

THE USE OF NEBULIZED KETAMINE TO REDUCE THE INCIDENCE AND SEVERITY OF POSTOPERATIVE SORE THROAT IN ADULT PATIENTS

Dr. Lina Ahmed Ridha^{1*}, Dr. Aimen Hameed Latif² and Dr. Ahmed Al-Mantafji¹

¹MBChB, FICMS, Specialist of Anesthesia and Intensive Care, Baghdad Teaching Hospital, Baghdad, Iraq.

²MBChB, D A, FICMS, Consultant Anesthesiologist, AlYarmook Teaching Hospital, Baghdad, Iraq.

Article Received date: 25 September 2024

Article Revised date: 15 October 2024

Article Accepted date: 05 November 2024



*Corresponding Author: Dr. Lina Ahmed Ridha

MBChB, FICMS, Specialist of Anesthesia and Intensive Care, Baghdad Teaching Hospital, Baghdad, Iraq.

ABSTRACT

Background: Endotracheal intubation is the prominent cause of airway mucosal injury which results in the postoperative sore throat (POST), In spite of it is a minor complication, if left without management, it produces significant dissatisfaction to the patient. **Aim of the study:** To assess the efficacy of ketamine nebulization in decreasing POST incidence with Endotracheal intubation. **Patient and Methods:** 70 patients undergoing General Anesthesia with endotracheal intubation participated in this prospective, randomized, placebo-control, and double-blind study. Patients were randomized into two groups, Group One were given ketamine 50 mg (1.0 ml) with 4.0 ml of normal saline nebulization, while Group 2 were given normal saline nebulization (5.0 ml) for 15 min both, POST assessment was started once patients had reached the recovery room at 0, 2, 4, 6, 12, and 24 hours after extubating, POST was graded on a four-point scale (0,1,2,3). **Results:** The incidence and severity of POST were significantly less in the ketamine group with time interval in compared with the 2nd group. There was a statistically significant lowering in the incidence of POST in the ketamine group when compared to saline, at 2, 4, 6,12, and 24 h postoperatively ($P < 0.05^*$), The severity of sore throat was also higher in the saline group when compared to ketamine at all time interval. **Conclusion:** Preoperative ketamine nebulization effectively reduced the incidence and severity of POST, with no adverse effects.

KEYWORDS: General anesthesia; intubation; ketamine; nebulization; sore throat.

INTRODUCTION

Despite rapid advancement in anesthetic techniques, sore throat following endotracheal intubation still is a long-standing concern for anesthesiologists^[1] the etiology is multifactorial, including patient-related factors such as age, sex, smoking, and intubation factors including technique, duration, tube size, intracuff pressure, cuff design, intraoperative tube movement, and suctioning.^[2]

Tracheal intubation is the foremost cause of trauma to the airway mucosa, resulting in the postoperative sore throat (POST) with a reported incidence of 21–65%^[3], Even though it is a minor complication, POST contributes to postoperative morbidity and patient dissatisfaction, POST had been rated by patients as the eighth-most adverse effect in the postoperative period. Various non-pharmacological and pharmacological trials have been used for attenuating POST with variable success.

Among the non-pharmacological methods, smaller-sized endotracheal tubes, lubricating the endotracheal tube with water-soluble jelly, careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, minimizing intra cuff pressure, and extubating when the tracheal tube cuff is fully deflated have been reported to decrease the incidence of POST.^[4] There is an increasing amount of experimental data showing that NMDA receptors are found not only in the central nervous system (CNS) but also in the peripheral nerves. Moreover, experimental studies point out that peripherally administered NMDA receptor antagonists are involved with antinociception^[5] and anti-inflammatory cascade.

It's noted that N-methyl -d-aspartate (NMDA) has a role in nociception and inflammation.^[6] Ketamine, an NMDA receptor antagonist has been used for decreasing POST because of its anti-nociceptive and anti-inflammatory action, as gargle as well as in nebulized form^[7], However, nebulized ketamine is better tolerated in

patients due to many reasons such as it saves the patient from the bitter taste of ketamine, also much lesser volumes required for gargle, this study was undertaken to evaluate the effectiveness of nebulization.

