

**COMPARATIVE STUDY TO EVALUATE THE EFFICACY OF ETORICOXIB VS PLACEBO AS PREEMPTIVE ANALGESIA FOR ACUTE POSTOPERATIVE PAIN RELIEF IN ORTHOPEDIC SURGERIES**B. Sowbhagya Lakshmi<sup>1</sup>, P. Krishna Prasad<sup>2</sup>, M. Santhi Sree<sup>3</sup>, Nageswar Rao<sup>4</sup>**HOW TO CITE THIS ARTICLE:**

B. Sowbhagya Lakshmi, P. Krishna Prasad, M. Santhi Sree, Nageswar Rao. "Comparative Study to Evaluate the Efficacy of Etoricoxib vs Placebo as Preemptive Analgesia for Acute Postoperative Pain Relief in Orthopedic Surgeries". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 30, July 28; Page: 8333-8339, DOI: 10.14260/jemds/2014/3051

**ABSTRACT: BACKGROUND:** Etoricoxib, a selective Cox-2 inhibitor has been found to be effective as preemptive analgesia for acute postoperative pain. This study evaluates the effect of preoperative use of oral etoricoxib on postoperative pain relief and sleep in patients undergoing lumbar laminectomies. **MATERIALS & METHODS:** In this prospective, randomized controlled study, fifty patients (ASA I & II) aged between 20-50yrs scheduled to undergo lumbar laminectomies were given either etoricoxib 120mg (Group E) or placebo (Group P) orally one hour before surgery. Visual analog score (VAS) was assessed at 0, 6, 12, 18, and 24 hours at rest and on movement. Sleep overnight, total fentanyl consumption, incidence of nausea and vomiting, intra-operative blood loss and patient satisfaction were noted. **RESULTS:** In our study we found that there was reduction in VAS at rest and on movement in the etoricoxib group when compared with the control group at all intervals till 24 hours postoperatively. Total fentanyl consumption was higher in control group in postoperative period. **CONCLUSION:** Single preoperative oral dose (120mg) of etoricoxib given one hour before surgery, has significantly reduced the postoperative pain at rest and on movement and improved sleep in patients undergoing lumbar laminectomies without any side effects and with good patient's satisfaction.

**KEYWORDS:** Etoricoxib, selective Cox-2 inhibitors, preemptive analgesia, postoperative analgesia.

**INTRODUCTION:** Multimodal analgesia using a combination of analgesics throughout perioperative period to control postoperative pain is an important part of anesthesia management and is well accepted.<sup>(1,2)</sup> Acute postoperative pain is usually treated with opioids and Non-steroidal anti-inflammatory agents (NSAIDs). Opioids are associated with side effects like sedation, respiratory depression, nausea and vomiting, urinary retention, ileus and constipation.<sup>(3,4)</sup> The nonselective NSAIDs inhibit both forms of cyclooxygenase (COX) enzymes and are associated with increased risk of perioperative bleeding, renal dysfunction and gastrointestinal disturbances.<sup>(5,6)</sup>

Among the NSAIDs is new generation of Cox-2 inhibitors of which etoricoxib is a member. Cox-2 selective inhibitor is a form of NSAID that directly targets cyclooxygenase-2, an enzyme responsible for inflammation and pain and devoid of side effects of Cox-1 enzyme inhibition like less gastrointestinal toxicity and no effects on platelet aggregation.<sup>(7)</sup>

Etoricoxib has been effective in providing analgesia in ambulatory surgeries, dental procedures, laparoscopic cholecystectomy and knee repair.<sup>(8)</sup> It is safe and effective in treating postoperative pain with minimal side effects. Pain in patients with spine pathology is different from other types of pain, because these people have chronic pain and this may flare up in acute

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postoperative period. Sleep disturbances are common in postoperative period and it adds to discomfort of patients.<sup>(9)</sup>

**PRE-EMPTIVE ANALGESIA:** Transmission of pain signals evoked by tissue damage leads to sensitization of peripheral and central pain pathways. Pre-emptive analgesia is a treatment that is initiated before the surgical procedure in order to reduce this sensitization owing to this protective effect on nociceptive system. We hypothesized that a single preoperative dose of etoricoxib (Cox-2 inhibitor) is effective as preemptive analgesic in control of acute postoperative pain following laminectomy.

**AIM OF THE STUDY:** Our aim of the study is to evaluate the efficacy of single preoperative dose of Etoricoxib (120mg oral) vs placebo (B-complex) as a preemptive analgesic in control of acute post-operative pain in laminectomy surgeries.

