

Effects of Nebulized Dexamethasone Versus Nebulized Ketamine on the Attenuation of Post-operative Sore Throat Following Endotracheal Intubation

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Abstract

Background: General anesthesia (GA) with endotracheal intubation is a frequent cause of airway mucosal trauma which results in the post-operative sore throat (POST), with an incidence of 21–65%. Although minor and self-limiting complication, it produces significant discomfort and annoyance to the patient. This study was aimed to compare the efficacy of nebulized dexamethasone versus ketamine in preventing POST.

Materials and Methods: After approval from the institutional ethics committee and written informed consent, 100 patients of the American Society of Anesthesiologists physical status 1–2, aged between 20 and 60 years of either sex, undergoing GA with endotracheal intubation were included in this prospective, randomized, and double-blind study. Patients were randomized into two groups of 50 each ($n = 50$); Group D: Patients received dexamethasone 8 mg (2 ml) with 3 ml of normal saline (total volume of 5 ml) for nebulization and Group K: Patients received ketamine (preservative free) 50 mg (1 ml) with 4 ml of normal saline (total volume of 5 ml) for nebulization. After 15 min of nebulization, induction was done, POST assessment was done at 0, 2, 4, 6, 12, and 24 h post-extubation. The severity of POST was graded on a 4-point scale (0–3).

Results: The total incidence of POST was 19% in this study. Five patients (10%) in dexamethasone group and 14 patients (28%) in ketamine group experienced POST (Fisher's exact test, $P = 0.039$). Reduction in the incidence and severity of POST in the dexamethasone group when compared to ketamine group at 2, 4, 6, and 12 h postoperatively is statistically significant ($P < 0.05^*$).

Conclusion: Pre-operative single dose of nebulized dexamethasone 8 mg effectively attenuates POST in patients following GA with endotracheal intubation compared to nebulized ketamine 50 mg without any detrimental effects.

Key words: Dexamethasone, General anesthesia, Intubation, Ketamine, Nebulization, Sore throat

INTRODUCTION

Post-operative sore throat (POST) is a frequent complaint that occurs in 21–65% of patients receiving general anesthesia (GA) with endotracheal intubation.^[1,2] Even

though considered as a minor and self-limiting complication, it may cause discomfort, distress to the patients and may even lead to significant post-operative morbidity.^[3]

Many treatment modalities both non-pharmacological and pharmacological have been tried for attenuating POST with varying results.^[4] Some of them include the use of small size endotracheal tubes, low intracuff pressures,^[5,6] minimizing laryngoscopy attempts, use of topical lidocaine,^[7] spraying the endotracheal tube with beclomethasone,^[8] gargling with ketamine and magnesium sulfate ($MgSO_4$),^[9,10] nebulization with ketamine and $MgSO_4$,^[11-13] $MgSO_4$ lozenges,^[14] and inhalational steroids.^[15]

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Corticosteroids have anti-inflammatory action and are widely used in clinical practice. The inhaled steroids distribute the drug to the airways and are devoid of systemic effects. Dexamethasone is a potent, long-acting synthetic steroid with anti-inflammatory effects, superior to other steroids. Various studies have been reported, supporting its use in effectively relieving POST.^[16]

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist with anti-nociceptive and anti-inflammatory effects and has been used successfully in the form of gargle for reducing POST. In view of a few disadvantages associated with ketamine gargle and lozenges such as the bitter taste, need for larger volumes, and risk of accidental aspiration, ketamine was used by the aerosol route to overcome these problems and for better patient tolerance.

The aim of this study was to assess and compare the effectiveness of nebulized dexamethasone versus ketamine in preventing the incidence and severity of POST following endotracheal intubation in patients under GA and also to detect any adverse effects.

MATERIALS AND METHODS

This prospective, randomized, and double-blind study was conducted in a tertiary care Government General and Teaching Hospital from March 2019 to September 2019. After obtaining the Institutional Ethical Committee approval and written, informed consent, 100 adult patients of ASA physical status I and II, aged between 20 and 60 years of either sex, undergoing elective surgeries under GA with endotracheal intubation, lasting <2 h duration were enrolled in this study. Exclusion criteria were patients with a history of pre-operative upper respiratory tract infection, asthma, sore throat, allergy to study drug, recent use of nonsteroidal anti-inflammatory drugs, anticipated difficult airway with Mallampati Grade >2, pregnancy, diabetes, undergoing head-and-neck surgeries, oral, nasal, and surgeries in the prone position.

The sample size was calculated based on the findings of the pilot study which was conducted with a sample of 20 patients, 10 per each group. To show 50% reduction in the incidence at α -error of 0.05 and power of 90%, we required sample size of 48 patients per group. Hence, 50 patients were included in each group to account for dropouts. The patients taken for the pilot study were not included in the original study.

