

## The Analgesic Efficacy of Preoperative Lornoxicam in Prevention of Postoperative Pain after Septoplasty

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### Abstract

**Background:** Septoplasty operation is a commonly performed procedure, usually done on short stay basis. Postoperative pain and bleeding are two major concerns that influence delayed discharge or readmission. Lornoxicam, nonselective anti-inflammatory drugs belongs to oxicam group with balanced cyclooxygenase inhibitor and is well tolerated by the patients. It is theoretically potential to reduce postoperative pain and perioperative bleeding. The role of preemptive analgesia in prevention of postoperative pain is controversial. Lornoxicam has proven role in the management of postoperative pain. However, comprehensive evidence is lacking regarding its preemptive use for postoperative pain relief.

**Materials and Methods:** After getting ethical committee approval and written informed consents from 88 adult patients of either sex, ASA physical status I and II scheduled for septoplasty under local anaesthesia and monitored anaesthesia care, were allocated in this prospective randomised double blinded placebo controlled study to receive either intravenous single dose lornoxicam 16 mg diluted into 100 ml normal saline (Group A) or Normal Saline (Group B) over 10 minutes 30 min before surgical incision. Dexmedetomidine was infused 1 microgram/kg over 10 min as initial loading dose and 0.2-0.7 microgram/kg/hr as maintenance of anaesthesia. Severity of postoperative pain was assessed with Visual Analogue Scale (VAS) Score 0-100 mm at immediate postoperative period, 30 min and every 1 hr till 4 hrs postoperatively and then 4 hrly upto 12 hrs and 6 hrly till 24 hrs. Oral paracetamol 1 gm was used as rescue analgesic on demand. Patients refractory to paracetamol treated with 10 microgram iv fentanyl increments. Patients were followed up for satisfaction and complications till 24 hrs.

**Results:** Patients of group A reported significantly lower pain score ( $p < 0.05$ ) and significantly less in patients of group A as compared to group B required rescue analgesia within first 6 hrs postoperatively. Time to first rescue analgesic request was also significantly prolonged in group A.

**Conclusion:** Preemptive single dose lornoxicam appears to be effective in management of acute postoperative pain following septoplasty.

**Keywords:** Septoplasty; Preemptive Lornoxicam non-steroidal anti-inflammatory drugs; Postoperative analgesia

### Introduction

Pain is a major concern of any type of surgery. Septoplasty operation is a commonly performed procedure, usually done on short stay basis. Postoperative pain is the major concern that may influence delayed discharge or readmission [1]. Moreover, inadequate pain management causes marked haemodynamic alteration and delayed recovery. Postoperative analgesia improves patient's quality of life, prevents clinical complications related to pain, encourages early postsurgical mobilization and results shorter hospital stay [2-6].

Currently multimodal approach of analgesia is a popular and safe approach. Drugs, mainly opioid and non-opioid with or without interventional pain management is the key to achieve early recovery and early hospital discharge after day-care or ambulatory surgery [7,8]. The concept of pre-emptive analgesia is still being practiced, though there is a focus of debate. Some reductions in postoperative pain

and/or analgesic requirements with pre-emptive analgesia were observed in 13 studies [9-21], whereas no significant differences were observed in 17 other studies [22-38]. Opioids are restricted in day care surgery due to their potential side effects like nausea, vomiting, urinary retention, sedation, and respiratory depression. Non-opioid analgesics are popular as it can effectively reduce postoperative pain with minimal adverse effects [39].

Lornoxicam (US FDA approved), a nonselective anti-inflammatory drug belongs to oxicam group, provides effective analgesia in postoperative period. Lornoxicam is the most potent balanced cyclooxygenase inhibitor (COX 1: COX 2=1:1). It exerts its analgesic effect not only by inhibition of cyclooxygenase, but also by releasing endogenous dynorphin and beta-endorphin [40]. Analgesic efficacy of lornoxicam for management of postoperative pain is well established [41]. Use of postoperative lornoxicam provides pain free postoperative hours with better patients' satisfaction and decreases need for opioids. But there is paucity of evidence regarding its preoperative use. Preemptive lornoxicam for postoperative analgesia in day care surgery needs more evaluation.