POST was graded on a four-point scale (0–3)^[8]

0 = no sore throat

1 = mild sore throat (complains of sore throat only on asking).

2 = moderate sore throat (complains of sore throat on his/her own).

3 = severe sore throat (change of voice or hoarseness, associated with throat pain).

Ketamine mainly used for starting and maintaining anesthesia, It induces a trance-like state while providing pain relief, sedation, and memory loss, Other uses include for chronic pain, sedation in intensive care, breathing and airway reflexes generally remain functional^[9], Effects typically begin within five minutes when given by injection and last up to about 25 minutes.

Common side effects include agitation, confusion, or hallucinations as the medication wears off^[10] and elevated blood pressure, Ketamine is an NMDA receptor antagonist, but it may also have other actions.^[11]

Ketamine was discovered in 1962, first tested in humans in 1964, and was approved for use in the United States in 1970, It was extensively used for surgical anesthesia in the Vietnam War due to its safety, It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system.

Aim of the study

To assess the efficacy of ketamine nebulization in decreasing POST incidence with Endotracheal intubation.

PATIENT AND METHODS

This study is prospective randomized double-blind clinical trial was conducted at Baghdad teaching hospital, medical city, Baghdad, Iraq, which started in 1st of February 2019 to 30th of October 2019.

Inclusion criteria

- They are ASA I and II.
- Age 18- 60 years.
- Weight ranging from 50 -100 kg from either gender.
- Blood pressure within the normal range.
- Expected duration of surgery from 30 minutes to 2 hours.

Exclusion criteria were:

- Patients with a history of preoperative sore throat.
- Upper respiratory tract infection.
- Chronic obstructive and restrictive pulmonary disease.
- Any contraindication to the drugs used in this study.
- Pregnant ladies.

- Suspected difficult to intubation.
- Oral, nasal, head-and-neck surgeries.
- Any patient on steroid or antihistamine drugs.

After approval of the scientific council of Iraqi Board, and the consent was obtained from all patients before included them in the study. A detailed history was taken from each patient's clinical examination was performed preoperatively.

The patient's baseline measurement of hemodynamic parameters blood pressure, pulse rate, oxygen saturation was recorded.

The patients enrolled for this study were kept fasting for 6 h preceding surgery.

Using sealed numbered cards were prepared by me, by which patients were randomized into two groups.

After opening the cards, the anesthesia assistant prepared the nebulized solution according to group allocation, the assistant who prepared the solution did not have a role in assessing the patients, Patients were blinded regarding the type of nebulized solution.

The enlisted 70 patients were randomly allocated into two groups of 35 each

Group 1: received ketamine 50 mg (1 ml) with saline (4 ml) nebulization for 15 minutes.

Group 2: received normal saline nebulization (5 ml), for 15 min (min).

On arrival at the operating room, wide-bore IV cannula inserted, All patients received 50mg ranitidine, 10mg metoclopramide, 8mg Dexamethasone.

The monitors including (pulse rate (PR), noninvasive BP, SpO₂, electrocardiogram (ECG), end-tidal CO₂ (ET CO₂).

General anesthesia was induced after completing nebulization, with intravenous (IV) 1 mg midazolam, IV ketamine 0.5mg/kg, IV propofol 2 mg/kg, IV rocuronium bromide 0.5 mg/kg.

Intubation was done smoothly with proper size ETT and its cuff inflated just to prevent air leak.

GA was maintained with oxygen and isoflurane. Analgesia during surgery was supplemented with paracetamol 1 g IV and Nefopam 20mg.

At the end of the surgery, patients oropharynx was gently suctioned with as minimal instrumentation as possible, Residual neuromuscular blockade was antagonized using neostigmine 2.5mg and atropine 1.2mg.

Each patient's trachea was extubated on the return of spontaneous respiration and the following ability to obey

the verbal command or have a sustained head lift for 5 seconds.

After extubation, each patient was transported to the recovery room for further observation and monitoring of vital signs.