Patients were randomized into two groups of 50 each using the randomization technique by an anesthesiologist who

was not involved in the study. The nebulization solution was prepared according to group allocation by anesthesia assistant who did not participate in further assessment of these patients. As both the nebulization solutions were colorless and tasteless, patients were blinded to the study drug preparations.

All the patients were kept nil oral overnight preceding surgery. On arrival at the operation theater, after securing IV cannula, all the standard monitors such as non-invasive blood pressure, electrocardiogram, pulse oximetry (SpO₂), and capnography were attached and baseline parameters were recorded. GA was administered as per the standard protocol for all the patients. Before the start of GA, 15 min before induction, all the enrolled patients received the study drugs by nebulization mask attached to wall-mounted oxygen source at 8 L/min, for 15 min according to group allocation.

Group D: Patients received dexamethasone 8 mg (2 ml) with 3 ml of normal saline (total volume of 5 ml) for nebulization.

Group K: Patients received ketamine (preservative-free) 50 mg (1 ml) with 4 ml of normal saline (total volume of 5 ml) for nebulization.

After 15 min of nebulization, patients were premedicated with intravenous (IV) injection glycopyrrolate 0.2 mg, injection fentanyl 2 mcg/kg, and midazolam 0.02 mg/kg. After preoxygenation with 100% oxygen for 3 min, induction was done with injection thiopentone IV 5 mg/kg. Tracheal intubation was done by smooth and gentle laryngoscopy 3 min after administering injection vecuronium bromide 0.1 mg/kg by an experienced anesthesiologist. Single-use, sterile, high-volume low-pressure cuffed polyvinyl chloride endotracheal tube with an internal diameter of 7–7.5 mm for females and 8–8.5 mm for males was used. The tracheal cuff was inflated with a volume of room air until no audible air leak and cuff pressure were set to 20 cm H₂O using hand gripped cuff pressure monitor and monitored every 30 min to maintain cuff pressure of 20 cm H₂O till the end of surgery. GA was maintained in both the groups with oxygen 33% in nitrous oxide 67%, sevoflurane 1–2%, and intermittent doses of IV vecuronium and fentanyl. Half an hour before the completion of surgery, injection IV ondansetron 4 mg was administered to prevent post-operative nausea and vomiting and then 8th hourly thereafter. At the end of the surgery, oropharynx was gently suctioned, and the neuromuscular block was reversed using injection IV neostigmine 0.05 mg/kg and injection glycopyrrolate 0.001 mg/kg. Tracheal extubation was performed in a

similar way in both the groups after complete recovery and the patient was fully awake.

After extubation, the patients were shifted to the post-anesthesia care unit for observation and assessment. Injection paracetamol 1 g IV was given 8th hourly. Patients were assessed for incidence and severity of POST at 0, 2, 4, 6, 12, and 24 h postoperatively, starting from the time of extubation by an anesthesia resident who was blinded to the study.

The incidence of POST was assessed by asking the patient for the presence or absence of soreness, pain, and change of voice or any discomfort in the throat. The severity of POST was graded on a 4-point scale (0–3)^[9] assessed as per the following clinical scores:

0–3 points scale

Grade 0 = no sore throat.

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

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

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

Any side effects such as cough, dry mouth, post-operative nausea vomiting, and respiratory depression were noted 8th hourly during the first 24 h postoperatively.

Statistical Analysis

All the collected data were entered into Microsoft Excel and statistical analysis was done using GraphPad.com software and Vassarstats.net software. Data were expressed as mean, standard deviation, and/or ratio or absolute numbers (%) and compared using Student's *t*-test, Fisher's exact test, and Chi-square test whichever were applicable. *P* < 0.05 was considered statistically significant.

RESULTS

A total of 103 patients were screened for this study. Out of these, three patients were excluded due to various reasons such as one patient had a history of asthma, one patient was morbidly obese with Mallampati Grade >2, and one patient with ASA physical status >2. Hence, a sum of 100 consented patients who fulfilled the inclusion criteria and randomized into two groups of 50 each was included in the study for their post-operative assessment of sore throat (POST) and completed the study successfully.

Demographic data were comparable between the two groups. There was no statistically significant difference between the two groups in terms of age, sex, body weight, ASA physical status, and duration of surgery [Table 1].

The comprehensive incidence of POST was 19% in the present study. Five patients (10%) in Group D and 14 patients (28%) in Group K contacted POST at 1 point of the study (Fisher's exact test, *P* = 0.039).

