

KETAMINE IMPROVES POSTOPERATIVE PAIN
AND EMERGENCE AGITATION FOLLOWING
ADENOTONSILLECTOMY IN CHILDREN.
A RANDOMIZED CLINICAL TRIAL

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Abstract

Background: Management of postoperative pain and emergence agitation following adenotonsillectomy in pediatrics has been a major challenge for anesthesiologists. Although analgesic sparing effect of ketamine has been studied during tonsillectomy in pediatrics, there is a lot of controversy about its efficacy. Present study was designed to evaluate the effect of intravenous low dose ketamine (0.25mg/kg) during induction of anesthesia on postoperative pain and emergence agitation following adenotonsillectomy in children.

Methods: In this randomized clinical trial 66 children aged 5 to 15 years who underwent elective adenotonsillectomy were randomly allocated into two groups. Patients in the control group received 5ml of normal saline while patients in the ketamine group received 0.25 mg/kg of ketamine in 5 ml volume during induction of anesthesia. After termination of surgeries and transferring the patients to recovery, emergence agitation, pain score, paracetamol requirements and incidence of postoperative nausea & vomiting were assessed every hour for 6 hours.

Results: Emergence agitation score was significantly lower in the ketamine group ($P=0.002$). Pain score at all hours was lower in the ketamine group than the control group ($P<0.05$). The requirements for intravenous paracetamol were significantly lower in the ketamine group ($P=0.0036$). There was no difference in the incidence of postoperative nausea and vomiting between the two groups ($P=0.99$).

Conclusion: Low-dose ketamine during induction of anesthesia improves emergence agitation and postoperative pain following adenotonsillectomy in children.

Conflict of interest: None.

Key words: Ketamine; Postoperative pain; Tonsillectomy; Children.

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Introduction

Adenotonsillectomy is one of the most common surgeries in pediatric age group¹. This procedure is usually associated with immediate moderate to severe postoperative pain and agitation that causes bleeding², laryngospasm, and delays discharge from recovery³. Traditionally opioids have been used for management of pain that have many complications such as respiratory depression specially in these patients with edema at the operative site that may cause airway obstruction and hypoxemia, nausea and vomiting and even central sensitization^{4,5,6}.

Other analgesics recommended for control of postoperative pain in adenotonsillectomy include local anesthetics, nonsteroidal anti-inflammatory drugs (NSAID) and N-methyl-D-aspartate receptor antagonist^{7,8,9}. Local anesthetics and NSAID are associated with vasoconstriction and increased risk of bleeding at site of operation respectively^{9,10}. Ketamine hydrochloride is a noncompetitive antagonist of NMDA receptors¹¹. In adult patients, it was found that ketamine has both analgesic-sparing and antisensitization effects^{12,13}. Although analgesic sparing effect of Ketamine has been studied both locally and

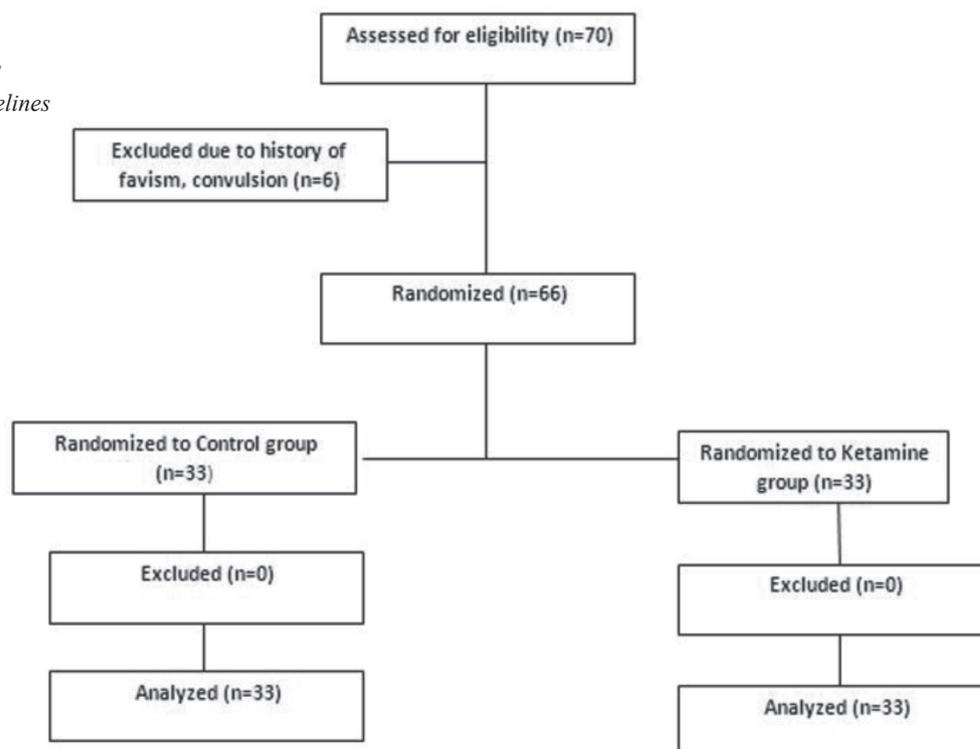
systemic during tonsillectomy in pediatrics¹⁴, there is a lot of controversy about its efficacy^{15,16}.

