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Comparison of Injectable Aceclofenac Vs Injectable Diclofenac in Post-operative Analgesia Following Laparoscopic Abdominal Surgeries

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Abstract

Introduction: To date various modalities of treatment are available ranging from opiods, multimodal therapy and Non-steroidal Anti-inflammatory Drugs (NSAIDs). Still NSAIDs are popular choice as they are easy to administer and their effects can easily be monitored. *Aims:* The aim of the present study is to "Compare intramuscular administration of Injectable Aceclofenac with Injectable Diclofenac in Post-operative Analgesia in patients undergoing Laparoscopic Abdominal Surgeries the efficacy and duration of action. *Materials and Methods:* It is a double blind prospective randomized study was conducted on 50 patients divided into two Groups of 25 each. Group I aceclofenac, Group II Diclofenac. Study done to compare the relative efficacy of injection aceclofenac and injection Diclofenac by intramuscular route for post-operative analgesia in patients undergoing laparoscopic abdominal surgeries. *Results:* The quality of analgesia with injection aceclofenac is better than that of injection Diclofenac post-operatively. Both the Groups exhibited hemodynamic stability. Incidence of rise inpulse rate and MAP in the post-operative period was higher with injection Diclofenac than Injection Aceclofenac. Injection aceclofenac in our study scores over injection Diclofenac in providing better quality of analgesia injection consistent with the pharmacokinetic profile of all the patients in Group II Diclofenac required for an additional dose of analgesic after 8 *hours*. Early ambulation was possible in both the Groups. The analgesia with injection aceclofenac is sustained over longer periods of time upto 24 hours. A single dose is required. *Conclusion:* We conclude that there is definite place for long acting NSAIDs like Injection Aceclofenac 150 *mg*/3 *ml* in the post-operative analgesia for patients undergoing laparoscopic abdominal surgeries in view of its good quality of analgesia, sustained and prolonged duration action upto 24 *hours* and better gastrointestinal tolerance.

Keywords: Aceclofenac; Diclofenac; Laparoscopic Abdominal Surgeries.

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Introduction

Optimal pain relief is a prerequisite for early post-operative recovery especially in patients undergoing Laparoscopic abdominal surgeries as these patients suffer from considerable pain most intense during the first *24 hours*. To date various modalities of treatment are available ranging from opiods, multimodal therapy and Non-steroidal Anti-inflammatory Drugs (NSAIDs). Still NSAIDs are popular choice as they are easy to administer and their effects can easily be monitored.[1]

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Aceclofenac is good and safe NSAID with negligible side effects on the kidney, liver and GIT. It is more popular than Diclofenac when used orally and can also be used for two to four weeks safely without any deleterious side effects. Earlier it was 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.

Relief from pain is by far the most frequent indication for surgical intervention, regardless of the nature of the operation. The incidence of post-operative 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. Its manifestation of autonomic, psychological and behavioral responses results in unpleasant sensory and emotional experience. It is of two characteristic types, a dull steady pain at rest or more severe stabbing pain associated with movement.[2] Post-operative pain is self limiting phenomenon, most intense during the first *24 hours* and diminishes during the next *24 hours*. Pain is minimal after *3–4 days* following surgery. Post-operative pain is often associated with increased incidence of other unpleasant symptoms like nausea, vomiting, sweating and can be cause of post-operative hemodynamic alterations.

Benefits from adequate pain control includes improvement of Post-operative pulmonary function, decreased length of post-operative stay in hospital, accentuation of the stress response to surgery, Improvement in recovery after surgery, maintenance of immune competence and earlier mobilization, which may lead to a decreased incidence of thrombotic sequel. NSAIDs are an important component in pharmacological management of post-operative pain.

NSAIDs are mainly used for chronic inflammatory painful conditions. Acute pain over short-periods of time like mild to moderate post-operative pain is usually controlled by injectable preparations. Diclofenac and Aceclofenac have already proven their worth in osteoarthritis and rheumatoid arthritis. Injectable Diclofenac is being used for intra-operative and post-operative analgesia for many years now as part of balanced multimodal analgesia.

