Open Access

Original Article

Comparison of Nebulized Ketamine with Intravenous Paracetamol Versus Paracetamol Alone For Post-Operative Analgesia In Pediatric Day Care Anesthesia

Hassan Nasir Minhas, Nabeel Tahir Butt, Chaudhry Raheel Ranjha, Muhammad Rashid Iqbal, Mobeen Ikram, Qaim Ali Bhatty

Department of Anesthesiology, Combined Military Hospital Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare the analgesic efficacy of nebulized Ketamine with intravenous Paracetamol versus Paracetamol alone for post-operative analgesia in pediatric cases undergoing general anesthesia for elective tonsillectomy as a day care procedure

Study Design: Quasi-experimental study

Place and Duration of Study: Department of Anesthesiology, Combined Military Hospital Rawalpindi, Pakistan from Jan-Jul 2022.

Methodology: Participants in Group-K received intravenous Paracetamol 10 mg/kg with nebulized Ketamine 2 mg/kg diluted in 5 ml given over 5 minutes 15 minutes before induction whereas Group-P received intravenous Paracetamol 15 mg/kg with nebulization with 5 ml Normal Saline as placebo 15 minutes before the procedure.

Results: Post-operative median pain scores calculated in the recovery showed median pain score of 4.00 (IQR=0.00) in Group-P versus 2.00 (IQR=0.00) in Group- K (p<0.001) assessed at 30 minutes. The same scores assessed at 60 minutes showed median pain score of 6.00 (IQR=0.00) in Group-P versus 4.00 (IQR=0.00) in Group -K (p<0.001) and pain scores at 120 minutes showed median score of 6.00 (IQR=0.00) in Group-P versus 4.00 (IQR=2.00) in Group-K (p<0.001).

Conclusion: We conclude that nebulized Ketamine offers better analgesia with improved pain scores and better per-operative hemodynamic stability when compared with NSAIDs alone.

Keywords: Analgesia, Day-care anesthesia, Ketamine, Nebulized, Paracetamol, Tonsillectomy

How to Cite This Article: *Minhas HN, Butt NT, Ranjha CR, Iqbal MR, Ikram M, Bhatty QA. Comparison of Nebulized Ketamine with Intravenous Paracetamol Versus Paracetamol Alone For Post-Operative Analgesia In Pediatric Day Care Anesthesia. Pak Armed Forces Med J 2026; 76(1): 17-20. DOI: https://doi.org/10.51253/pafmj.v76i1.10665*

INTRODUCTION

Pediatric anesthesia is both difficult and challenging for the anesthetist. From anatomical differences to modified physiology when compared to the adult, pediatric anesthesia must be given with extra vigilance and requires continuous monitoring.[1] When giving anesthesia to these patients, care must be taken about the type and the doses of the drugs given.[2] With the advent of the concept of day care anesthesia, many procedures of the pediatric group are increasingly being done as day care cases with the patient expected to make a full recovery and stable enough to be sent home the same day.[3] This makes it challenging in certain cases when the drugs used for routine anesthesia in these patients prolong the recovery time for the patient to be sent home as a day care case.[4]

Pain is one of the chief complaints of the patient in the post-anesthesia care unit and opioids are generally not preferred in full physiological doses or omitted to hasten the sedative recovery of patients so they can be sent home.[5] This acts as a double-edged sword; while preventing the incidence of deep sedation and respiratory depression, inadequate pain relief can result in failed early recovery and possible admission in certain cases.[6] Alternate drugs have been proposed in day care procedures to provide opioid free analgesia. These include Lignocaine, Dexmedetomidine and Ketamine.[7] Even though ketamine has found itself as an established agent for induction with added analgesic effect in the intravenous form, it's sedative and analgesic efficacy in the nebulized form has been proposed recently with scarce literature especially in the pediatric age group. Since the intravenous form is associated with hypertension, tachycardia and post-operative delirium, the nebulized form needs to be studied further to see whether it provides acceptable analgesia as an adjunct to non-sedative analgesics for use in day care procedures, where opioids are to be avoided for better patient compliance without compromising pain relief.[8]

Correspondence: Dr Hassan Nasir Minhas, Department of Anesthesiology, Combined Military Hospital Rawalpindi Pakistan

Received: 21 Jul 2023; revision received: 01 Nov 2023; accepted: 02 Nov 2023

This study aimed to study the analgesic efficacy of the nebulized form Ketamine with intravenous Paracetamol versus Paracetamol alone for post-operative analgesia in pediatric cases undergoing general anesthesia for elective tonsillectomy as a day care procedure.