The aim of the present study is to determine the effect of intravenous low dose ketamine (0.25mg/kg) on postoperative pain score, needs to paracetamol as a rescue analgesic following adenotonsillectomy in pediatric patients.

Methods: In this double blind randomized control trial, seventy pediatric patients aged 5 -15 years old who underwent elective adenotonsillectomy were enrolled in this study. Patients with history of convulsion, high intracranial pressure, common cold, favism, congenital heart disease, hypersensitivity to paracetamol or ketamine and pediatrics with developmental or cognitive disorder were excluded from the study. After our institutional board approval, written informed consent was obtained from parents. Eligible pediatric patients were randomly allocated in two groups by computer base program, the ketamine group and the control group (Figure 1).

Upon arrival of patient to operating room, routine monitors including: blood pressure, electrocardiogram and pulse oximetry were applied to all children. Anesthesia was induced with intravenous sodium

Fig. 1
Flowchart of the patients
according to the consort guidelines



thiopental 5-7mg/kg and 0.6mg/kg atracurium as muscle relaxant. In the ketamine group, patients received ketamine 0.25 mg/kg in 5 ml total volume and in the control group, patients received physiologic normal saline in 5 ml total volume. A nurse in anesthesia prepared the ketamine and placebo drugs in two identical 5 ml syringes. At induction of anesthesia, an anesthesiologist unaware of the prepared drug delivered the solution as per the allocation of the patients to the relevant groups. After oral endotracheal intubation, general anesthesia was maintained with 1.2% isoflurane, 50% N2O in oxygen and controlled ventilation to maintain end tidal about CO2 30-35 mmHg. Adenotonsillectomy was done by dissection by the same surgeon and upon the end of operation and discontinuation of general anesthesia the patients were transferred to recovery room and remained intubated till became fully awake. Emergence from anesthesia was recorded by same resident from anesthesia who was blinded to the groups of patients. Emergence agitation was assessed using a simple assessment scale as follows: 1: asleep; 2: awake but calm; 3: agitated but comfort; and 4: severely agitated and difficult to comfort. Then pain score of both groups was assessed ten minutes after extubation using the Baker-Wong faces pain rating scale every one hour till six hours after extubation. The Wong-Baker FACES Pain scale is often useful for assessing pain in patients who do not have ability to use language to describe pain. This scale uses faces: Face 0 is very happy because he doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little more. Face 6 hurts even more. Face 8 hurts a whole lot. Face 10 hurts as much as you can imagine (Figure 2).

If pain score was ≥ 4 then patients received 15mg/kg intravenous paracetamol as rescue analgesic. Postoperative nausea and vomiting (PONV) were

recorded every one hour during these six hours. Vomiting was defined as the forceful expulsion of gastric contents from the mouth and was brought about by the powerful sustained contraction of the abdominal muscle; nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.

Statistical analysis

By using the power static software collection (SSC), sample size calculation was based on the assumption that the primary end point was the number of patients required paracetamol as a rescue analgesic in postoperative period. Power calculations indicated with a power of 80% and α level of 0.05, a sample size for each group of at least 33 patients (total of 66patients) would detect a 50% reduction in number of patients that required rescue analgesic drug during the first 6 hours post operation.

The data were prospectively transferred into a computer database for further analysis by SPSS for Windows; Version 19.0 (SPSS Inc., Chicago, IL, USA). Independent t-test and chi- square was used to compare sex, weight, age between two groups. For test hypothesis, chi-square, t test and Mann- Whitney U were used. Data were reported as means \pm SD. The statistical significance was considered at $P < 0.05$.

Results

Sixty six pediatric patients undergoing elective adenotonsillectomy, were randomly allocated to the ketamine group (n=33) and the control group (n=33). There were no significant differences in the demographic variables in the two groups (Table 1).

Fig. 2
Wong-Baker FACES Pain Rating Scale



Table 1
Demographic data in both groups

	Control Group(n=33)	Ketamine Group(n=33)	P Value
Age(Years)	8.24±3.07	9.12±3.29	0.07
Weight(Kg)	25.67±12.95	28.41±9.65	0.33
Sex(M/F)	20/13	19/14	0.80

The pain scores during the first 6 postoperative hours were significantly lower in the ketamine group compared to the control group (Figure 3). The percentage of patients requiring paracetamol for postoperative pain control was significantly lower in the ketamine group compared to the control group (Table 2).

