries under general anaesthesia. In two groups containing 25 patients each the group A received injection (Inj) aceclofenac intramuscularly and group B received injection diclofenac intramuscularly. Perioperative haemodynamics were assessed and monitored. Postoperatively visual analogue score, pulse rate and mean arterial pressure were recorded at 2, 4, 6, 8, 12 and 24 hours duration intervals.

Results: Both aceclofenac and diclofenac are efficient for providing postoperative analgesia in patients undergoing elective laparoscopic abdominal surgeries. Both the groups exhibited haemodynamic stability. Incidence of rise in pulse rate and MAP in the postoperative period was higher with inj. diclofenac than inj. aceclofenac. Inj. aceclofenac in our study scores over inj. diclofenac in providing better quality of analgesia.

Keywords: Aceclofenac, Diclofenac, Laparoscopy

Date of Acceptance: 20th December, 2016 **Date of Manuscript Receive:** 23rd June, 2016

Introduction

Optimal pain relief is a prerequisite for early postoperative recovery in patients undergoing laparoscopic abdominal surgeries as these patients suffer from considerable pain most intense during the first 24 hours. The incidence of postoperative pain varies with the individual patients, but is largely governed by the site and nature of the operation. Pain after surgery is largely result of direct injury caused to the tissues, but may be further aggravated by associated reflex muscle spasm or visceral distension. Postoperative pain is often associated with increased incidence of other unpleasant symptoms like nausea, vomiting, sweating and can be a cause of postoperative haemodynamic alterations.[(1)] To date various modalities of treatment are available ranging from opiods, multimodal therapy and non-steroidal anti inflammatory drugs (NSAIDS).

The most established and accepted mode of pain relief in many surgeries are the parenteral narcotics but they carry certain disadvantages like depression of respiration, cough reflexes, consciousness and can cause nausea and vomiting.[(2,3)] In view of these disadvantages, it may not be possible to achieve active participation and cooperation of the patient in carrying out chest physiotherapy which may lead to pulmonary complications. Non-narcotic analgesics and neuronal blockade techniques provide equipotent analgesia with fewer side effects, now the concept is balanced multimodal analgesia.[(4,5)] NSAIDS make an important component in pharmacological management of postoperative pain.[(6)] NSAIDS are popular choice as they are easy to administer and to monitor the effects.

Among NSAIDS, Aceclofenac is a good and safe drug with negligible renal, hepatic and GIT side effects. Earlier parenteral preparation was available as 1 ml ampoules containing 150mg of aceclofenac. The drug was intended only for deep intragluteal, intramuscular injection. In view of the severe pain caused due to the intramuscular injection, the drug never became popular.

The newer parenteral form of aceclofenac is an improvised intramuscular version containing 150 mg of aceclofenac in 3 ml, made of stable lyophilized aqueous solution by adding additive urea and sodium citrate thereby minimizing the pain on intramuscular injection. It is sustained release injection with improved efficacy, prolonged duration of action and good tolerability profile.

Materials and Methods

The present study was undertaken to compare the relative efficacy of aceclofenac and diclofenac by intramuscular route for postoperative analgesia in patients undergoing laparoscopic abdominal surgeries.

After approval from Institutional Ethical committee and written informed consent from the patients, a randomized study was conducted on 50 patients, planned for laparoscopic abdominal surgeries under

general anaesthesia, divided into two equal groups containing 25 patients each.
Group A: Aceclofenac, Group B: Diclofenac.

Inclusion Criteria:

- ASA grade I and II
- Age group: 25 to 55 years of either sex
- Patients undergoing elective laparoscopic abdominal surgeries
- Cholecystectomy
- Appendectomy
- Hysterectomy

Exclusion Criteria:

- Patients with history of hypersensitivity to NSAIDS
- Peptic ulcer disease GI bleeding or other bleeding disorders.
- Patients with abnormal liver or renal function tests
- Patients on concomitant medication—Aspirin, corticosteroids anticoagulants or antihistaminics.
- Patients with Motion sickness and migraine

The patients were allocated into two groups. The patient were advised to take night before surgery group A[study] tablet aceclofenac 100 mg orally and group B[control] tablet diclofenac 50 mg orally. Uniform standard technique of general anaesthesia with endotracheal intubation and controlled ventilation was planned for all patients. On arrival into operation theatre patient was connected to standard Anesthesia Monitoring. After intubation group A was given inj. aceclofenac 150mg/3m1 intramuscularly and group B was given inj. diclofenac 75mg/3m1 intramuscularly on deltoid region.

After satisfying the extubation criterion, trachea was extubated and patients were transferred to post anaesthesia care unit, (PACU). In the postoperative period, oxygen with mask was given to all patients, vital parameters — PR, BP, degree of analgesia by visual analogue score at intervals of 2, 4, 6, 8, 12, and 24 hours was recorded. In the postoperative period patients were observed for any side effects like nausea and vomiting.

