

PRE-EMPTIVE EFFECT OF INTRAVENOUS PARACETAMOL VERSUS INTRAVENOUS KETOROLAC ON POST-OPERATIVE PAIN AND SHIVERING AFTER SEPTOPLASTY UNDER GENERAL ANESTHESIA: A COMPARATIVE STUDY

Sanum Kashif, M Nasir Kundi, Taimur Azam Khan*

Frontier Corps Hospital, Quetta Pakistan, *63 Medical Battalion, Multan Pakistan

ABSTRACT

Objective: To observe the pre-emptive effect of intravenous paracetamol versus intravenous ketorolac in preventing post-operative shivering and pain after septoplasty in postoperative care unit.

Study Design: Prospective comparative study.

Place and Duration of Study: Main Operation Theatre of Frontier Corps Hospital Quetta, from Sep to Dec 2019.

Methodology: After ethical committee approval, 90 American Society of Anaesthesiologist (ASA-I patients, aged between 18-45 years, scheduled for septoplasty, were recruited and divided into three equal groups, Paracetamol (PA), Ketorolac (KE) and Placebo (PL) as per computer generated table. The paracetamol (PA) group (n=30) received 1gm intravenous paracetamol, ketorolac (KE) group (n=30) received 30mg intravenous ketorolac and group placebo (PL) received 100ml normal saline, 20 minutes before completion of surgery. Postoperative shivering and pain was assessed via four-point scale and visual analogue scale (VAS) respectively, in post-anesthesia care unit at 10 and 30 minutes post-extubation.

Results: Mean visual analog scale (VAS) score in paracetamol group was 2.7 ± 1.41 , ketorolac group was 2.3 ± 1.24 and in placebo group was 3.6 ± 1.44 , with a *p*-value of 0.002. Mean four point shivering score in paracetamol group was 0.3 ± 0.55 , ketorolac was 0.7 ± 0.78 and placebo group was 1.4 ± 1.00 , with a *p*-value of <0.001.

Conclusion: The effect of paracetamol is better than ketorolac in preventing pain and shivering after septoplasty under general anesthesia.

Keywords: Ketorolac, Pain, Paracetamol, Pre-emptive, Shivering.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Pain and shivering are one of the most common complications after surgeries under general anesthesia. Effective postoperative pain management is an essential component of enhance recovery after surgery¹. Persistent uncontrolled pain and shivering may adversely affect the body's endocrine, cardiovascular, immune, neurologic and musculo-skeletal systems. Poorly controlled acute postoperative pain and shivering are associated with increased morbidity, functional and quality-of-life impairment, delayed recovery time, prolonged duration of opioid use, and higher health-care costs².

Septoplasty is one of the commonly performed ENT procedure. Post-operative pain or tenderness occurs on the front of the nose due to stuffiness and swelling³. It is associated usually with mild to moderate post-operative pain. Multimodal analgesia is an effective method, to improve peri-operative analgesia with reduced dosage and limited side effects⁴.

There is a wide range of analgesic agents used to control post-septoplasty pain e.g. Non steroidal anti-

inflammatory drugs (NSAIDs), opioids, intravenous paracetamol, dexmedetomidine^{5,6}. Among all, paracetamol and ketorolac have been widely used for mild to moderate pain post-operatively. Ketorolac is an NSAID (non-steroidal anti-inflammatory drug), commonly use in peri-operative pain management but should be avoided in bleeding diathesis and renal dysfunction⁷. The analgesic effect of ketorolac is comparable to other analgesic drugs like pethidine, morphine, or pentazocine in previous studies for postoperative pain management⁸.

Intravenous paracetamol (acetaminophen) is commonly used for peri-operative pain management. Phenacetin is an active metabolite of paracetamol and has central analgesic action is via inhibiting cyclooxygenases, doesn't effect coagulation or renal functions like NSAIDs and its side effects are extremely rare (<1/10,000)^{9,10}.

The rationale of this study was to compare the pre-emptive effect of intravenous paracetamol versus intravenous ketorolac in preventing postoperative pain and shivering after septoplasty.

METHODOLOGY

It was a prospective comparative study, conducted at Main Operation Theater of Frontier Corps

Correspondence: Dr Sanum Kashif, Classified Anaesthesia, Frontier Corp Hospital, Quetta Pakistan

Received: 08 May 2020; revised received: 29 Mar 2021; accepted: 02 Apr 2021

Hospital Quetta, from September to December 2019, 90 ASA-I patients were selected via non-probability consecutive sampling. Inclusion criteria included patients of American Society of Anesthesiology Score (ASA-1), of either gender with age between 18-45 years, scheduled for septoplasty. Patients with ASA Score more than 1, history of allergy to the study drugs and not given consent were excluded from the study.