Fig. 3

Postoperative pain intensity in the ketamine and control both groups during six hours post-operation

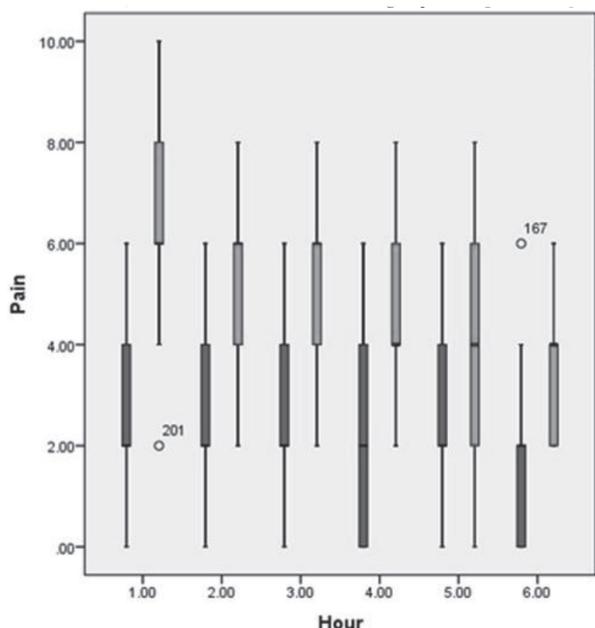


Table 2

Postoperative emergence, nausea and vomiting, and paracetamol use in both groups

	Control Group(n=33)	Ketamine Group(n=33)	P Value
Agitation Score(1:2:3:4)	3:0:17:13	14:9:7:3	0.002
PONV	4(12.1)	5(15.1)	0.996
Paracetamol Use (number of patients)	24(75%)	12(36.4%)	0.003

Emergence agitation score: 1: asleep; 2: awake but calm; 3: agitated but comfortable; and 4: severely agitated and difficult to become comfortable. PONV: Postoperative nausea and vomiting.

Furthermore emergence agitation was lower in the ketamine group than the control group and this differences were statistically significant between two groups (P=0.002) (Table 2).

There was no significant difference between two groups regarding incidence of the postoperative nausea and vomiting (P=0.996) (Table2).

Discussion

The present study showed that intravenous low dose ketamine (0.25 mg/kg) at induction of anesthesia may reduce postoperative pain, reduce paracetamol need as a rescue analgesic, and reduce emergence agitation.

Abu-Shahwan showed that ketamine 0.25mg/kg at induction time did not decrease postoperative pain in pediatric patients undergoing tonsillectomy¹⁵. Batra et al in another study found that postoperative pain score after tonsillectomy in pediatric patients was not decreased by small dose ketamine¹⁶. However, all these studies used remifentanyl in the maintenance of anesthesia which could have made ketamine effective in reducing postoperative pain¹⁷. DA Conceição et al reported that a single small dose of ketamine (0.5mg/kg) in the pediatric patients undergoing tonsillectomy could reduce postoperative pain and use of rescue analgesia¹⁸. Likewise Murray et al concluded that ketamine (0.5 mg/kg) was effective in reducing postoperative pain in pediatric population undergoing tonsillectomy¹⁹. In our study a further decrease in the ketamine dose e (0.25mg/kg) was effective in reducing postoperative pain and in reducing rescue analgesic usage.

Emergence agitation in pediatric population undergoing adenotonsillectomy remains a major problem. Emergence agitation is reflected by self aggressive movement during emergence of anesthesia in recovery room²⁰. Yoon Sook Lee et al found that ketamine was effective in the prevention of emergence agitation without delay in awakening and both sub-hypnotic doses of ketamine 0.25 and 0.5 mg/kg were effective²¹. Also Kararmaz et al concluded that oral ketamine was effective in reducing incidence of emergence agitation²². Similarly in the present study we showed that low dose ketamine (0.25mg/kg) is effective in preventing of emergence agitation in pediatric patients following adenotonsillectomy.

The incidence of postoperative nausea and vomiting (PONV) after adenotonsillectomy is more than 70% and may cause serious complications such as pulmonary aspiration, hypoxemia, increase chance of bleeding^{23,24} and may cause unplanned hospitalization in 3-4.7% of patients²⁵. This complication may result from using opioids^{26,27}. Hasnain et al in their study that compared ketamine with morphine for management

of postoperative pain following tonsillectomy in pediatrics reported that postoperative nausea and vomiting in the ketamine group was significantly less than the morphine group²⁸. The other studies that used low dose ketamine to decrease postoperative pain showed that low dose ketamine did not increase the incidence of PONV^{29,30}. Similarly, the current study showed that the incidence of PONV did not increase in the ketamine group as compared to the control group.

In conclusion intravenous low dose ketamine (0.25mg/kg) was effective in reducing postoperative pain following adenotonsillectomy in pediatric patients, in decreasing incidence of emergence agitation, and in decreasing the incidence of PONV in these patients.

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