METHODOLOGY

This Quasi-experimental study was carried out at the Department of Anesthesiology, Combined Military Hospital Rawalpindi, Pakistan from Jan-Jul 2022 after approval form the ethical review board (vide Sr no.261/2021). A total of 190 patients (WHO minimum sample size 181) were included in the study keeping the confidence interval at 95%, margin of error at 5% with the incidence of pediatric elective tonsillectomy as a day care procedure at 13.6%9. The method of sampling was non-probability consecutive sampling by lottery method.

Inclusion Criteria: All ASA-I and II male and female pediatric patients aged 7-12 years coming to the pre-anesthesia clinic for elective tonsillectomy as a day care procedure were included.

Exclusion Criteria: Patients with any co-morbidity requiring admission, history of upper or lower respiratory tract infection in the last 2 weeks, major cardiovascular abnormalities and non-consenting patients were excluded.

The study method included all patients as per the inclusion criteria furnished. Patients were divided into two groups: Group- K (n=95) and Group-P (n=95) with Group-P to receive intravenous Paracetamol 10 mg/kg pre-operatively while Group- K to receive pre-operative intravenous Paracetamol at 10 mg/kg along with nebulized Ketamine at 2 mg/kg 15 minutes before induction. (Figure)

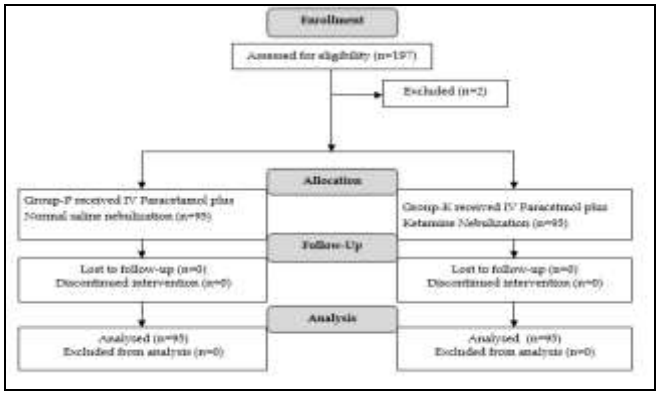

Figure: Phases of Study

Patients were received in the recovery room 1 hour before the procedure. Consent was obtained from parents/guardians. Double-blind method was used to put the patients in 2 groups to prevent bias. Participants in Group-K received intravenous Paracetamol 10 mg/kg with nebulized Ketamine 2 mg/kg diluted in 5 ml given over 5 minutes 15 minutes before induction whereas Group-P received intravenous Paracetamol 15 mg/kg with nebulization with 5 ml Normal Saline as placebo 15 minutes before the procedure. The anesthetist preparing the solutions was given sealed non-descript bottles with the nebulizing preparations and the trainee in the operating room did not know of the drug in the nebulizer while also unaware of the study protocol.

Anesthesia was induced in both groups with intravenous Propofol 2 mg/kg and maintained with Isoflurane at 1 MAC, paralysis done with Atracurium 0.5 mg/kg and maintained with bolus doses 0.1 mg/kg. At the end of the procedure, reversal of residual neuromuscular block was done with intravenous Neostigmine 0.04 mg/kg and Glycopyrrolate 0.01 mg/kg. Patients were kept in the recovery room post-procedure and discharged according to the PADSS scoring system[10].

Primary variables measured were mean heart rate and mean arterial pressure, 10 minutes post-surgical incision per-operatively to assess for response to pain during surgical stress and median pain scores post-operatively at 15, 30 and 120 minutes after the procedure in PACU (post-anesthesia care unit) by a standardized Wong Baker faces scale by the anesthetist.[11]

Demographic data were statistically described in terms of mean and SD. Independent samples t-test was used evaluate mean values for heart rate and MAP. Statistical significance between median pain scores was calculated using Mann Whitney U test. A p value of <0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.00.

RESULTS

A total of 190 patients were included in the study protocol divided into Group-P (n=95) and Group-K (n=95). Mean age of patients was 9.37±1.45 years in Group-P versus 9.12±1.41 years in Group-K (p=0.228). Mean duration of surgery was 38.00±4.75 minutes in Group-P versus 37.10±4.62 minutes in Group-K (p=0.190) (Table-I).

When analyzing the primary per-operative parameters for pain due to surgical stress, mean heart rate was 94.76±2.63 beats per minutes versus 88.27±2.88 beats per minutes between Group-P and K respectively (p<0.001). Mean arterial pressure was 84.81±2.16 mm Hg in Group-P versus 84.89±2.23 mm Hg in Group-K (p=0.869) (Table-II).