After approval of ethics committee, 90 patients (for sample size, data from previous similar studies were taken into consideration¹¹, sample of 90 patients were divided into three equal groups by random allocation. The paracetamol (PA) group (n=30) received 1gm intravenous paracetamol, ketorolac (KE) group (n=30) received 30mg intravenous ketorolac and group placebo (PL) received 100ml normal saline 20 minutes before completion of surgery. All drugs were issued by hospital pharmacy in a sealed box and handed over to anesthetist, who was unaware of the drug formulation. The anaesthesia was induced with propofol 2mg/kg, nalbuphine 0.1 mg/kg and atracurium 0.5mg/kg. It was maintained with isoflurane 1.5% and air 50% in oxygen. Axillary temperature was measured immediately 10 min after induction. An investigator, blinded to the treatment group, graded postoperative shivering using a 4-point scale (table-I) and postoperative pain

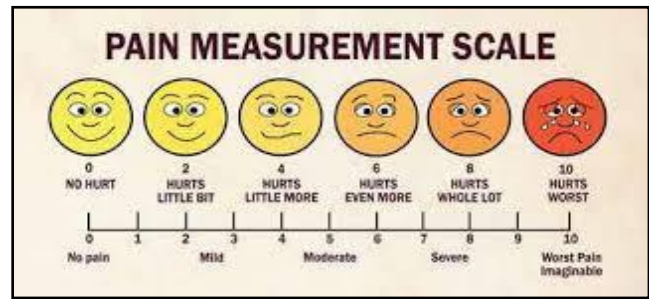


Figure: Visual analog scale (VAS) for Pain.

using a visual analogue scale (VAS) (figure) ranging between 0-10, at 10 and 30 minutes post-extubation in post-anesthesia care unit. Descriptive statistics was performed. Categorical variables (i.e. Four Point Shivering scale and VAS and Gender) presented as frequency & percentage. Continuous variables (i.e. age) presented as mean ± SD. Four Point Shivering scale and VAS were compared using one-way ANOVA.

RESULTS

A total of 90 patients were selected and divided into three groups. Seventy one (78.9%) patients were male and 19 (21.1%) patients were female. Mean age in paracetamol group was 25.3 ± 3.46, ketorolac group was 25.9 ± 4.12 and placebo group (PL) was 31.9 ± 3.48. Mean VAS score in paracetamol group was 2.7 ± 1.41, ketorolac group was 2.3 ± 1.24 and in placebo group was 3.6 ± 1.44, with a p-value of 0.002. Mean four-point shivering score in paracetamol group was 0.3 ± 0.55, ketorolac was 0.7 ± 0.78 and placebo group was 1.4 ± 1.00, with a p-value of <0.001 (table-II & III).

DISCUSSION

Postoperative shivering and pain are the two common problems after surgery, which should be managed adequately to improve patient’s satisfaction and outcome after surgery, as shivering and pain may increase blood pressures, cardiac output, intraocular and intracranial pressures due to increase secretions of catecholamines¹¹. Septoplasty is commonly performed day case procedure, in which pain and bleeding aggravates by shivering. Perioperative pain and shivering

Table-I: Post-operative 4 point shivering scale.

Score	Definition
0	None: no shivering noted on palpation of the masseter, neck, or chest wall
1	Mild: shivering localized to the neck and/or thorax only
2	Moderate: Shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Severe: Shivering involves gross movements of the trunk and upper and lower extremities

using a visual analogue scale (VAS) (figure) ranging between 0-10, at 10 and 30 minutes post-extubation in post-anesthesia care unit.

Table-II: Comparison of mean age, shivering score and visual analog scale score among groups.

Group		Age	Shivering	p-value	Pain (VAS)	p-value
Paracetamol	Mean ± SD	25.53 ± 3.46	0.36 ± 0.55	<0.001	2.73 ± 1.41	0.002
	n	30	30		30	
Ketorolac	Mean ± SD	25.90 ± 4.12	0.73 ± 0.78		2.36 ± 1.24	
	n	30	30		30	
Placebo	Mean ± SD	31.96 ± 3.48	1.46 ± 1.00		3.60 ± 1.42	
	n	30	30		30	

Data was recorded on a pre-designed structured Performa which were analyzed by using SPSS-16 for

may be prevented or treated by different techniques such as intravenous pethidine, clonidine, tramadol, do-

xapram, alfentanil, busipron, dexmedetomidine, ondansetron, pregabalin and dexamethasone¹².

Dahl *et al*, showed in study, the use of analgesic drugs (gabapentin and pregabalin) as protective medication, before different kind of surgeries. The basic principle behind protective medications is that, they reduce the pain after injury¹³.

Table-III: Comparison of shivering score and visual analog scale score among groups.

