

# Comparative Evaluation Of Intramuscular Ketoprofen And Diclofenac Sodium For Post-Operative Pain Relief

H Prabhakar, S Shrirao, V Shelgaonkar, A Ghosh

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## Abstract

**Objectives:** The treatment of pain after surgery is central to the care of postoperative patients. Non-steroidal anti-inflammatory drugs are devoid of side effects of opioids like respiratory depression, vomiting, cardiac depression etc. Ketoprofen, a non-steroidal anti-inflammatory drug, being in use since 1974, is not a much-studied drug. We decided to compare Ketoprofen and Diclofenac sodium for postoperative pain relief. We used the intramuscular route of administration for both the drugs, as postoperatively, this route is easier, safer and practically simple.

**Methods:** 100 patients of ASA-I undergoing cesarean section under subarachnoid block were enrolled for the study. The patients were randomly divided into 2 groups of 50 patients each to receive either ketoprofen 100-mg or diclofenac sodium 75-mg intramuscularly at the onset of bearable pain after surgery. The analgesic was assessed at regular intervals using visual analogue scale. The onset of action and total duration of action for the study drugs was calculated. Summing up the weightage points of pain score, onset of action and duration of action assessed the overall efficacy.

**Results:** The change in the mean pulse rate was statistically significant in both groups. The change in the mean respiratory rate in both the groups before and after administration of study drugs was significantly reduced. The mean duration of action of ketoprofen was found to be significantly longer than diclofenac.

**Discussion:** In all patients of the study groups the result ranged from Good to Excellent showing their comparable efficacy. Ketoprofen may be a better alternative to the more commonly used drug diclofenac for postoperative pain relief.

## INTRODUCTION

Pain is a protective mechanism designed to alert the body to potentially injurious stimuli. The treatment of pain after surgery is central to the care of postoperative patients; failure to relieve pain is morally and ethically unacceptable. Familiarity with the pharmacology of analgesic drugs makes an anesthesiologist a logical choice to provide pain relief in the immediate post-operative period. Various methods of treating postoperative pain are available with opioids and non-opioid analgesics. Non-steroidal anti-inflammatory drugs (NSAIDs) are devoid of side effects of opioids like respiratory depression, vomiting, cardiac depression etc. Although various NSAIDs have been tried for pain relief, Diclofenac sodium has become widely popular and acceptable for the relief of pain. Ketoprofen, another non-steroidal anti-inflammatory drug, being in use since 1974, is not a much-studied drug.

We decided to study the two drugs, namely Ketoprofen and Diclofenac sodium for postoperative pain relief. We decided to use the intramuscular route of administration for both the drugs, as postoperatively, this route is easier, safer and practically simple.

## MATERIALS AND METHODS

This prospective, double blind, randomized study was carried out after taking clearance from the local ethics committee and an informed consent from the patient. A total of 100 patients of ASA-I/II undergoing cesarean section under subarachnoid block were enrolled for the study. Patients with a history of allergy to NSAIDs, peptic ulcer disease, renal disease and coagulopathies were excluded from the study. No pre-operative or intra-operative sedation was given. Preoperative pulse rate, systolic blood pressure and respiratory rate were noted. All patients were pre-loaded with 500 ml Ringer lactate solution prior to the subarachnoid

block. Lumbar puncture was performed aseptically in lateral position with 22-G lumbar puncture needle and hyperbaric lignocaine 5 percent was injected in the dose of 1.2 cc. In all patients spinal anesthesia was successful and surgery could be undertaken in all of them without encountering any major side effects or complications. The patients were randomly divided into 2 groups of 50 patients each to receive either ketoprofen 100-mg or diclofenac sodium 75-mg intramuscularly at the onset of bearable pain after surgery. The pulse rate, systolic blood pressure and respiratory rate were recorded immediately before the injection. The visual analogue scale (VAS), which was explained to the patient in the pre-operative visit, was used to assess the pain.