**MATERIALS & METHODS:** This prospective randomized double blind, placebo controlled study was conducted in orthopedic OT and ward, Government general Hospital attached to Rangaraya Medical College, Kakinada between May 2013 to August 2013. After obtaining institutional ethical committee approval & informed consent from patients, 50 patients belonging to ASA grade I&II, of both sexes, aged between 20-50years were taken up for study.

They were randomly divided into 2 groups, Group E and Group P each comprising of 25 patients.

### Inclusion Criteria

Age between 20-50years  
 Patients posted for laminectomy  
 ASA grade I&II  
 Uncontrolled HTN  
 Lactating women  
 Hypersensitivity to NSAIDS

### Exclusion Criteria

Age < 20years, H/o of asthma  
 Gastritis, coagulation disorders  
 Hepatic & renal dysfunction

**Group E:** Patients received Tab. Etoricoxib 120mg orally 60mins before surgery with sips of water.

**Group P:** Patients received Tab. B-complex orally 60mins before surgery with sips of water. All the patients in both the groups were pre medicated with tab. Lorazepam 1mg and tab. Rabiprazole 10mg in the night before surgery.

Study drug and placebo were identical and were given in a folded cover to the patients by the assistant as it was a double blinded study. Base line parameters like pulse rate, NIBP, respiratory rate and SpO<sub>2</sub> were recorded in both the groups. Both Groups were given standard general anesthesia with inj. Glycopyrrolate 10µg/kg IV, inj. Ondansetron 0.1mg/kg IV., inj. Fentanyl 1µg/kg IV as premedication and induced with inj.

Thiopentone sodium 5mg/kg IV, intubated after giving vecuronium 0.1mg/kg IV with appropriate sized endotracheal tube. Anaesthesia was maintained with increments of vecuronium, oxygen & nitrous oxide mixture 40%: 60% and isoflurane 1-1.5%. Intra operatively, inj. Fentanyl

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1µg/kg increments were given when there was considerable rise in heart rate and NIBP. After surgery, patients were reversed with inj. Glycopyrrolate 10µg/kg IV and Neostigmine 50-70µg/kg IV, extubated and shifted to recovery room after complete recovery from neuromuscular blockade, monitored for 24 hours in the PACU. In all the patients continuous monitoring of heart rate, NIBP, SpO<sub>2</sub> was done throughout the surgery and for 24 hours in the PACU.

In both the groups we observed & compared severity of post-operative pain at rest and on movement, sleep at night, total fentanyl consumption, total drain output at the end of 24 hours, incidence of side effects like nausea and vomiting, satisfaction from pain in terms of facial expression and body language

**Statistical Analysis:** Data analysis was performed by unpaired student's t-test and chi-square test. SPSS 14.0 was used for statistical analysis.  $P < 0.05$  was considered statistically significant and a  $p$  value  $< 0.0001$  was considered statistically very significant.

**RESULTS:** The demographic profiles of the patients in both the groups were comparable with regards to age, sex, height, weight and duration of surgeries (Tab-I). Pain score was assessed using visual analogue scale (0-100mm) at time points 0, 6, 12, 18, 24 hours when patient was at rest (static) and on movement (dynamic), (Fig-I).

Patients in group E had lower VAS score compared to group P at 0, 6, 12, 18, 24 hours both at rest and during movement and it is statistically significant ( $p < 0.05$ ) (Bar-dia-I, II). Patients were given rescue analgesic dose when VAS pain score was  $> 40$ . (Inj. Fentanyl 1µg/kg IV). Less opioid consumption (µg/kg/hr) in group E compared to group P and is statistically significant ( $p = 0.007$ ) (Tab-II). Sleep, facial expression, body language were assessed after 24 hours following surgery, i.e.

Pain satisfaction scale (Tab-III) Sleep at night was assessed subjectively as 1=good, 2=interrupted, 3=no sleep. Facial expression was assessed as 1=contented, 2=sad, 3=frightened. Body language was assessed as 1=relaxed, 2=tensed, 3=unhappy.

**DISCUSSION:** Our results demonstrated that preoperative use of oral etoricoxib, 120mg one hour before surgery reduced the postoperative analgesic requirement after lumbar laminectomy. Sleep at night, facial expression and body language were better with the use of etoricoxib whereas there was no increase in intra-operative blood loss and side effects.