Injectable Aceclofenac is the newer non-steroidal/non-narcotic agent with good analgesic potency extending up to *twenty four hour* duration. Recently *150 mg/3 ml* stable lyophilized aqueous injections have been developed. However, there has been no proper evaluation of this drug for the treatment of post-operative pain. The present study is undertaken to evaluate the efficacy and duration of action of intramuscular injectable Aceclofenac in comparison to intramuscular injectable Diclofenac.

Materials and Methods

The present study to compare the relative efficacy of injection aceclofenac and injection Diclofenac by intramuscular route for post-operative analgesia in patients undergoing laparoscopic abdominal surgeries was undertaken at Osmania General Hospital in the *year 2014*. After approval from Departmental Ethics committee and written informed consent, a double blind prospective randomized study was conducted on 50 patients divided into two Groups of 25 each. Group I Aceclofenac, Group II Diclofenac.

Inclusion Criteria

ASA Grade I and II, Age group: *25* to *55 years* of either sex in Patients undergoing Elective Laparoscopic Abdominal Surgeries (Cholecystectomy, Inguinal Hernia Repair and Appendectomy under general anesthesia.

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 antihistamines, Any significant abnormality in preclinical trial screening and Patients with Motion sickness and migrane.

All the patients were assessed clinically pre-operatively and presence of any medical disorder and history of drug intake was ruled out. All the patients underwent the following investigation. Hemogram, blood chemistry, μ complete urine examination, *X*-ray chest and pre-operative ECG.

The patients were randomly allocated into two Groups. Night before surgery Group I was advised to take Tablet Aceclofenac *100 mg* orally and Group II was advised to take Tablet Diclofenac *50 mg* orally. Uniform standard

technique of general anesthesia with endotracheal intubation and controlled ventilation was planned for all patients.

On the day of surgery after shifting the patient in to the waiting area of the operation theatre intravenous canulation was done with 18 G cannula and connected to a drip of ringer lactate solution. Pre-medication with glycopyrrolate *4 µg/kg*, ondansetron *15 µg/kg*, ranitidine *1 mg/kg* fentanyl *2 µg/kg* were given slowly intravenously *20 minutes* before induction.

On arrival into operation theatre patient was connected to non-invasive blood pressure monitors, pulse oximeter probe and electrocardiographic leads, (limb lead II). Baseline PR, BP, SpO_2 were recorded. After pre-oxygenating the patient with 100% oxygen for *3 minutes*, patients were induced with IV Thiopentone Sodium *5 mg/kg*. Intubation was facilitated by using vecuronium bromide *0.1 mg/kg*. The lungs were ventilated for 180 seconds. Intubation was achieved with an appropriate size oral cuffed, portex endotracheal tube by the aid of Macintosh Laryngoscope blade. After intubation Group I was given injection aceclofenac *150 mg/3 ml* intramuscularly, Group II was given injection Diclofenac *75 mg/3 ml*.

Anesthesia was maintained with IV vecoronium bromide *0.08 mg/kg* top up doses and intermittent positive pressure ventilation with nitrous oxide and oxygen in the ratio of 66%: 33% and 0.5% isoflurane using circle absorber system connected to the Boyle's Anesthetic workstation. Adequate IV fluids were given, vitals monitored and maintained. At the end of the surgery neuromuscular blockade was reversed with IV neostigmine *60 µg/kg* and IV glycopyrrolate *10 µg/kg*. After satisfying the extubation criterion, trachea was extubated and patients were transferred to Post-anesthesia Care Unit, (PACU). In the post-operative period, oxygen with polymask was given to all patients, vital parameters–PR, BP, degree of analgesia by visual analog score at intervals *of 2, 4, 6, 8, 12,* and *24 hours* was recorded.