Assuming the duration of action of Aceclofenac and diclofenac 6-8 hrs, No rescue analgesia was given to either groups for 8 hours. After, 8 hours rescue analgesia of injection diclofenac 75 mg/3m1 was given on demand by the patient or when the visual analog score was more than 5. At the end of study, all data was compiled and analysed statistically. The data obtained was analyzed using SPSS software version 17.0. Appropriate statistical tests were used to determine the efficacy of drugs.

Visual Analogue Scale: VAS is a simple and reliable measure of subjective pain (for adults and children above 8yrs). It consists of a 10cm horizontal or vertical line with two end points[7, 8]. In our study we preferred this scale in view of ease to get information from patient.
0 = No pain
10=Worst imaginable pain
It provides numerical index of severity of pain

Sample size calculation: Studies have shown that the analgesic duration with group A (Aceclofenac) was 12 hrs and with group B (Diclofenac) was 8 hrs Mean VAS score was 4 and 6 respectively in both groups. In the present study expecting similar results and to get 80% power, 95% confidence interval and considering minimal difference between two groups as 60 min, the study requires minimum of 25 patients in each group.

Observation and Results

The data obtained was analyzed using SPSS software version 17.0. Descriptive results are expressed as mean and SD of various parameters in different groups. Probability value (p value) was used to determine the level of significance, p-value < 0.05 was considered as significant, p-value < 0.01 was considered as highly significant.

Table 1: Age and pre op PR and pre op MAP of both groups

Parameter	Group A		Group B		t value	p value
	Mean	SD	Mean	SD		
Age (yrs)	38.12	7.84	38.8	8.9	0.286	0.77
Pre OP PR (/min)	79.7	5.96	80.8	5.03	0.71	0.47
Pre OP MAP (mm of Hg)	89.2	6.36	89.8	5.64	0.4	0.68

From Table 1, there was no statistical significant difference in mean ages in either group (p > 0.05). There was no statistically significant difference, in the pre-operative PR and MAP between the groups.

There was no statistically significant difference in the type of surgeries performed in both Groups (Table 2c). Group A included 10 patients of cholecystectomy 9 patients of appendectomy and 6 patients of hysterectomy Group — B included 10 patients of Cholecystectomy 10 patients of appendecetomy 5 patients of hysterectomy.

Table 2: Type of surgery performed

Type of surgery	Group A		Group B	
	No. of patients	%	No. of patients	%
Cholecystectomy	10	40	10	40
Appendectomy	9	36	10	40
Hysterectomy	6	24	5	20

Pulse rate was compared at different time interval, postoperatively. It was observed that, there was no statistical significance in the mean pulse rate. There was no statistical significance in the mean pulse rates at 24 hours between group A and group B ($p > 0.05$).

Table 3: Pulse rate (per min) comparison in two groups at different time interval post operatively

Time interval	Group A		Group B		T value	P value
	Mean	SD	Mean	SD		
2 hours	78.44	6.04	80.72	5.51	1.39	0.17
4 hours	77.84	5.91	81.3	5.88	2.08	0.04
6 hours	78.24	5.75	86.04	4.24	5.45	<0.001
8 hours	78.3	5.43	88.56	3.76	7.7	<0.001
12 hours	79.5	5.09	80.8	5.40	0.39	0.45
24 hours	83.4	6.11	82.7	5.35	0.41	0.67

Table 4: MAP (in mm Hg) comparison in two groups at different time interval postoperative Period

Time interval	Group A		Group B		T value	P value
	mean	SD	Mean	SD		
2 hours	79.8	8.17	94.1	3.34	8.03	<0.001
4 hours	81.52	8.17	93.7	3.4	6.85	<0.001
6 hours	80.8	8.67	101.3	4.8	10.31	<0.001
8 hours	82.16	7.97	101.36	4.68	10.4	<0.001
12 hours	84.8	8.32	93.84	3.6	4.98	<0.001
24 hours	88.24	8.85	93.8	3.78	2.92	0.005

Mean arterial pressure was compared at different time interval postoperatively. It was observed that, mean arterial pressure a was significantly higher in group B, compared to group A ($p<0.001$).

Table 5: VAS (pain score) comparison in two groups at different time interval postoperatively

Time (hrs)	Group A Mean	SD	Group B Mean	SD	t – value	P – value
2	0.8	0.4	1	0	2.44	0.018
4	0.96	0.2	2.32	0.74	8.77	<0.001
6	1.16	0.37	3.48	1.04	10.44	<0.001
8	1.48	0.5	5.36	0.63	23.7	<0.001
12	1.96	0.78	3.68	0.62	8.52	<0.001
24	3.48	1	4.24	0.96	2.72	0.009

Pain scoring at different time interval postoperatively was measured using VAS score. It was observed that the mean VAS score at 2, 4, 6, 8, 12, and 24 hrs in group A was , significantly lower than group B ($p<0.001$).