Four Point Shivering Score	Paracetamol	Ketorolac	Placebo	p-value
No Shivering	20 (22.2)	14 (15.6)	6 (6.7)	<0.001
Mild	9 (10)	10 (11.1)	9 (10)	
Moderate	1 (1.1)	6 (6.7)	10 (11.1)	
Severe	-	-	5 (5.6)	
Mean ± SD	0.3 ± 0.55	0.7 ± 0.78	1.4 ± 1.0	
Visual Analog Scale				
Mild	26 (28.9)	25 (27.8)	15 (16.7)	0.002
Moderate	3 (3.3)	5 (5.6)	14 (15.6)	
Severe	1 (1.1)	-	1 (1.1)	
Mean ± SD	2.7 ± 1.41	2.3 ± 1.24	3.6 ± 1.44	

In one of the study on Jordanian patients, underwent septoplasty surgery under general anesthesia required more remifentanil dose in the A-118 G gene group in comparison with patients with homozygous for the A allele involving nucleotide 118 of OPRM1. The muopioid receptors genetic variation also associated with different doses of intra-operative intravenous remifentanil infusion¹⁴.

Ketorolac is a potent nonsteroidal anti-inflammatory drug (NSAID), when administered for acute and chronic pain management. NSAIDs are cyclo-oxygenase inhibitor and they effectively reduced postoperative pain. They provide preemptive analgesia, like lornoxicam is used effectively in the management of post-septoplasty pain¹⁵. Maximum plasma concentrations are achieved in 45-50 minutes with peak analgesic effects in 1-2 hours following intramuscular injection. The efficacy of ketorolac, in emergency management, has been demonstrated and it has no sedative effect as it is a non-opioid medication, which is a main concern in management of emergency department¹⁶. The mechanism to prevent shivering in NSAIDs is either through reduction of perioperative pain or by inhibiting the release of vasoconstrictor and pyrogenic cytokines. Unlike opioids, ketorolac neither has respiratory depressant effect nor it has other side-effects such as nau-

sea, pruritis and constipation etc. According to Khezri *et al*, there was no significant difference between meperidine and ketorolac groups in terms of prevalence of shivering, although both groups were different from the placebo group ($p < 0.04$)¹⁷.

Among recent randomized controlled trials, 12 out of 14 were in favor of using intravenous paracetamol for perioperative analgesia. Its routes of administration can be oral, rectal, intramuscular and intravascular. Mode of excretion occurs through liver via conjugation. Its peak of action is achieved at 1 hour and duration of action is of 4-6 hours.

Kela *et al*, compared paracetamol and tramadol and found comparable results i.e. 10.0% of paracetamol group and 13.3% out of total cases in tramadol group suffered nausea and vomiting¹¹. Aghamir *et al*, compared tramadol and propacetamol in open urological procedures and found propacetamol effective in mild to moderate pain but not adequate for severe pain while Akcali *et al*, on extracorporeal shockwave lithotripsy patients, compared the efficacy of tramadol, paracetamol and lornoxicam and found same efficacy in all three drugs¹³. Cattabriga *et al*, in study on postoperative median sternotomies, compared tramadol and paracetamol and found paracetamol, more effective than tramadol¹⁸.

Kossick *et al*, reviewed multiple studies and concluded that for pediatric surgical patients 15 years of age and younger, ketorolac was not found to improve discharge times, decrease the incidence of unplanned hospital admissions, or cut down on total opioid consumption^{19,20}.

In the study Heo *et al*, compared the analgesic efficacy of 8 g of propacetamol and 180 mg of ketorolac as a PCA dose. Despite the relatively low dose of propacetamol, as compared to that of ketorolac, the analgesic efficacy of the propacetamol group was comparable to that of the ketorolac group in postoperative patients using patient-controlled analgesia with fentanyl. This suggests that propacetamol is effective when used for the management of postoperative pain and combined with fentanyl PCA²¹.

CONCLUSION

The effect of paracetamol is better than ketorolac in preventing pain and shivering after septoplasty under general anesthesia.

CONFLICT OF INTEREST

The study has no conflict of interest to be declared by any author.