Post-operative median pain scores calculated in the recovery showed median pain score of 4.00 (IQR=0.00) in Group-P versus 2.00 (IQR=0.00) in Group-K (p<0.001) assessed at 30 minutes. The same scores assessed at 60 minutes showed median pain score of 6.00 (IQR=0.00) in Group-P versus 4.00 (IQR=0.00) in Group-K (p<0.001) and pain scores at 120 minutes showed median score of 6.00 (IQR=0.00) in Group-P versus 4.00 (IQR=2.00) in Group-K (p<0.001) (Table-II).

Table-I: Demographic and Per-Operative Parameters of both Groups (n=190)

Variable(s)	Group-P (n=95)	Group-K (n=95)	*p* value
Mean Age (Years)	9.37±1.45	9.12±1.41	0.228
Mean Duration of Surgery (Minutes)	38.00±4.75	37.10±4.62	0.190
Mean Heart Rate (Beats Per Minute)	94.76±2.63	88.27±2.88	<0.001
Mean Arterial Pressure (Mm Hg)	84.81±2.16	84.89±2.23	0.869
Gender			
Male	72 (75.8%)	23 (24.2%)	-
Female	71 (74.7%)	24 (25.3%)	

Table-II: Comparison of Median Pain Scores Among Groups (n=190)

Median Pain Scores	Group-P (n=95)	Group-K (n=95)	*p* value
30 Min Post-Procedure	4.00 (IQR=0.00)	2.00 (IQR=0.00)	<0.001
60 Min Post-Procedure	6.00 (IQR=0.00)	4.00 (IQR=0.00)	<0.001
120 Min Post-Procedure	6.00 (IQR=0.00)	4.00 (IQR=2.00)	<0.001

DISCUSSION

The results of our study showed that nebulized Ketamine offered better analgesia with improved pain scores and better per-operative hemodynamic stability when compared with NSAID alone.

Day care anesthesia has now been adopted by various medical setups to decrease patient stay in the hospital resulting in better patient recovery and early mobilization to home[12]. Various ERAS protocols adopted along with selected anesthesia care aim to decrease post-operative recovery times and early discharge practices to ensure that patient can be sent home on the same day of surgery[13].

Ketamine is an NMDA receptor antagonist and has been used outside of the operating room for the treatment of migraine, asthma and as an attractive adjunct to opioid free analgesia[14]. Our study aimed at finding out the efficacy of the nebulized form of the drug and whether it provided any advantages over intravenous form with respect to its side effect profile and its comparison to the commonly used non-opioid analgesics in the pediatric age group. The use of opioids in the pediatric age groups especially for day care surgery has not gained wide acceptance due to its incidence of respiratory depression, nausea and vomiting and deep sedation resulting in longer hospital stay and requiring possible admission overnight[15].

A study carried out by D Dove *et al*[16] found that pain scores for analgesia in the emergency room through the nebulizer route offered better and improved pain toleration. An added finding was seen that increasing doses did not have a linear relationship with improvement of pain and physiological doses at 2 mg/kg offered the same analgesic efficacy when doses were increased. Similar study to see the efficacy of the nebulized route for minor dental procedures for the pediatric age group as day cases showed that pre-procedure nebulization resulted in better patient comfort and improved pain scores[17]. International studies for short ENT procedures also recommended that nebulized ketamine is an attractive adjunct to non-opioid analgesic for early discharge of patients8. Local studies done for the same were conclusive in finding better analgesia as well as decreased incidence of sore throat after general anesthesia in patients. This confers added benefit to the anesthetist to recommend the regime in prolonged surgeries where intubation inadvertently ends in sore throat causing considerable patient discomfort[18]. When comparing nebulized route of Ketamine with nebulized corticosteroids, there was a comparable analgesic efficacy, however, the incidence of sore throat was less with Ketamine and the recommendation of inhalational corticosteroids has still not gained wide acceptance[19].

RECOMMEDATION

The study recommends the use of inhaled Ketamine as an excellent adjunct for short procedure

analgesia for pediatric age group undergoing day care surgeries.

CONCLUSION

We conclude that nebulized Ketamine offers better analgesia with improved pain scores and better per-operative hemodynamic stability when compared with NSAIDs alone.

LIMITATION OF STUDY

The limitations are that the study is single center only. A multi-center study would result in a wider demographic area with more confirmative results. The study does not include pediatric age group below 6 years of age and further studies would be needed to see analgesic efficacy in the group.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HNM & NTB: Data acquisition, data analysis, critical review, approval of the final version to be published.