After the administration of the drugs, the analgesic effect was assessed at 0 hour, 15 min, 30 min, 60 min, 120 min, and then every hour till 6 hours by a blinded observer. At the same intervals the patients' blood pressure, pulse rate and respiratory rate were also recorded. The rescue analgesic was intramuscular pentazocine 15 mg, which was administered whenever the pain score on VAS was equal to or more than 5. The onset of action and total duration of action for the study drugs was calculated. The duration of action was taken as the time interval between the onset of action and first recurrence of pain or demand for analgesic. Summing up the weightage points of pain score, onset of action and duration of action assessed the overall efficacy. The weightage points were given as follows:

**Figure 1**

	Weightage point
1. Pain score	
No pain (0,1)	3
Mild pain (2-5)	2
Moderate pain (6-9)	1
Severe pain (10)	0
2. Onset of action	
0-15 mins	2
15-30 mins	1
More than 30 mins	0
3. Duration of action	
Upto 4 hours	0
5-8 hours	1
More than 8 hours	2
4. Efficacy	Total score
Excellent	6-7
Good	3-5
Poor	0-2

Applying Student's 't' test compared the mean values and the overall efficacy of the analgesics was thus evaluated on comparative basis. The value of  $p < 0.05$  was considered significant.

## RESULTS

Before giving the analgesic drug postoperatively, vital signs were recorded so that any fluctuations in the clinical parameters after giving the drug could be analyzed. As the patients were in their reproductive age group, their ages were comparable. The mean pulse rate in Group I was  $87.32 \pm 8.3$  beats per minute just before injection of drug and  $85.67 \pm 8.1$  beats per minute upto 2 hours after injection of drug. The change was statistically significant. Similar result was found in Group II also. The mean systolic blood pressure in both groups before and after the administration of study drugs was statistically insignificant. However the change in the mean respiratory rate in both the groups before and after administration of study drugs was significantly reduced. [Table 1] The time of onset of action of drugs in both the groups was comparable. However the mean duration of action of ketoprofen was found to be significantly longer than diclofenac. [Table 2] In all patients of the study groups the result ranged from Good to Excellent showing their comparable efficacy. It was observed that 14% of patients in ketoprofen group and 22% patients in diclofenac group showed minor side effects like nausea, vomiting and headache. Three patients in diclofenac group experienced local tenderness. [Table 3]

**Figure 2**

Table 1: Mean values of heart rate, systolic blood pressure and respiratory rate before and after injection of study drugs.

Mean	Group I		Group II	
	Pre-Inj	Post-Inj	Pre-Inj	Post-Inj
Heart rate (b/m)	$87.32 \pm 8.38$	$85.67 \pm 8.10^*$	$90.64 \pm 5.66$	$86.99 \pm 5.396^*$
Systolic BP (mmHg)	$115 \pm 7.28$	$115.12 \pm 7.03$	$111.8 \pm 9.314$	$112.24 \pm 6.628$
Respiratory rate (bpm)	$22.08 \pm 2.82$	$20.06 \pm 2.66^*$	$20.24 \pm 2.10$	$17.62 \pm 1.49^*$

b/m ~ beats per minute, bpm ~ breaths per minute

\*p value less than 0.05

**Figure 3**

Table 2: Mean time of Onset of action and Duration of action of study drugs in both groups

	Group I	Group II
Onset (minutes)	$18.5 \pm 3.04$	$19.0 \pm 3.60$
Duration (hours)	$7.72 \pm 3.04$	$6.68 \pm 1.24^*$

\*p value less than 0.05

**Figure 4**

Table 3: Frequency of side effects encountered by the patients in the two groups

	Group I (n)	Group II (n)
Nausea	2	3
Vomiting	1	3
Headache	4	2
Local tenderness	-	3

n ~ number of patients

## DISCUSSION

This prospective, randomized, double blind clinical trial included a total of hundred patients of ASA-I physical status undergoing subarachnoid block for elective cesarean section. There have been very few comparative studies of ketoprofen after administration via intramuscular route [1,2]. Ketoprofen is a propionic acid derivative and a non-steroidal anti-inflammatory drug. Besides inhibiting enzyme cyclooxygenase, the analgesic effect of ketoprofen also has a central component inhibiting the spinal cord nociceptor reflex activity and reducing the central sensitization in the cord. This centrally mediated effect is also believed to reduce the opioid induced respiratory depression [3]. Ketoprofen is used in musculoskeletal and joint disorders such as rheumatoid arthritis, osteoarthritis, periarticular disease such as tendinitis and bursitis. It is also used in the management of mild to moderate pain such as primary dysmenorrhea. Ketoprofen has been used extensively in the management of all tissue disease and postoperative pain. Still, the drug has failed to gain wider acceptance and popularity. Our search in English literature revealed no study showing the effects of ketoprofen in post-cesarean patients. Ours is probably the first study of its type comparing ketoprofen and diclofenac sodium administered via intramuscular route for post operative pain relief in cesarean section patients.