In this study, an effort has been made to find out analgesic efficacy of preemptive lornoxicam for management of postoperative pain after septoplasty operation.

## Materials and Methods

With approval from the institutional ethics committee and written informed consent from 98 adult patients of 18-40 years of age, of either sex with ASA physical status I or II, scheduled for elective septoplasty, the authors have conducted this prospective randomised double blinded placebo controlled study. Patients who refused to participate, younger than 18 year, BMI>30 kg/m<sup>2</sup>, alcohol abuse, smoker, pregnant, psychiatric patients and patients having history of significant cardiac, pulmonary, hepatic, renal or haematological disease, granulocytopenia, thrombocytopenia, aplastic anaemia, on chronic analgesic therapy, patients having hypersensitivity to any of the study drugs, peptic ulcer disease, asthma, chronic obstructive pulmonary disease were excluded from the study.

Considering 15 mm decrease in pain intensity would be clinically relevant with a power of 80% ( $\beta=0.2$ ) at  $\alpha$  value 0.05; this two tailed study required 44 patients in each group [42]. We enrolled total 98 patients considering the dropout. Patients were randomised by sealed envelope on the day of surgery, into two groups; Group A (n=44) and Group B (n=44) to receive either lornoxicam or normal saline, respectively.

During preoperative check-up all patients were made conversant with the use of visual analogue scale (VAS) to express postoperative pain (0 mm=no pain, 100=worst pain). In the night before surgery, patients were prescribed to take tab diazepam (5 mg). On the day of surgery, patients were transferred to a monitored procedure room where intravenous infusion of lactated Ringer's solution as maintenance fluid was started. Baseline necessary parameters like pulse rate, non-invasive blood pressure (NIBP), respiratory rate and peripheral arterial oxygen saturation (SpO<sub>2</sub>) were recorded. Half an hour before surgical incision, single dose intravenous 16 mg lornoxicam diluted into 100 ml normal saline was infused over 10 minutes to all the patients of group A. Group B received infusion normal saline 100 ml over 10 min, half an hour before surgical incision. The infusion set and bottle were wrapped with black paper to mask the colour of the solution from the patient. The investigator who prepared and administered the drug were not involved in the outcome assessment. Continuous monitoring was done throughout the operative procedure. Operations were done under local anaesthesia (10 ml of 1% lignocaine with adrenaline) and monitored anaesthesia care. Dexmedetomidine was infused 1 mcg/kg over 10 min as initial loading dose and 0.2-0.7 mcg/kg/hr titrated to maintain sedation with easy arousability. Heart rate and mean arterial pressure were maintained within 20% of the baseline values. This infusion was stopped when last stitch was applied. Duration of surgery was noted in all cases. Duration of surgery was defined as the time between surgical incision and application of adhesive dressing after proper closure of wound in both the groups.

After operation, all patients were shifted to postoperative recovery room where they were monitored for the first 24 postoperative hours. Postoperative pain was assessed with the help of VAS score immediately after shifting of patient to recovery room by the on duty resident who was not present in the OT procedure. Thereafter, patients were assessed for pain at 30 min, 1, 2, 3, 4, 8, 12, 18 and 24 postoperative hours. Patients who were complaining of pain (VAS

score  $\geq$  40 mm) were treated with rescue analgesic tablet paracetamol 1 gm with sips of water. Any episode of pain refractory to paracetamol was treated with a backup analgesic intravenous fentanyl aliquots of 10  $\mu$ g titrated to keep VAS  $\leq$  40 mm, not exceeding 100  $\mu$ g/hr. The number of patients who required additional analgesics was noted. The total dose of both the analgesics (paracetamol and fentanyl) required in the first 24 postoperative hours were recorded. Duration of postoperative analgesia was defined as the time between application of adhesive dressing and request for first rescue analgesic at VAS score  $\geq$  40 mm. Patients were also assessed for postoperative nausea, vomiting and treated accordingly. Patients were monitored continuously throughout the study period for any complications.