Patients were asked for the presence of pain on swallowing as a symptom of postoperative sore throat or throat pain when patients fully awake, prior to discharge toward, who do the assessment was unaware of the group allocation of the patient.

Assessment starts at 0 hours in a recovery room and later in the ward at 2, 4, 6, 12, and 24 h postoperatively.

POST was graded on a four-point scale (0–3)
 0 = no sore throat
 1 = mild sore throat (complains of sore throat only on asking).
 2 = moderate sore throat (complains of sore throat on his/her own).
 3 = severe sore throat (change of voice or hoarseness, associated with throat pain).

Statistical Analysis

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25, The data presented as mean, standard deviation and ranges, Categorical data presented by frequencies and percentages.

Pearson’s Chi-square test was used to assess the statistical association between study groups and postoperative sore throat development, A level of P – value less than 0.05 was considered significant.

Differences in sex, age, gender, weight, and duration of surgery were done by using the student t-test.

ASA grading and differences in the incidence of POST were analyzed using Fisher’s exact t-test or Chi-square test and Odd ratio.

RESULTS

The total number of study patients was 70, all of them were undergone elective surgical procedures under general anesthesia.

Before giving GA, 35 patients were received ketamine nebulizer solution (Group A) (for prevention of postoperative sore throat), other 35 patients were received normal saline nebulizer (Group B).

Both groups were comparable in the distribution of age, gender, body weight, ASA 1&2, blood pressure, pulse rate and duration of surgery, we noticed that there was no statistically significant difference [Table1], [Figure 1].

Table 1: Descriptive and statistical tests of demographic variables among groups.

Parameters	Groups				T-test	p value
	Ketamine		Saline			
	Mean	SD	Mean	SD		
Age	35.2	12.35	38.4	9.4	1.217	0.228
Sys. BP	129.71	14.035	131.34	11.550	0.53	0.598
Dia. BP	74.8	9.1	77.4	7.6	0.53	0.2
PR	87.54	11.97	84.31	12.45	1.29	0.273
Duration	53.86	27.841	68.29	32.96	1.978	0.052
weight	79.31	7.88	82.11	9.27	1.36	0.178

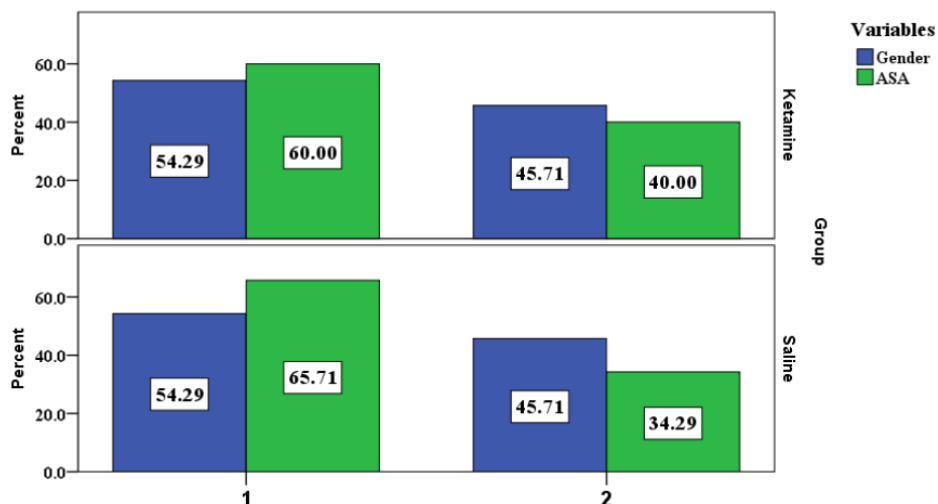


Figure 2: Comparison in the distribution gender, ASA and groups.

The comparison between study groups by postoperative sore throat complain is shown in table {2}, In this study.

• **At zero hour**

71.43% of patients in the control group (Group B) complained from postoperative sore throat while 28.57 % in ketamine group with a highly significant association (P= 0.001) between study groups and development of postoperative sore throat.