Hanna MH et al [1], reported good analgesic efficacy of intramuscular ketoprofen in terms of opioid-sparing and pain control after major orthopedic surgery. In a study by Rorarius et al [4], the effects of a constant infusion of diclofenac and ketoprofen for pain treatment after elective cesarean section, was found to result in significant less consumption of the rescue analgesic oxycodone, as compared to the placebo group. Commandre et al [5] studied the use of intramuscular piroxicam as a single daily dose in comparison with ketoprofen and diclofenac. His study group

included patients with acute sprain of ankle or knee or those with acute tendinitis. In their study to evaluate intramuscular ketoprofen as analgesic in mild to moderate pain in children undergoing squint surgery, Alam et al [6] found ketoprofen better than pethidine in providing postoperative pain control. Using intravenous route of administration, Elhakim et al [7] found significantly less pain post-operatively in their patients receiving ketoprofen than pethidine.

In our study, there was a significant reduction in the mean pulse rate after administration of study drugs in both the groups. Though the reduction in the mean systolic blood pressures before and after administration of the study drugs was not significant. These findings of our study are in accordance with studies by Elhakim et al [7], Kostamovaara et al [8] and Rorarius et al [4]. We also found a statistically significant reduction in the respiratory rates after administration of the study drugs. Though there was a fall in the respiratory rate, it was not corresponding to patients in whom there was a decrease in pulse rate. Bradycardia or peripheral cyanosis was not seen in any of the patients. It is likely that the patients were comfortable and having adequate analgesia. The mean onset of time in both the groups was comparable and showed no statistical significance.

We are not aware of any previous study indicating the onset of action of the two study drugs in comparison with one another given through intramuscular route. In our study, the mean duration of action in ketoprofen group was  $7.72 \pm 3.04$  hours and  $6.68 \pm 1.24$  hours in the diclofenac group. The difference was statistically significant. Ketoprofen produced analgesia for a longer duration as compared to diclofenac. The over-all efficacy of ketoprofen was found to be significantly more than diclofenac. In the present study it was found that 14% of patients in ketoprofen group and 22% patients in diclofenac group experienced minor side effects like, nausea, vomiting, and headache. Three patients in diclofenac group reported local tenderness. No side effect requiring active management was noted.

To summarize, our study compared only a single dose of the two drugs in question, to know the efficacy and duration of action during the early post-operative period. Our study clearly indicates the overall good tolerability of the drugs ketoprofen and diclofenac. Both drugs exhibited a fairly rapid onset of action with the mean duration of action being significantly more in ketoprofen group as compared to the diclofenac group, although both provided good to excellent

analgesia. There were minimal side effects with both the drugs.

We conclude that ketoprofen may be a better alternative to the more commonly used drug diclofenac for postoperative pain relief and the former can be considered marginally superior.

#### **ADDRESS FOR CORRESPONDENCE**

Dr.Hemanshu Prabhakar Department of  
Neuroanaesthesiology 7th Floor, CN Center All India  
Institute of Medical Sciences, New Delhi- 110029  
Telephone: 9868398205(mob) Fax: 91-11-26862663 E-mail:  
prabhakarhemanshu@rediffmail.com

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**Author Information**

**Hemanshu Prabhakar, M.D.**

Assistant Professor, Department of Neuroanesthesiology, All India Institute of Medical Sciences

**Subhash A. Shirao, M.D.**

Honorary Professor, Department of Anesthesiology, Indira Gandhi Medical College and Hospital

**Vaishali C. Shelgaonkar, M.D.**

Associate Professor, Department of Anesthesiology, Indira Gandhi Medical College and Hospital

**Alok A. Ghosh, M.D.**

Ex-Professor and Head, Department of Anesthesiology, Indira Gandhi Medical College and Hospital