

# Comparison of Efficacy of Diclofenac versus Aceclofenac in Post Operative Pain in Lower limb fractures: a Double blind, Randomized Study

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## Abstract

**INTRODUCTION:** Providing effective postoperative analgesia is a significant challenge in patients undergoing orthopedic surgery. Non steroidal anti-inflammatory group of drugs is used mostly to achieve it. This clinical study was done to investigate efficacy of Injectable Aceclofenac over inj. Diclofenac in patients with severe postoperative pain in lower limb fractures. **METHODS:** 100 patients (aged 18-60 yr) of lower limb fractures were enrolled as per inclusion criteria. They were randomly assigned to Group A or Group B (50 patients each). Severe pain was postoperative pain 7 or >7 on Numerical Rating Scale. For postoperative analgesia, in Group A Inj. Aceclofenac (12 hourly) and in Group B Inj. Diclofenac (8 hourly) was given. To abort pain in case of no relief Inj. Tramadol was given. Decrease in Numerical Rating Scale score in either the group and associated adverse effects were noted. Patients' overall subjective response to therapy was rated as poor, fair, good or excellent. **RESULTS:** After treatment at 10 min. only the mean pain score had 47.8% fall in Group A and 40.3% in Group B. At the end of 20 min. percentage fall was more in Group A (88.1%) than Group B patients (68.9%). Group A patients received less rescue analgesia than Group B ( $p < 0.05$ ). At the end of 24 hr period 60% patients in Group A and 40% patients in Group B reported outcome as good or excellent. **CONCLUSION:** The study demonstrated superiority of Inj. Aceclofenac to Inj. Diclofenac in providing postoperative pain relief. Aceclofenac demonstrated a favourable tolerability profile than Diclofenac along with lesser frequency of administration due to longer half life.

## INTRODUCTION

Postoperative pain remains a routine problem in orthopedic surgery. Parenteral Nonsteroidal Ant inflammatory Drugs (NSAIDS) are an attractive option in providing postoperative analgesia. They are effective in a wide range of postoperative pain states as adverse effects with them are considerably less<sup>1</sup>. Aceclofenac a phenylacetic acid derivative (2-(2,6-dichlorophenyl) amino Phenylacetooxyacetic acid) is related to Diclofenac. In injectable form it is clinically useful in reduction of postoperative pain<sup>2</sup>. It acts by inhibition of cyclo-oxygenase, thus reducing bio synthesis of pain mediating and inflammatory prostaglandins and also by direct inhibition of spinal nociceptor processing<sup>3,4</sup>.

The present study aims at the evaluation of the analgesic activity, efficacy and safety of Aceclofenac injection 150mg/ml versus Diclofenac injection 75 mg/3 ml in management of postoperative pain of severe intensity in patients with Lower Limb Fractures.

## MATERIALS AND METHODS

This was a prospective double blind randomized study conducted at Dr. Rajendra Prasad Medical College and Hospital Kangra (Tanda) in the year 2006-2008. Written informed consent was obtained from all participating patients. A total number of 100 patients, male and female aged 18-60 years with Lower Limb Fractures distal to knee joint, scheduled to undergo surgery were selected. Exclusion criteria for the present study were hypersensitivity to NSAID, severe hepatorenal or cardiac dysfunction, gastrointestinal bleed/clotting disorders, pregnant or lactating mothers and patients unwilling to comply with protocol requirements.

At a presurgical visit, patients were evaluated for inclusion. Baseline assessment was performed including a medical history, diagnosis and nature of lower limb surgery to be performed. A careful examination including pulse rate and blood pressure recording was done prior to surgery and

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postoperatively immediately and at 10 min,20 min,30 min,1hr,4 hr,8hr and 12 hrs. Biochemical, hematological, urine examination and ECG were done in all the patients pre and postoperatively. Treatment with any analgesic was forbidden 8 hrs following injections of study medication. Alcohol, Anticoagulant therapy or any other cross reacting drugs were forbidden. Study medication was to be given to the patients on first postoperative day intramuscularly. The therapy was administered to the patient postoperatively with severe pain ( 7 or > 7 ) on an 11 point Numerical Rating Scale (NRS) of 0-10 (0=none, 10=unbearable). Patients and doctors were blinded for the type of injection being given . Inj. Tramadol i/m was used as rescue analgesia for patients who did not achieve adequate analgesia with study medication. The first dose of study medication that was given to patient on demand (NRS 7 or >7) was taken as 0 minute. Using the NRS scale the patients recorded onset and duration of effect of analgesia of study medication . Postoperatively pain intensity was noted on NRS at 0 min, 10 min,20 min,30 min,1hr,4 hr,8hr and 12 hrs.

Both the groups were compared for percentage fall in NRS , adverse effects (0.5-4 hours) and any withdrawal from the study. These comparisons were analysed by chi-square test and p value .Overall patient response to therapy was graded as poor (0), fair (1), good (2), excellent (3) .

### RESULTS

Both the groups were comparable for age , sex and weight. The population was predominantly male (61%) with male to female ratio of 65/35. Mean age and weight were 37+-13.47 yrs (range 18-65 yrs) by student t test and 58.88+-6.79(range 44-75 kg) respectively. At enrolment there were 50 patients each in group A and group B. Mean time interval from completion of surgery to starting study medication was 4 hours. No significant changes were noted in routine lab investigations and blood pressure measurements before and after study medication.