• **At 2nd hour**

62.85% of patients in the control group (Group B) complained from postoperative sore throat while 22.86 % in the ketamine group with a highly significant association (P= 0.001) between study groups and development of postoperative sore throat.

• **At 4th hour**

54.29% of patients in the control group (Group B) complained from postoperative sore throat while 14.29% in ketamine group with a highly significant association (P= 0.001) between study groups and development of postoperative sore throat.

• **At 6th hour**

40.00% of patients in the control group (Group B) complained from postoperative sore throat while 14.29 % in ketamine group with a significant association (P=

0.031) between study groups and development of postoperative sore throat.

• **At 12th hour**

37.14% of patients in the control group (Group B) complained from postoperative sore throat while 8.57 % in ketamine group with a highly significant association (P= 0.009) between study groups and development of postoperative sore throat.

• **At 24th hour**

31.43% of patients in the control group (Group B) complained from postoperative sore throat while 5.7 % in ketamine group with a highly significant association (P= 0.011) between study groups and development of postoperative sore throat.

Results illustrate that in all time intervals, the percentage of the presence of the sore throat post-operative in the saline group is higher than with ketamine one with the highly significant association.

Table 2: Association between sore throat and groups in each time interval.

Variables		Group				FEPT*	Odd ratio (K./Saline)	Total	
		Ketamine		Saline				N.	%
		N.	%	N.	%				
0 h	Absent	25	71.43	10	28.57	0.001	6.25	35	50
	Present	10	28.57	25	71.43			35	50
2 h	Absent	27	77.14	13	37.14	0.001	5.71	40	57.14
	Present	8	22.86	22	62.86			30	42.86
4 h	Absent	30	85.71	16	45.71	0.001	7.12	46	65.71
	Present	5	14.29	19	54.29			24	34.29
6 h	Absent	30	85.71	21	60	0.031	4.0	51	72.86
	Present	5	14.29	14	40			19	27.14
12 h	Absent	32	91.43	22	62.86	0.009	6.3	54	77.14
	Present	3	8.57	13	37.14			16	22.86
24 h	Absent	33	94.29	24	68.57	0.011	7.56	57	81.43
	Present	2	5.71	11	31.43			13	18.57

*: FEPT=Fisher exact probability test.

Comparing the severity of POST in both groups, {Table 3}, clarify that the percentage of the absence of the sore throat grade 0 in all-time intervals are higher in the Ketamine group than in the saline one while the grade1 (mild) and the grade 2(moderate score) are higher in the saline than those in the ketamine one with statistically significant association in the first, third and fifth time interval while statistically highly significant association in the other ones.

No patients had a severe sore throat (Grade 3) in both groups. No adverse effects such as nausea, vomiting, cough, stridor, laryngospasm, dry mouth, hoarseness, hallucinations, respiratory depression, or hemodynamic instability were noticed throughout the observation.

Table 3: Association between postoperative sore throat scores of severity and groups.

Variables		Group				FEPT	Total	
Time	POST	Ketamine		Saline			N.	%
		N.	%	N.	%			
0 h	0	25	71.43	10	28.57	0.010	35	50
	1	8	22.86	17	48.57		25	35.71
	2	2	5.71	8	22.86		10	14.29
2 h	0	27	77.14	13	37.14	0.004	40	57.14
	1	5	14.29	15	42.86		20	28.57
	2	3	8.57	7	20		10	14.29
4 h	0	30	85.71	16	45.71	0.012	46	65.71
	1	3	8.57	16	45.71		19	27.14
	2	2	5.71	3	8.57		5	7.14
6 h	0	30	85.71	21	60	0.001	51	72.86
	1	5	14.29	13	37.14		18	25.71
	2	0	0	1	2.86		1	1.43
12 h	0	32	91.43	22	62.86	0.031	54	77.14
	1	3	8.57	12	34.29		15	21.43
	2	0	0	1	2.86		1	1.43
24 h	0	33	94.29	24	68.57	0.001	57	81.43
	1	2	5.71	10	28.57		12	17.14
	2	0	0	1	2.86		1	1.43

DISCUSSION

Post-operative sore throat [POST] related to endotracheal tube may be caused by aseptic inflammation, edema, congestion, pain. It suggested that Ketamine decreases the incidence and severity of POST because of their analgesic and anti-inflammatory effects.