Discussion

To date various modalities of treatment are available to address the issue of postoperative pain ranging from opiods, multimodal therapy[9] and NSAIDS. Still NSAIDS are popular choice as analgesia for postoperative pain as they are easy to administer and their effects can easily be monitored and as they do not suppress cough reflex and breathing. The present study was undertaken to compare the relative efficacy and safety of injection aceclofenac 150 mg/3 ml with injection diclofenac 75mg/3ml by intramuscular route in postoperative pain relief in patient's undergoing laparoscopic abdominal surgeries.

There have been many studies conducted on these two drugs diclofenac and aceclofenac. Diclofenac is being used for intraoperative and postoperative analgesia for or

many years. Now it is found to be an effective analgesic and having opiod sparing affect.[10] This fact is supported by various studies such as a study conducted by Anirbanpal et al[11] which concluded diclofenac to be more effective for post-operative analgesia in patients undergoing lower abdominal gynecological surgeries. Another study by Ozcan S, et al A[12] concluded that diclofenac sodium was found to be safe and effective analgesic with minimal or negligible side-effects. In a study of efficacy and safety of aceclofenac in the treatment of osteoarthritis: a randomized double-blind comparative clinical trial versus diclofenac - an Indian experience by Pareek A, et al S[13] concluded that aceclofenac is an effective and well tolerated drug in osteoarthritis, statistically superior to diclofenac in terms of compliance.

Another study by V Sharma, et al[14] comparison of efficacy of diclofenac versus aceclofenac in postoperative analgesia in lower limb fractures: a double blind, randomized study, it was concluded that aceclofenac in injectable form is superior to diclofenac in providing postoperative pain relief of severe intensity in patients with lower limb fractures Furthermore it possesses a more favourable tolerability profile.

Newer NSAIDs like aceclofenac (tablet and injectible form) has been preferred therapy for pain relief in various studies as in the study by Lemmel Em, et al S.[10] Tablet aceclofenac was considered by the patients to be highly efficacious treatment with excellent and fast analgesic activity, well tolerated and low incidence of side effects in the management of inflammatory pain. Aceclofenac was earlier launched in the injectable form for intramuscular use as 1 ml ampoules containing 150 mg of aceclofenac. The drug was intended only for deep intragluteal, intramuscular injection. In view of the severe pain caused due to the intramuscular injection, the drug never became popular and had a poor acceptance from both the doctor and patient.

The present parenteral form of aceclofenac is an improvised intramuscular version mitaining 150 mg of aceclofenac in 3 ml, each ml contains 50 mg. The ampoule contains urea and sodium citrate as an additive to make it a stable lyophilized aqueous solution thereby minimizing the pain on intramuscular injection, and also can be given into the deltoid which is an advantage. It is sustained release injection with improved efficacy, 18-24 hours duration of action and good tolerability profile. This is supported by the study of formulation and evaluation of aceclofenac injection made by mixed hydrotropic solubilization technique by Rajesh kumar.[15]

Present study showed the results as mean pain scores by VAS showed significantly less pain scores in Group A - aceclofenac when compared to Group B diclofenac at 2,4,6,8,12 and 24 hours. After 8 hours all the Group B patients were given injection diclofenac in 75mg/3ml as rescue analgesia on patient demand or scores more than 5 as can be explained by the pharmacokinetic properties of both the drugs. The onset of action of injection aceclofenac is10 minutes and injection diclofenac is 20 minutes. The peak action of diclofenac being 2 hours, the peak action of aceclofenac is 1 hour. Because of controlled release of injection aceclofenac its duration of action is prolonged.

There was no statistical difference in pulse rate at 2 hours. Both the drugs have reached the peak action by then. Mean pulse rate was significantly lower at the 4th 6th & 8th hours in Group A suggesting the superior analgesia provided by injection acelciofenac. There was no statistical significance in the mean pulse rate at 12 and 24 hours between Group A and Group B this can be explained as rescue analgesia was given to Group B after 8 hours. Mean arterial pressures were significantly higher in Group B compared to Group I suggesting the excellent analgesia provided by the injection aceclofenac upto 24 hours.

Inj. aceclofenac is better tolerated in the present study. There were almost negligible complications in patients treated by aceclofenac like pain at injection site. The results of this study shows that patients treated with injection aceclofenac 150mg/3ml tended to have a greater overall percentage reduction in pain intensity and achieved a larger peak pain intensity difference score and prolonged action than by injection diclofenac 75mg/3ml.

Conclusions

From the study we conclude that there is definite place for long acting NSAIDs like injection aceclofenac 150 mg/3m1 in the postoperative analgesia for patients undergoing laparoscopic abdominal surgeries in view of its good quality of analgesia, sustained and prolonged duration of action upto 18-24 hours and negligible side effects on kidney & GIT.

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