In the post-operative period patients were observed for any side effects, or complications. No rescue analgesia was given to either Groups for *8 hours*. After, *8 hours* rescue analgesia of injection Diclofenac *75 mg/3 ml* was given to Group II on demand by the patient or when the visual analog score was more than *5 cm*. At the end of study, all data is compiled and analysed statistically.

Three frequently considered aspects of pain are:

1. Subjective (measured by self report);
2. Behavioral (measured by observation and coding of behavior);
3. Biological (measured by sampling of physiological fluids and electrical potentials).

IASP emphasizes that pain is always subjective and self report measures should be regarded as "Gold Standard".

Subjective pain assessment

Visual analogue scale

VAS is a simple and reliable measure of subjective pain (for adults and children above *8 yrs*). It consists of a *10 cm* horizontal or vertical line with two end points. Requires certain level of cognitive function to co-operate with it.

Visual Analogue Scale

0-No pain

1, 2, 3-Mild pain

4, 5, 6-Moderate pain

7, 8, 9-Severe pain

10-Worst ever felt pain

The data obtained was analyzed using SPSS software version 17.0. Appropriate statistical tests were used to determine the efficacy of drug. 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.

Results

Table I: Demographic details in study

Parameter	Group I		Group II		*p* - value
	Mean	SD	Mean	SD	
Age (*yrs*)	38.12	7.84	38.8	8.9	0.77
Pre-OP PR (*min*)	79.7	5.96	80.8	5.03	0.47
Pre-OP MAP (*mm* of *Hg*)	89.2	6.36	89.8	5.64	0.68
Gender					
Male	13	52	13	52	
Female	12	48	12	48	
Type of surgery					
Cholecystectomy	10	40	10	40	
Inguinal hernia repair	9	36	10	40	
Appendectomy	6	24	5	20	

Shown as in (Table 1), the mean age in Group I was 38.2 compared to Group II where the mean age was 38.8 there was no statistical difference in mean ages in either Group ($p > 0.05$). The mean Pre-operative PR in Group I was 79.7 compared to Group II 80.8 ($p > 0.05$). The mean Pre-operative MAP in Group I was 89.2 compared to Group II 89.8 ($p > 0.05$). there was no statistically significant difference in the pre-operative PR and MAP in either Groups. In the present study male to female ratio was same in either Groups, shows in (Table 2).

Table 2: Pulse rate (*per min*) comparison in two Groups at different time interval post-operatively

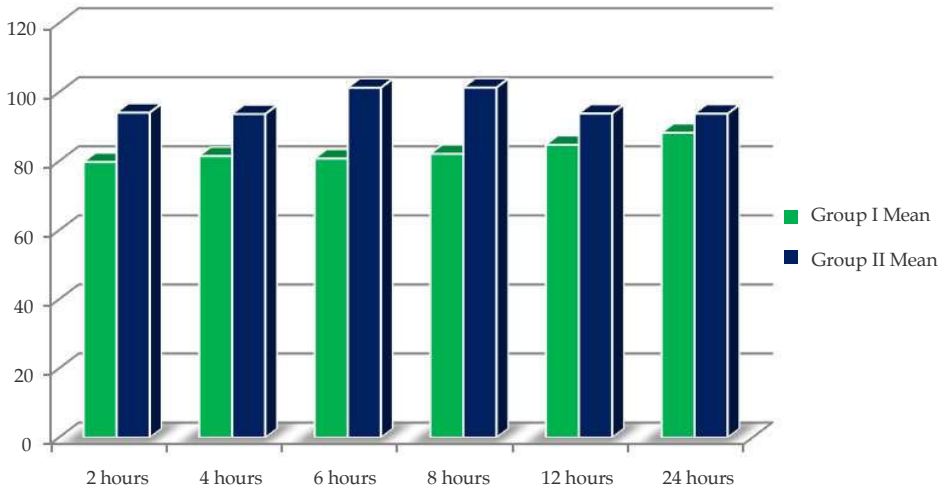
Time	Group I		Group II		t - value	*p* - value
	Mean	SD	Mean	SD		
2 hours	78.44	6.04	80.72	5.51	1.39	0.17
4 hours	77.84	5.91	81.3	5.88	2.08	0.04
6 hours	78.24	5.75	86.04	4.24	5.45	< 0.001
8 hours	78.3	5.43	88.56	3.76	7.7	< 0.001
12hours	79.5	5.09	80.8	5.4	0.86	0.39
24 hours	83.4	6.11	82.7	5.35	0.41	0.67