This study showed that preoperative ketamine nebulization (50 mg) for 15 minutes prior to endotracheal intubation has a beneficial effect in the prophylaxis of postoperative sore throat attributable to endotracheal intubation with all-time interval.

So our result show, 50.00% of patients in ketamine group were complained from postoperative sore throat at zero time with a significant association ($P= 0.001$) between study groups and development of postoperative sore throat at zero time, after 2hr We noticed that 42.86% of patients in ketamine group were complained from postoperative sore throat with a significant association ($P= 0.001$) between study groups and development of postoperative sore throat.

After 4 h, 6h, 12h, 24h we noticed that 34.29%, 27.14 %, 22.86%, 13.57%, of patients complained from post-operative sore throat, so the ratio decrease with time interval and this also for severity and that approved the benefit of ketamine nebulization in reducing postoperative sore throat incidence and severity.

Mechanism of action of ketamine could be involved in the explanation of its reducing effect of POST, is its local anesthetic effect and was evidenced in several studies; Tekelioglu et al found that topically applied ketamine to tonsillar fossa for 5 min after tonsillectomy reduce postoperative pain^[13], Kargi et al showed that local

infiltration with 50mg ketamine was similar to 2% lidocaine in tendon repair surgery of the hand.^[14]

Therefore, used the studies of other NMDA antagonists, and by the different route of administration, the study of can bay et al^[15] and the study of Shrestha et al^[16] they found that preoperative gargling with ketamine 50mg reduced the incidence and severity of POST after endotracheal intubation similar to our study. This could be explained by Zhu et al that found that locally administrated ketamine inhibits the inflammatory response as NMDA receptors are present in the CNS and peripheral nerves.^[17]

Another NMDA antagonist, magnesium sulfate, has an anti-inflammatory effect and decreases the inflammatory mediators like histamine and leukotriene^[18] and it's found to be effective in reducing the severity of POST as shown in a study of Gupta et al^[19] he found that preoperative Mg nebulization reduces the incidence of POST.

Also, another NMDA antagonist, Tramadol, involved in reducing the effect of POST, shown in a local study done by Dr. Marwa Najat and her supervisor Consultant Anesthetist prof. Dr. ALI ABDULHAMEED 2019, the Scientific Council of Iraqi Board of Anesthesia and Intensive care^[20], by preoperative gargling with tramadol decreased the incidence and severity of POST inpatient undergoing cesarean section C/S the early postoperative period.

AK bay et al. showed that topical 5% tramadol applied to the tonsillar fossa provides good analgesia after tonsillectomy.^[21]

The criteria of inclusion was well-defined. We nebulized ketamine in this study instead of its other forms, mainly due to the fact that it was safe and easier to administer to the patient, especially at a time immediately before surgery.

CONCLUSION

Preoperative administration of nebulized ketamine effectively attenuated the incidence and severity of POST in patients with endotracheal intubation undergoing General Anesthesia, with no notable adverse effects.

RECOMMENDATIONS

We recommend for using Ketamine nebulizer preoperatively for reduction of postoperative sore throat in general anesthesia with endotracheal intubation.