## Results

All the data were tabulated and analysed by SPSS for Windows (version 11.0 SPSS Inc, Chicago, IL, USA). Discrete categorical data are expressed as n (%) and median; continuous data are expressed as means  $\pm$  SD. Continuous data were analysed by independent Student's t-test and categorical data by Chi-square test.

One patient of group A and 2 patients of group B received inj. diclofenac in immediate postoperative period. One patient of group A and group B who were refractory to paracetamol, received inj. tramadol due to unavailability of inj. fentanyl at that certain moment. These 5 patients were excluded from the study and data of 83 patients were analysed finally.

Demographic profile and preoperative parameters were similar in both the groups. Duration of surgery were  $39 \pm 3.7$  min and  $38 \pm 4.2$  min in group A and group B respectively ( $P=0.3$ ). Intraoperative vital parameters were comparable between the two groups ( $P>0.05$ ). Two groups were comparable with respect to age, sex, ASA physical status and duration of surgery. Though body mass index (BMI) has just got the value of statistical significance but it has not clinical significance (Table 1).

Parameters	Gr. A (n=42)	Gr. B (n=41)	P value
Age (years)	28.3 $\pm$ 4.48	28.4 $\pm$ 4.57	0.995
Sex (M/F) *	26/18	25/19	0.893
BMI (kg/m <sup>2</sup> )	22.2 $\pm$ 2.65	23.5 $\pm$ 2.2	0.075
Duration of surgery (minutes)	39 $\pm$ 3.7	38 $\pm$ 4.2	0.339

**Table 1:** Demographic and preoperative parameters (Data expressed in mean  $\pm$  SD. Statistical test: independent sample t' test. P value<0.05 is considered significant. \* Chi Square test. n=number of patients. BMI: Body mass index).

Postoperative VAS scores of patients were significantly lower in the A group at immediate postoperatively, 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 8<sup>th</sup>, 12<sup>th</sup>, 18<sup>th</sup>, and 24<sup>th</sup> postoperative hrs (Table 2).

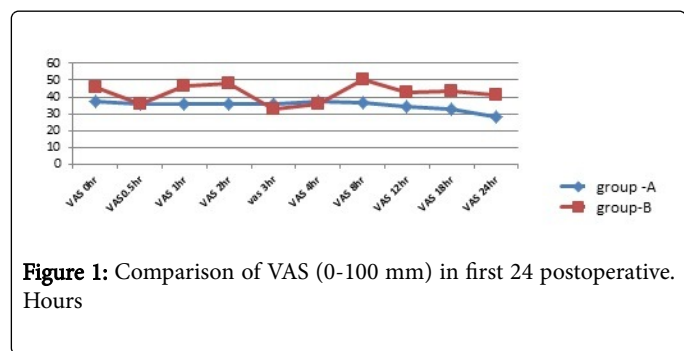
## Discussion

Pain is a subjective phenomenon. But postoperative pain depends on type of surgery, time and route of drug administered. Age, race, patient factors, presence of additives, drug dose may affect pain score as well. Preoperative lornoxicam 16 mg iv provides effective postoperative analgesia in the first 24 postoperative hours in different

surgical procedures. Such pain free postoperative period enhances patients' satisfaction which helps in early recovery, quick resumption of daily activity, also reduces the duration of hospital stay. It is very important in all type of operations, mainly day care surgery. Reduction of incidence of postoperative nausea, vomiting, which may influence increase chance of post-operative bleeding, is the added advantage of proper pain control in postoperative period.