Pulse rate was compared at different time interval post-operatively it was observed that, Mean pulse rate at *2 hours* in Group I was *78.44/min* compared to Group II *80.72/min* there was no statistical difference in the mean pulse rates at *2 hours* ($p > 0.05$). Mean pulse rate at *4 hours* was significantly lower in Group I *77.84/min* compared to Group II *81.3/min* ($p = 0.04$). Mean pulse rate at *6 hours* was significantly lower in Group I *78.24/min* compared to Group II *86.04/min* ($p < 0.001$). Mean pulse rate at *8 hours* was significantly lower in Group I *78.3/min* compared to Group II *88.56/min* ($p < 0.001$). There was no statistical significance in the mean pulse rates at *12 hours* between Group I *79.5/min* and Group II 80.8, ($p > 0.05$). There was no statistical significance in the mean pulse rates at *24 hours* between Group I *83.4/min* and Group II 82.7, ($p > 0.05$).

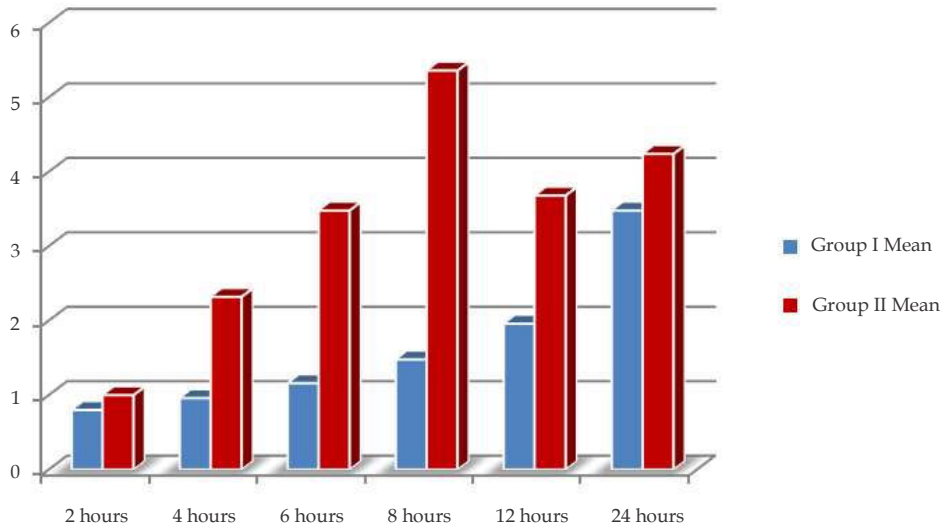
Shown in (Graph 1), mean arterial Pressure was compared at different time interval post-operatively it was observed that, Mean arterial pressure at *2 hours* was significantly higher in Group II *94.1 mm Hg* compared to Group I *79.8 mm Hg* ($p < 0.001$). Mean arterial pressure at *4 hours* was significantly higher in Group II *93.7 mm Hg* compared to Group I *81.5 mm Hg* ($p < 0.001$). Mean arterial pressure at *6 hours* was significantly higher in Group II *101.3 mm Hg* compared to Group I *80.8 mm Hg* ($p < 0.001$). Mean arterial pressure at *8 hours* was significantly higher in Group II *101.3 mm Hg* compared to Group I *82.1 mm Hg* ($p < 0.001$). Mean arterial pressure at *12 hours* was significantly higher in Group II *93.8 mm Hg* compared to Group I *84.8 mm Hg* ($p < 0.001$). Mean arterial pressure at *24 hours* was significantly higher in Group II *93.8 mm Hg* compared to Group I *88.2 mm Hg* ($p = 0.005$).