REFERENCES

1. Ocalan R, Akin C, Disli ZK, Kilinc T, Ozlugedik S. Preoperative anxiety and postoperative pain in patients undergoing septoplasty. *B-ENT* 2015; 11(1): 19-23.
2. Locketz GD, Brant JD, Adappa ND, Palmer JN, Goldberg AN, Loftus PA, et al. Postoperative opioid use in sinonasal surgery. *OTO Open* 2019; 160(3): 402-408.
3. Du E, Farzal Z, Stephenson E, Tanner A, Adams K, Farquhar D, et al. Multimodal analgesia protocol after head and neck surgery: effect on opioid use and pain control. *OTO Open* 2019; 161(3): 424-30.
4. Kallush A, Riley CA, Kacker A. Role of complementary and alternative medicine in otolaryngologic perioperative care. *Ochsner J* 2018; 18(3): 253-59.
5. Dogan R, Erbek S, Gonencer HH, Erbek HS, Isbilen C, Arslan G. Comparison of local anaesthesia with dexmedetomidine sedation and general anaesthesia during septoplasty. *Eur J Anaesth* 2010; 27(11): 560-64.
6. Akça B, Arslan A, Yılbaş AA, Canbay Ö, Çelebi N. Comparison of the effects of patient-controlled analgesia (PCA) using dexmedetomidine and propofol during septoplasty operations: a randomized clinical trial. *Springer* 2016; 5(1): 572-75.
7. Amini S, Mahdavi E, Soltani G, Zirak N, Tashnizi MA, Vakili V et al. Efficacy and Safety of Ketorolac for Pain Management After Congenital Heart Surgery: A Comparison to Paracetamol. *Arch Crit Care Med* 2016; 1(4): e8278-82.
8. Szychta P, Antoszewski B. Assessment of early post-operative pain following septorhinoplasty. *J Laryngol Otol* 2010; 124(11): 1194-99.
9. Caliskan E, Sener M, Kipri M, Yilmaz I, Aribogan A. Comparison of the effects of intravenous Dexketoprofen Trometamol versus Paracetamol on postoperative analgesia in patients undergoing Septoplasty: A randomised double-blind clinical trial. *Pak J Med Sci* 2018; 34(3): 546-48.
10. Ceyhan D, Bilir A, Güleç MS. Evaluation of the analgesic efficacy of dexketoprofen added to paracetamol. *Turk J Anaesthesiol Reanim* 2016; 44(6): 312-15.
11. Kela M, Umbarkar S, Sarkar M, Garasia M. Comparative study of efficacy of IV paracetamol vs. IV tramadol for postoperative pain relief after cardiac surgery. *Bombay Hosp J* 2011; 53(3): 582-86.
12. Yildiz I, Bayir H, Sereflican M, Demirhan A, Yurttas V, Bilgi M. The effect of topical lidocaine plus dexamethasone on postoperative analgesia in septoplasty surgery. *Biomed* 2016; 27(3): 1-4.
13. Akcali GE, Iskender A, Demiraran Y, Kayikci A, Yalcin GS, Cam K. Randomized comparison of efficacy of paracetamol, lornoxicam, and tramadol representing three different groups of analgesics for pain control in extracorporeal shockwave lithotripsy. *J Endouro* 2010; 24(4): 615-20.
14. Al-Mustafa MM, Al Oweidi AS, Al-Zaben KR, Qudaisat IY, Abu-Halaweh SA, Al-Ghanem SM, et al. Remifentanyl consumption in septoplasty surgery under general anesthesia: Association with humane mu-opioid receptor gene variants. *Saudi Med J* 2017; 38(2): 170-74.
15. Nguyen BK, Yuhan BT, Folbe E, Eloy JA, Zuliani GF, Hsueh WD, et al. Perioperative analgesia for patients undergoing septoplasty and rhinoplasty: an evidence based review. *Laryng* 2019; 129(6): E200-12.
16. Keidan I, Zaslansky R, Eviatar E, Segal S, Sarfaty SM. Intraoperative ketorolac is an effective substitute for fentanyl in children undergoing outpatient adenotonsillectomy. *Paediatr Anaesth* 2004; 14(4): 318-23.
17. Khezri MB, Mosallaei MA, Ebtehaj M. Comparison of preemptive effect of intravenous ketorolac versus meperidine on postoperative shivering and pain in patients undergoing cesarean section under spinal anesthesia: A prospective, randomized, double-blind study. *Caspian J Intern Med* 2018; 9(2): 151-54.
18. Cattabriga I, Pacini D, Lamazza G, Talarico F, Di Bartolomeo R, Grillone G, et al. Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial. *Eur J Cardiothorac Surg* 2007; 32(3): 527-31.
19. Sclafani AP, Kim M, Kjaer K, Kacker A, Tabae A. Postoperative pain and analgesic requirements after septoplasty and rhinoplasty. *Laryng* 2019; 129(9): 2020-25.
20. Kossick MA. Intravenous acetaminophen and intravenous ketorolac for management of pediatric surgical pain: a literature review. *Aana J* 2014; 82(1): 53-56.
21. Heo BH, Park JH, Choi JL, Kim WM, Lee HG, Cho SY, et al. A comparative efficacy of propacetamol and ketorolac in postoperative patient-controlled analgesia. *Korean J Pain* 2015; 28(3): 203-206.