VAS	Gr. A (n=42)	Gr. B (n=41)	P value
VAS0 min	36.95 ± 9.2	45.36 ± 13.08	0.001
VAS30 min	35.98 ± 6.44	35.83 ± 9.034	0.935
VAS1 hour	35.73 ± 9.10	48.79 ± 15.7	0.000
VAS2 hour	35.46 ± 6.80	47.81 ± 14.2	0.000
VAS3 hour	35.63 ± 7.3	32.43 ± 3.14	0.011
VAS4 hour	37.24 ± 6.9	35.83 ± 7.5	0.379
VAS8 hour	36.29 ± 7.9	50.24 ± 9.2	0.000
VAS12 hour	34.05 ± 6.2	42.38 ± 8.7	0.000
VAS18 hour	32.39 ± 3.5	43.57 ± 7.8	0.000
VAS24 hour	27.85 ± 5.04	40.86 ± 9.92	0.000

**Table 2:** Pain intensity at different time intervals (Data expressed in mean ± SD. Statistical test: independent sample't' test. P value<0.05 is considered significant. n=number of patients. BMI: Body mass index VAS: Visual analogue scale).



**Figure 1:** Comparison of VAS (0-100 mm) in first 24 postoperative hours

Total paracetamol consumption during the first 24 postoperative hours was significantly higher in group B (3.24 ± 0.759 mg) than group A (1.34 ± 0.693 mg), p < 0.05

	Gr. A (n=44)	Gr. B (n=44)	P value
Total oral paracetamol consumption (gm)	1.34 ± 0.693	3.24 ± 0.759	0.000
Total parenteral opioid (Fentanyl) requirement (µgm)	1.46 ± 3.5	13.57 ± 8.7	0.000

**Table 3:** Total analgesic requirement in first 24 postoperative hours (Data expressed in mean ± SD. Statistical test: independent sample't' test. P value < 0.05 is considered significant. n=number of patients. BMI: Body mass index VAS: Visual analogue scale).

In our study, patients were blinded as to the type of medication administered. The resident who prepared and administered the drug, were not involved to note the outcome assessments. A standard surgical procedure was followed for all the patients by two ENT surgeons with similar expertise to avoid interindividual variation.

This study shows, that VAS score was significantly lower in those patients who received lornoxicam and they were maintaining adequate analgesia throughout 24 postoperative hours. But in group B there was much variability in pain scores and it is much higher than A group and even higher at 24<sup>th</sup> postoperative hours (figure.1). This high pain score in B group was due to inadequate pain management by postoperatively administered analgesics whereas patients who received lornoxicam preoperatively had adequate analgesia which is reflected by decreased pain score. Adequate analgesia was defined as VAS score ≤ 40 mm with movement. When analyzing the graph of VAS score, it has been shown that there are so many peaks and valleys in group B whereas group A is maintaining a constant level of analgesia. This gross variation of group B can be explained by the effect of preemptive analgesia. Preoperative use of lornoxicam provides a sustained reduced level of pain throughout the 24 postoperative hours. The essence of preemptive analgesia is that it suppresses the pain receptors before they get stimulated. In our study, pain score in group B is higher than group A even at 24<sup>th</sup> postoperative hours. This is also because of preemptive use of lornoxicam in patients of group A. As the effect of preemptive analgesia is supposed to be persisting beyond the analgesic in the biophase, the analgesia achieved by preoperative lornoxicam was still maintaining lower VAS score in 24<sup>th</sup> postoperative hour.

VAS score was comparable between the two groups at 30 minutes (min) of postoperative period. This is probably due to the effect of residual local anaesthetic (1% lignocaine). We have used infusion dexmedetomidine for sedation. The analgesic property of dexmedetomidine may also affect the score of 30 min. At 4<sup>th</sup> postoperative hour VAS score was also not significant between the two groups in this study because paracetamol and fentanyl administration resulted in better analgesia for certain period of time. They do not have prolonged duration of action, so patients suffered from pain after few hours and pain score was increased.

This study showed that total paracetamol required in group B (3.24 ± 0.75) was higher than group A (1.34 ± 0.69), which proves clearly that preoperative lornoxicam reduced the need for rescue analgesic (paracetamol) during immediate postoperative period. Time to first request of rescue analgesic was also prolonged in group A. This can be explained as preemptive analgesia of lornoxicam provided adequate analgesia for long duration. Patient satisfaction was also higher in group A than compare to group B. Total parenteral fentanyl requirement was also significantly higher in group B (13.57 ± 8.7) than group A (1.46 ± 3.5).