Pre-emptive analgesia is a new strategy of postoperative pain management. The key concept is to prevent the altered sensory processing from surgical process. There are a number of medications being tested for pre-emptive analgesia, including opioids, anesthetic drugs and NSAIDs with conflicting results.<sup>(10-12,4,13,14)</sup> Our results found that etoricoxib was efficacious for use as pre-emptive analgesia after major orthopedic surgeries.

Etoricoxib is a second generation Cox-2 inhibitor with 100 fold increases in selectivity for Cox-2 over Cox-1. This reduces prostaglandin (PGS) generation from arachidonic acid. It has been found to be safe and effective in management of acute pain in different surgical conditions.<sup>(15-17)</sup>

NSAIDs (Nonselective Cox) have analgesic effect and opiate sparing effect and proven to be effective in major surgeries, but gastrointestinal bleeding and bleeding from operative site are the major concerns. So selective Cox-2 inhibitors are used as pre-emptive analgesics.

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Etoricoxib with its convenient single daily dosing and long half-life (24.8hrs) was found to be superior in relief of postoperative pain.

Etoricoxib due to its short onset and long duration of action was also proved to be useful as a pre-emptive analgesic, in ambulatory gynecological surgeries.<sup>(8)</sup> Preoperative use of etoricoxib 120mg was found to be equally effective with etoricoxib and paracetamol combination for postoperative pain relief after laparoscopic cholecystectomy, when pain intensity and opioid sparing effects were compared.<sup>(4)</sup> Kitti J- et al showed that parecoxib reduces postoperative pain in spinal surgery patients and this study is comparable with our study.<sup>(18)</sup>

Studies have shown that adequate postoperative pain control is an important determinant of patient satisfaction.<sup>(19, 20)</sup> Better satisfaction expressed as contented facial expression and relaxed body language was due to superior postoperative pain relief in patients of etoricoxib group in our study. Postoperative sleep disturbance may contribute to the development of episodic hypoxemia, haemodynamic instability and altered mental states, all of which have an influence on postoperative morbidity and mortality.

In our study we found that group which received etoricoxib had better quality of sleep. This is due to decreased pain, reduced stress response and less need for opioids which inhibit random eye movement (REM) sleep and slow wave sleep (SWS).<sup>(21)</sup> Common side effects of Cox-2 inhibitors and other NSAIDS are fluid retention, hypertension and renal damage, particularly in the elderly. None of such problems have been encountered in any of our cases.

**CONCLUSION:** Based on this study we conclude that preoperative oral etoricoxib is an effective preemptive analgesic as it resulted in significantly less post-operative pain scores both at rest and during movement and less consumption of opioid postoperatively and a better satisfaction from pain with less incidence of side effects.

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GROUPS	GROUP E (n=25)	GROUP P (n=25)
AGE (YEARS)	39.9 10.3	39.6 11.1
SEX (M/F)	15/10	13/12
WEIGHT (Kg)	62.4 + 11.2	61.2 + 12.2
HEIGHT (cm)	165.8 + 6.3	167.6 + 7.1
DURATION OF ANAESTHESIA (min)	155 + 30.0	160 + 28.2
INTRA OPERATIVE BLOOD LOSS (ml)	186.20 + 48.6	190.6 + 53.5
<b>TABLE 1: SHOWING DEMOGRAPHIC VARIABLES</b>		

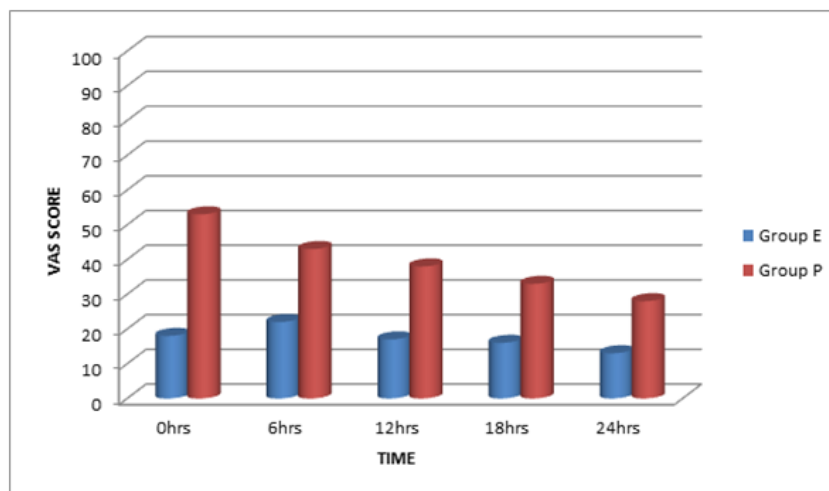
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TIME	GROUPS	GROUP - E	GROUP - P	P VALUE
0 HOURS	AT REST	20	55	0.001
	MOVEMENT	30	55	0.003
6 HOURS	AT REST	22.5	45	0.008
	MOVEMENT	27.5	50	0.003
12 HOURS	AT REST	20	40	0.001
	MOVEMENT	27.5	45	0.006
18 HOURS	AT REST	20	35	0.06
	MOVEMENT	30	40	0.02
24 Hours	AT REST	15	30	0.012
	MOVEMENT	20	35	0.33
TOTAL FENTANYL CONSUMTION (ug/kg/hr)		450.8	668	0.007