CRR & MRI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MI & QAB: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Cote C, Lerman J, Anderson B. Coté and Lerman's :A practice of anesthesia for infants and children: 6th Ed. Philadelphia Elsevier; 2019.
2. Grubb TL, Perez Jimenez TE, Pettifer GR. Neonatal and pediatric patients. Veterinary Anesthesia and Analgesia: Lumb and Jones: 5th Ed; 2015: 983-987.
3. Butz SF. Pediatric ambulatory anesthesia challenges. Anesthesiol Clin 2019; 37(2): 289-300. https://doi.org/10.1016/j.anclin.2019.01.002
4. Almaz ME, Oba AA, SÖNMEZ IŞ. Postoperative morbidity in pediatric patients following dental treatment under general anesthesia. Eur Oral Res 2019; 53(3): 113-118. https://doi.org/10.26650/eor.20190023
5. Suandika M, Muti RT, Tang W-R, Haniyah S, Astuti D. Impact of Opioid-Free Anesthesia on Nausea, Vomiting and pain Treatment in Perioperative Period: A Review. Bali Med J 2021; 10(3): 1408-1414.
6. Cravero JP, Agarwal R, Berde C, Birmingham P, Coté CJ, Galinkin J, et al. The Society for Pediatric Anesthesia recommendations for the use of opioids in children during the perioperative period. Paediatr Anesthes 2019; 29(6): 547-571. https://doi.org/10.1111/pan.13639
7. Siu EY, Moon TS. Opioid-free and opioid-sparing anesthesia. Int Anesthesiol Clin 2020; 58(2): 34-41. https://doi.org/10.1097/aia.0000000000000270
8. Abdel-Ghaffar HS, Abdel-Wahab AH, Roushdy MM, Osman AM. Preemptive nebulized ketamine for pain control after tonsillectomy in children: randomized controlled trial. Braz J Anesthesiol 2019; 69: 350-357. https://doi.org/10.1016/j.bjane.2019.04.005
9. Šumilo D, Nichols L, Ryan R, Marshall T. Incidence of indications for tonsillectomy and frequency of evidence-based surgery: a 12-year retrospective cohort study of primary care electronic records. Br J Gen Pract 2019; 69(678): e33-e41. https://doi.org/10.3399/bjgp18X699833
10. Fang L, Wang Q, Xu Y. Postoperative Discharge Scoring Criteria After Outpatient Anesthesia: A Review of the Literature. J PeriAnesth Nurs 2023: 38(4): 642-649. https://doi.org/10.1016/j.jopan.2022.11.008
11. Chandran R. Pain assessment in children using a modified wong baker faces pain rating scale. Int J Clin Prevent Dent 2019; 15(4): 202-205. https://doi.org/10.15236/ijcpd.2019.15.4.202
12. Bhatia A, Buvanendran A. Anesthesia and postoperative pain control—multimodal anesthesia protocol. J Spine Surg 2019; 5(Suppl 2): S160-S165. https://doi.org/10.21037%2Fjss.2019.09.33
13. Smith Jr TW, Wang X, Singer MA, Godellas CV, Vaince FT. Enhanced recovery after surgery: a clinical review of implementation across multiple surgical subspecialties. Am J Surg 2020; 219(3): 530-534. https://doi.org/10.1016/j.amjsurg.2019.11.009
14. Pribish A, Wood N, Kalava A. A review of nonanesthetic uses of ketamine. Anesthesiol Res Pract 2020; 2020: 5798285. https://doi.org/10.1155/2020/5798285
15. Mehrotra S. Postoperative anaesthetic concerns in children: Postoperative pain, emergence delirium and postoperative nausea and vomiting. Indian J Anaesth 2019; 63(9): 763-770. https://doi.org/10.4103%2Fija.IJA_391_19
16. Dove D, Fassassi C, Davis A, Drapkin J, Butt M, Hossain R, et al. Comparison of nebulized ketamine at three different dosing regimens for treating painful conditions in the emergency department: a prospective, randomized, double-blind clinical trial. Ann Emerg Med 2021; 78(6): 779-787. https://doi.org/10.1016/j.annemergmed.2021.04.031
17. Zanaty OM, El Metainy SA. A comparative evaluation of nebulized dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery. Anesth Analg 2015; 121(1): 167-171. https://doi.org/10.1213/ane.0000000000000728
18. Zia R, Iqbal S, Khan MBA, Butt MM, Nazeer T, Hanif MZ. Post Operative Sore Throat (POST), Comparison Between Nebulization with Ketamine and Placebo. Pak J Med Health Sci 2022; 16(5): 1036-1038. https://doi.org/10.53350/pjmhs221651036
19. Kuriyama A, Maeda H, Sun R. Aerosolized corticosteroids to prevent postoperative sore throat in adults: A systematic review and meta-analysis. Acta Anaesthesiol Scand 2019; 63(3): 282-291. https://doi.org/10.1111/aas.13275