Among the all NSAIDs, the authors have chosen Lornoxicam as it is better tolerated by the patients and its duration of action is longer than other NSAIDs [40,43]. Its plasma half-life is 3-5 hrs [44] and it has less side effects as compared to other NSAIDs. Instead of oral preparation, the patients in this study have intravenous lornoxicam administered. Parenteral lornoxicam is preferred for immediate postoperative pain management mainly in those patients where perioperative nausea, vomiting may adversely affect postoperative outcome. It is more important in head, neck, oesophageal, oropharyngeal and nasal surgeries. So, in our study oral administration is not desirable. The dose of iv16 mg has been chosen on the basis of previous studies [45-48], though there are some studies where iv 8 mg lornoxicam has

produced postoperative analgesia efficiently [49]. However, 16 mg lornoxicam may produce more potent analgesia and of longer duration [45,47,48]. In this study, lornoxicam was infused 30 min before surgical incision, as the time to reach peak plasma concentration ( $T_{max}$ ) was determined to be 30 min [50].

Daglar et al. [51] found that lornoxicam and diclofenac are equipotent for management of postoperative pain after cardiac surgery and it also shows similar efficacy as parecoxib for the management of postoperative pain after laparoscopic cholecystectomy [52]. There are so many studies which demonstrate that lornoxicam is more effective than paracetamol for management of postoperative pain in minor gynecologic operations. It is even more efficacious in reducing postoperative pain than ketoprofen after abdominal hysterectomy [53] or either ketoprofen or ketorolac after oncologic surgery [54]. In a recent study, preoperative lornoxicam shows adequate postoperative analgesia than tramadol after tonsillectomy [55]. It has been proved that lornoxicam is as potent as morphine [44], meperidine [56], pethidine [56], fentanyl [57].

Postoperative bleeding is a serious problem and it may limit the use of NSAIDs in perioperative period. NSAIDs inhibit cyclooxygenase, leading to inhibition of platelet thromboxane A<sub>2</sub> production and platelet aggregation, resulting in prolongation of bleeding time. Among all NSAIDs, oxicam group is safe one which does not cause perioperative bleeding that may alter the positive outcome of the patient. In this present study, there was no incidence of perioperative bleeding that needed intervention; though incidence of bleeding in septoplasty is as high as 6 to 13% [1].

Postoperative nausea, vomiting may restrict the discharge of patients after day-care surgery. Perioperative use of opioid usually further complicates the situation. Our study result shows that in group A 11.9% and in group B 9.7% patients complaining of nausea and vomiting. They were treated with 8 mg ondansetron intravenous. It is not statistically significant. This result is probably due to small sample size. No patient at any time after recovery had hypoxia ( $SpO_2 \leq 94\%$ ) or excessive sedation (Ramsay sedation scale score  $\geq 3$ ). No patient developed postoperative bleeding requiring treatment.

In this study perioperative bleeding could not be assessed properly due to lack of investigational backup as in the setting of resource constraint in a developing third world country. Assessment of pain also may depend on subjective variation of pain threshold, intelligence of patient to understand and express the "VAS" score. The major limitation of this study is that, use of local anaesthetics and dexmedetomidine can act as confounding factors which may alter the pain score. The available data could not enable the authors to analyze additive and synergistic effect of lornoxicam, paracetamol and fentanyl, which has influence on 'VAS' score. If large sample size would have been taken, the result will be more reliable. This result may not be extrapolated in situation like major abdominal surgery where visceral component of pain is present.

The present study provides strong evidence that preemptive single dose 16 mg intravenous lornoxicam significantly lowers VAS score over first 24 hr postoperative period in elective septoplasty operation. The need of analgesics in first 24 postoperative period, both fentanyl and paracetamol were significantly less.

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