Table 3: VAS (pain score) comparison in two groups at different time interval post operatively

Time	Group I		Group II		*t* - value	*p* - value
	Mean	SD	Mean	SD		
2 hours	0.8	0.4	1	0	2.44	0.018
4 hours	0.96	0.2	2.32	0.74	8.77	< 0.001
6 hours	1.16	0.37	3.48	1.04	10.44	< 0.001
8 hours	1.48	0.5	5.36	0.63	23.7	< 0.001
12 hours	1.96	0.78	3.68	0.62	8.52	< 0.001
24 hours	3.48	1	4.24	0.96	2.72	0.009



Graph 1: MAP (in *mm Hg*) comparison in two Groups at different time interval post-peratively



Graph 2: VAS score comparison in two groups at different time interval post-operatively

Shown in (Table 3), Pain scoring at different time interval post-operatively was measured using VAS score it was observed that the mean VAS score at *2 hr* in Group I was 0.8, significantly lower than Group II 1.0 (p = 0.018). The mean VAS score at *4 hrs* was significantly lower in Group I, 0.96 compared to Group II, 2.32 p (< 0.001). The mean VAS score at *6 hrs* was significantly lower in Group I, 1.16 compared to Group II, 3.48 p (< 0.001). The mean VAS score at *8 hrs* was significantly lower in Group I, 1.48 compared to Group II, 5.36 p (< 0.001). The mean VAS score at *12 hrs* was significantly lower in Group I, 1.96 compared to Group II, 3.68 p (< 0.001). The mean VAS score at *24 hrs* was significantly lower in Group I, 3.48 compared to Group II, 4.21 p (p = 0.009), displays in (Graph 2).

Discussion

To date various modalities of treatment are available to address the issue of post-operative pain ranging from opiods, multimodal therapy and NSAIDs. Still NSAIDs are popular choice as analgesia for post-operative pain as they are easy to administer and their effects can easily be monitored. The present study was undertaken to compare the relative efficacy and safety of injection Aceclofenac *150 mg/3 ml* with injection Diclofenac *75 mg/3ml* by intramuscular route in post-operative pain relief in patients undergoing laparoscopic abdominal surgeries.

There have been many studies conducted on these two drugs Diclofenac and Aceclofenac. Diclofenac is being used for intra-operative and post-operative analgesia for many years now. It is found to be an effective analgesic and having opioid sparing effect. This fact is supported by various studies such as a study conducted by Anirban Pal *et al*. which concluded Diclofenac to be more effective for post-operative analgesia in patients undergoing lower abdominal gynecological surgeries.[3] Another study by Ozcan S *et al*. concluded that Diclofenac sodium was found to be safe and effective analgesic with lower side-effects.[4]

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*. Acecloefenac 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.[6]

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 containing 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, so also, can be given into the Deltoid which is an advantage. It is sustained release injection with improved efficacy, 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 Maheshwari and Arpna Indurkhya.[6]

Mean pain scores by VAS showed significantly less pain scores in Group I - Aceclofenac when compared to Group II Diclofenac at *2, 4, 6, 8, 12* and *24 hours*. After *8 hours* all the Group II patients were given Injection Diclofenac in *75 mg/3 ml* as rescue analgesia by patient demand or VAS scores more than *5 cm*. This can be explained by the pharmacokinetic properties of both the drugs. The onset of action of injection aceclofenac is *10 minutes* and injection diclofenac is *20 minutes*.

The peak action of Dicloenac being *2 hours*. The peak action of aceclofenac is *1 hour*. Because of sustained release of injection aceclofenac its duration of action is prolonged.