REFERENCES

- Morgan & Mikhail's, clinical anesthesiology, 5th edition, 2016.
- Lehmann M, Monte K, Barach P, et al. Postoperative patient complaints: a prospective interview study of 12, 276 patients. *J Clin Anesth*, 2010.
- Ahuja V, Mitra S, Sarna R. Nebulized ketamine decreases the incidence and severity of postoperative sore throat. *Indian J Anaesth*, 2015; 59: 37-42.
- Thomas S, Beevi S. Dexamethasone reduces the severity of postoperative sore throat. *Can J Anaesth*, 2007; 54: 897-90.
- Davidson EM, Carlton SM. Intraplantar injection of dextrorphan, ketamine or memantine attenuates formalin-induced behaviors. *Brain Res.*, 1998; 785: 136.
- Zhu MM, Zhou QH, Zhu MH, Rong HB, Xu YM, Qian YN, et al. Effects of nebulized ketamine on allergen-induced airway hyperresponsiveness and inflammation in actively sensitized Brown-Norway rats. *J Inflamm (Lond)*, 2007; 4: 10.
- Rudra A, Ray S, Chatterjee S, Ahmed A, Ghosh S. Gargling with ketamine attenuates the postoperative sore throat. *Indian J Anaesth*, 2009; 53: 40-3.
- Green, Steven M.; Roback, Mark G.; Kennedy, Robert M.; Krauss, Baruch (May 2011). "Clinical Practice Guideline for Emergency Department Ketamine Dissociative Sedation: Update". *Annals of Emergency Medicine*, 2011; 57(5): 449-461.
- Strayer, RJ; Nelson, LS. "Adverse events associated with ketamine for procedural sedation in adults". *American Journal of Emergency Medicine*, 2008.
- Tyler, Marshall W.; Yourish, Harmony B.; Ionescu, Dawn F.; Haggarty, Stephen J. "Classics in Chemical Neuroscience: Ketamine". *ACS Chemical Neuroscience*, 21 April, 2017.
- Domino, EF (September 2010). "Taming the ketamine tiger". *Anesthesiology*, 2010; 113(3): 678-84.
- Almashhadani M.M, Abd Janabi A.H, Kareem M.A Effect of nebulized ketamine in prevention of postoperative pharyngeal pain. *AJMS*, 2023; 9(2): 230-43.
- U.Y. Tekelioglu, T. Apuhan, A. Akkaya, A. Demirhan, I. Yildiz, T. Simsek, U. Gok, H. Kocoglu Comparison of topical tramadol and ketamine in pain treatment after tonsillectomy *Paediatr Anaesth*, 2013.
- E. Kargi, O. Babuccu, H. Altunkaya, M. Hosnuter, Y. Ozer, B. Babuccu, C. Payasli Tramadol as a local anaesthetic in tendon repair surgery of the hand *J Int Med Res*, 2008; 36(5): 971-978.
- O. Canbay, N. Celebi, A. Sahin, V. Celiker, S. Ozgen, U. Aypar, Ketamine gargle for attenuating postoperative sore throat, *Br J Anaesth*, 2008; 100: 490-493.
- S.K. Shrestha, B. Bhattarai, J. Singh, Ketamine gargling and postoperative sore throat, *J Nepal Med Assoc*, 2010; 50(180): 282-285.
- M.M. Zhu, Q.H. Zhou, M.H. Zhu, et al. Effects of nebulized ketamine on allergen-induced airway hyper responsiveness and inflammation in actively sensitized Brown-Norway rats, *J Inflamm (Lond)*, 2007; 4: 10.
- A. Mazur, J.A. Maier, E. Rock, E. Gueux, W. Nowacki, Y. Rayssiguier, Magnesium and the inflammatory response: potential pathophysiological implications, *Arch Biochem Biophys*, 2007; 458: 48-56.
- S.K. Gupta, S. Tharwani, D.K. Singh, G. Yadav, Nebulized magnesium for prevention of postoperative sore throat *Br J Anaesth*, 2012; 108(1): 168-169.
- Dr. Marwa Najat, consultant anasthetist Dr. ALI ABDULHAMEED, the Scientific Council of Iraqi Board of Anesthesia and Intensive care, by preoperative gargling with tramadol decreased the incidence and severity of POST inpatient undergoing cesarean section C/S the early postoperative period, 2019.
- Agarwal A, Nath SS, Goswami D, Gupta D, Dhiraaj S, Singh PK. An evaluation of the efficacy of aspirin and benzydamine hydrochloride gargle for attenuating postoperative sore throat: A prospective, randomized, single-blind study. *Anesth Analg.*, 2006; 103: 1001-3.