**TABLE 2: SHOWING TOTAL FENTANYL CONSUMPTION**

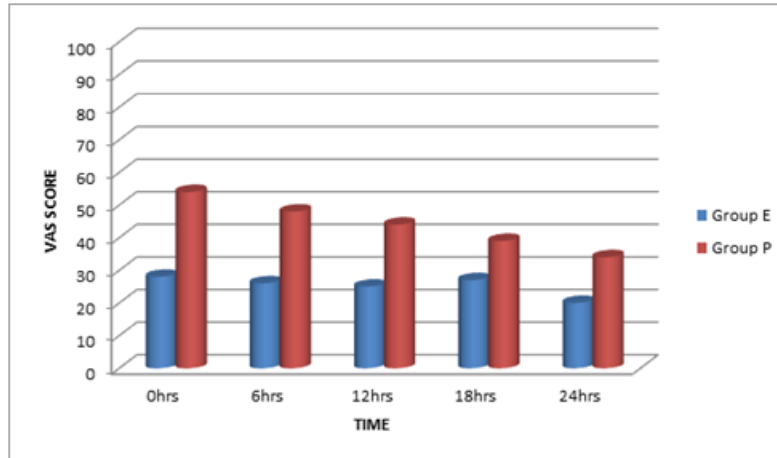
GROUP		GROUP - E (n-25)	GROUP - P (n-25)
SLEEP (p - 0.00)	GOOD	15	7
	INTERRUPTED	8	14
	NO SLEEP	2	4
FACIAL EXPRESSION (p - 0.003)	CONTENDED	15	6
	SAD	7	13
	FRIGHTENED	3	6
BODY LANGUAGE (p - 0.004)	RELAXED	16	8
	TENSED	6	12
	UN HAPPY	3	5

**TABLE 3: SHOWING SLEEP, FACIAL EXPRESSION, BODY LANGUAGE SCORING**

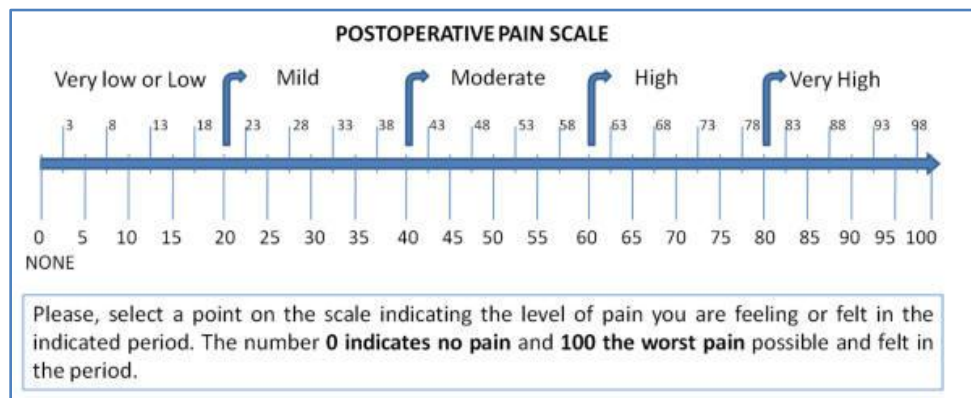


**BAR DIAGRAM I: SHOWING VAS SCORE AT REST**

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**BAR DIAGRAM II: SHOWING VAS SCORE AT MOVEMENT**



**Figure 1: Showing Visual Analogue Scale**

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Date of Submission: 14/07/2014.

Date of Peer Review: 15/07/2014.

Date of Acceptance: 21/07/2014.

Date of Publishing: 22/07/2014.