There was no statistical difference in pulse rate at *2 hours*. Both the drugs were have reached the peak action by then. Mean pulse rate was significantly lower at the 4^{th}, 6^{th} *hours* in Group I suggesting the superior analgesia provided by injection Acelclofenac. There was no statistical significance in the mean pulse rate at *12* and *24 hours* between Group I and Group II. This can be explained as rescue analgesia was given to Group II after *8 hours*. Mean arterial pressures were significantly higher in Group II compared to Group I compared to Group I suggesting the excellent analgesia provided by the injection aceclofenac up to *24 hours*. Injection 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 were treated with Aceclofenac *150 mg/3 ml* 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 *75 mg/3 ml*.

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*. concluded that Aceclofenac is an effective and well-tolerated drug in osteoarthritis, statistically superior to Diclofenac in terms of compliance.[7]

Another study by V Sharma *et al*. concluded that Aceclofenac in injectable form is superior to Diclofenac in providing post-operative pain relief of severe intensity in patients with lower limb fractures.[8] Furthermore, it possesses a more favorable 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 post-operative pain.[9,10]

Conclusion

Injection aceclofenac in our study scores over injection Diclofenac in providing better quality of analgesia injection consistent with the pharmacokinetic profile of all the patients in Group II Diclofenac required for an additional dose of analgesic after *8 hours*. Early ambulation was possible in both the Groups. Good patient compliance in both the Groups were found. The analgesia with injection aceclofenac is sustained over longer periods of time upto *24 hours*. A single doe is required. From the study we conclude that there is definite place for long acting NSAIDs like Injection Aceclofenac *150 mg/3 ml* in the post-operative analgesia for patients undergoing laparoscopic abdominal surgeries in view of its good quality of analgesia, sustained and prolonged duration action upto *24 hours* and better gastrointestinal tolerance.

References

1. Kehlet H, Holte K. Effect of post-operative analgesia on surgical outcome. Br J Anesth 2001;87(1):62–72.
2. Wheeler M, Oderda GM, Ashburn MA, *et al*. Adverse events associated with post-operative opioid analgesia: A systemic review. J Pain 2002;3:159–80.
3. Pal A, Biswas J, Mukhopadhyay P, *et al*. Diclofenac is more effective for post-operative analgesia in patients undergoing lower abdominal: Anesthesia. Essays and Researches, 2014 8(2):192–96.
4. Ozcan S, Tabuk M, Baltaci B, *et al*. Is epidural pre-emptive analgesia effective in lower abdominal surgery: Agri. 2004 Jan;16(1):58–63.
5. Lemmel EM, Leeb B, De Bast J, *et al.* Patient and physician satisfaction with aceclofenac: Results of the European Observational Cohort Study (experience with aceclofenac for inflammatory pain in daily practice). Aceclofenac is the treatment of choice for patients and physicians in the management of inflammatory pain. Curr Med Res Opin. 2002;18(3):146–53.
6. Maheshwari RK, Indurkhya A. Formulation and evaluation of aceclofenac injection made by mixed hydrotropic solubilization technique. Iran J Pharm Res. 2010 Summer;9(3):233–42.

7. Pareek A, Chandanwale AS, Oak J, *et al*. Efficacy and safety of aceclofenac in the treatment of osteoarthritis: A randomized double-blind comparative clinical trial *vs* diclofenac: An Indian experience. Curr Med Res Opin. 2006 May;22(5):977–88.
8. Sharma V, Rana S, Sharma S *et al*. Comparison of Efficacy of Diclofenac *vs* Aceclofenac in post-operative pain in lower limb fractures: A Double blind Randomized study. The Internet Journal of Orthopedics. 2012;19(2).
9. Villa H, Smith RA, Augustyniak MJ. The efficacy and safety of pain management before and after implementation of hospital–wide pain management standards: Is patient safety compromised by treatment based solely on numerical pain ratings? Anesth Analg. 2005;101:474–80.
10. Reuben SS, Buvanendran A. Preventing the development of chronic pain after orthopedic surgery with preventive multimodal analgesic techniques. J Bone Joint Surg Am. 2007;89:1343–58.