**Figure 1**

Table 1 MEAN NRS SCORE BEFORE AND AFTER THE TREATMENT

	Group A		Group B	
	Before Treatment	After Treatment	Before Treatment	After Treatment
0	7.10+-1.15	3.30+-0.70	6.80+-1.24	3.60+-0.70
10	*3.70+-1.10	*1.70+-0.52	*4.10+-1.40	*2.00+-0.70
20	*0.83+-0.95	*0.23+-0.44	*2.13+-1.32	*0.84+-0.70
30	*0.11+-0.35	*0.11+-0.35	*0.05+-0.20	0
60	*0.01+-0.12	0	0	0
240	0	0	0	0
480	*0.54+-0.80	*0.70+-0.90	*0.70+-0.90	*0.63+-0.70
720	*3.25+-0.82	*2.53+-1.03	*3.62+-0.72	*2.10+-1.02

\* P<0.05 Significant

Onset of analgesia occurred in 10 minutes (median) in both groups but tended to be quicker with Group A. The median duration of analgesia was 8.7 hrs with Group A and 4.5 hrs with Group B .Mean NRS score were 7.10 and 6.80 respectively in both the groups at basal ( P>0.05) . At 10 minutes the mean pain score had significant fall in both the groups (47.8% in Group A , 40.3% in Group B). At 20 min. percentage fall was more with Group A (88.1%) than Group B ( 68.9%). By 4 hours both the groups had achieved maximum analgesia (minimum pain score at this point). Only 3 patients from Group B needed additional analgesia (inj Tramadol i.m.) in the present study (p<0.05) (Table 2).A small number of patients from both groups reported mild adverse reactions in the form of pain at injection site (2%) .

In the overall subjective assessment that was performed at the end of 24 hour period 60% of patients in Group A( on Aceclofenac) and 40% patients in Group B (on Diclofenac) reported outcome as excellent .

**Figure 2**

Table 2 ADVERSE EVENTS

	Group A	Group B
Patients reporting adverse events (%)	2	2
No. of adverse events reported	1	1
Severity of adverse events		
Mild	1	1
Moderate		
Severe		
Relationship to study medication		
Unlikely		
Possible	yes	yes

## DISCUSSION

Optimal (dynamic) pain relief is a prerequisite for early postoperative recovery<sup>5</sup>. To date various modalities of treatment are available to address the issue of postoperative pain ranging from opioids, multimodal therapy and NSAIDS. Opioids act upon opioid receptors in the central nervous system, reduce postoperative pain and improve patient outcome. But because of dependence coupled with various adverse effects<sup>6</sup>, they lead to increased overall cost of therapy and delay in discharge from hospital<sup>7,8,9,10,11</sup>. Recently a preventive multimodal analgesic regimen utilizing regional blocks, nonsteroidal antiinflammatory drugs,  $\mu_2$ -agonists, ketamine,  $\mu_2$ -ligands, opioids administered throughout the perioperative period has also been advised<sup>12</sup>. Still NSAIDS are a popular choice for postoperative pain as they are easy to administer and their effects can be easily monitored. Diclofenac sodium was found to be an effective analgesic having opioid sparing effect<sup>13</sup>. It has also been found to be equally effective as fentanyl and tramadol in postoperative pain management<sup>14</sup>. The main problem with tablet or injectable diclofenac on long term use is gastrointestinal side effects.

Newer NSAIDS like Aceclofenac (tablet and injectable form) has been preferred therapy for pain relief in various studies<sup>15</sup>. Tablet Aceclofenac (100mg bd) was found to be statistically superior to tab. Diclofenac (75mg bd) in terms of its efficacy, safety and compliance in patients of osteoarthritis<sup>16</sup>. The onset of action is improved by injection of Aceclofenac. Pain relief has been shown to reduce the onset of chronic pain syndrome<sup>17</sup>.

In the present study postoperative pain from lower limb fractures has been used as a model as pain after orthopedic surgery is of severe intensity. To date no study has compared postoperative analgesia from Injection Aceclofenac with Injection Diclofenac in these patients. Aceclofenac scored significantly better in patients having severe postoperative

pain as compared to Diclofenac in present study.

Aceclofenac was well tolerated in this study. There were almost negligible complications in patients treated by Aceclofenac like pain at injection site. The majority of complications experienced with Aceclofenac were mild and improved spontaneously. Only inj. Tramadol (rescue medication) presented with some complications like abdominal discomfort and nausea. With Tramadol some other studies also have documented such complications<sup>18,19</sup>.

In this study the overall assessment of therapy performed favoured Inj. Aceclofenac over Inj. Diclofenac while treating patients with severe postoperative pain. After treatment at 10 min. only mean pain score had significant fall in both the groups i.e. 47.8% in Aceclofenac and 40.3% in Diclofenac group. Percentage fall in NRS was more in Aceclofenac than Diclofenac group. At the end of 20 min. percentage fall was 88.1% among Aceclofenac and 68.9% in other group. Patients treated with Aceclofenac tended to have a greater overall percentage reduction in pain intensity and achieved a larger peak pain intensity difference score than patients receiving Diclofenac. In this study the overall assessment of therapy performed favoured Inj. Aceclofenac over Inj. Diclofenac while treating patients with severe postoperative pain. After treatment at 10 min. only mean pain score had significant fall in both the groups i.e. 47.8% in Aceclofenac and 40.3% in Diclofenac group. Percentage fall in NRS was more in Aceclofenac than Diclofenac group. At the end of 20 min. percentage fall was 88.1% among Aceclofenac and 68.9% in other group. Patients treated with Aceclofenac tended to have a greater overall percentage reduction in pain intensity and achieved a larger peak pain intensity difference score than patients receiving Diclofenac.

A smaller number of patients received Inj. Tramadol rescue analgesia in Group A as compared to Group B ( $p < 0.05$ ) which was significant. No study is presently available regarding the efficacy and safety of injectable Aceclofenac in the relief of postoperative pain in patients of orthopedic trauma.

## CONCLUSION

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. It has a long half life, Therefore frequency of administration is less. Hence Aceclofenac represents a better alternative to Diclofenac in patients with severe postoperative pain.

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