In the immediate post-operative period at 0 h, there was no significant difference in the incidence of POST in between the two groups (*P* = 0.066). Incidence of POST was significantly lower in Group D at 2, 4, 6 and 12 h post-extubation when compared to Group K. At 2 h and 4 h post-extubation, 5 patients in Group D developed POST compared to 14 patients in Group K (*P* = 0.039) which was statistically significant. At 6 h postoperatively,

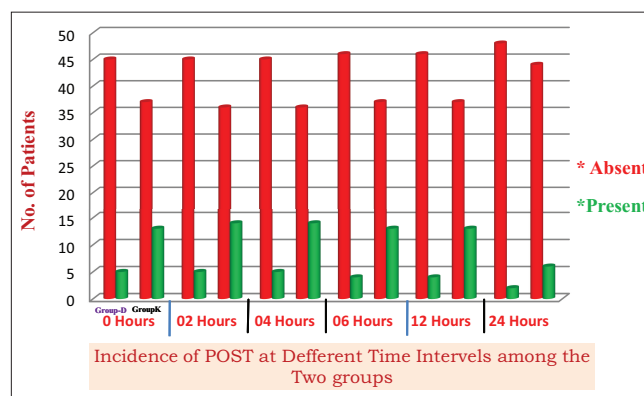


Figure 1: Incidence of post-operative sore throat at different time intervals among the two groups

Table 1: Demographic data of the patients

Parameters	Mean±SD (n=50)		<i>P</i>
	Group D	Group K	
Age in years	39.42±10.31	41.30±9.56	0.150
Weight in kg	64.57±8.45	66.29±7.82	0.322
Gender (male/female) (n)	29/21	26/24	0.687*
ASA I/II	31/19	33/17	0.835
Duration of surgery (min)	88.29±18.62	91.81±15.6	0.308

Data expressed as mean (SD) or ratio or absolute numbers, Student's *t*-test, *Fischer's exact test, SD: Standard deviation

Table 2: Incidence of post-operative sore throat in patients

Time period (hour)	Sore throat incidence	Group D n=50	Group K n=50	<i>P</i>
0	Absent	45	37	<i>P</i> =0.066
	Present	5	13	
2	Absent	45	36	<i>P</i> =0.039
	Present	5	14	
4	Absent	45	36	<i>P</i> =0.039
	Present	5	14	
6	Absent	46	37	<i>P</i> =0.010
	Present	4	13	
12	Absent	46	37	<i>P</i> =0.010
	Present	4	13	
24	Absent	48	44	<i>P</i> =0.268
	Present	2	6	

Values are expressed as absolute numbers. Fischer's exact test used, *P* < 0.05 statistically significant.

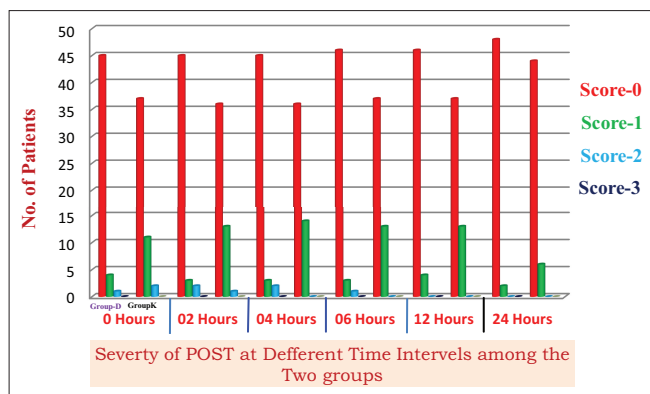


Figure 2: Severity of post-operative sore throat at different time intervals among the two groups

Table 3: Severity of post-operative sore throat in patients

Time period (hour)		Sore throat grade				P
		0	1	2	3	
0	Group D	45	4	1	0	P=0.223
	Group K	37	11	2	0	
2	Group D	45	3	2	0	P=0.040
	Group K	36	13	1	0	
04	Group D	45	4	1	0	P=0.020
	Group K	36	14	0	0	
06	Group D	46	3	1	0	P=0.025
	Group K	37	13	0	0	
12	Group D	46	4	0	0	P=0.031
	Group K	37	13	0	0	
24	Group D	48	2	0	0	P=0.135
	Group K	44	6	0	0	

Values are expressed as absolute numbers. *Chi-square test used, $P < 0.05$ statistically significant.

POST was observed in 4 patients in Group D compared to 13 patients in Group K ($P = 0.010$) which was statistically significant and identical statistically significant results were observed at 12 h postoperatively ($P = 0.010$). There was no significant difference at 24 h post-extubation in between the groups ($P = 0.268$) [Table 2 and Figure 1].

When comparing for the severity of POST in between the two groups using a 4-point scale, POST was significantly abated in Group D at 2 h ($P = 0.04$), 4 h ($P = 0.012$), 6 h ($P = 0.041$), and 12 h ($P = 0.044$) postoperatively when compared to Group K. There was no significant difference in the severity of POST at 24 h post-extubation ($P = 0.537$). None of the patients experienced severe sore throat (POST Score 3) in both the groups [Table 3 and Figure 2]. No adverse effects were observed throughout the study.

DISCUSSION

GA with endotracheal intubation is associated with a number of major and minor complications, of which

POST is one of the most commonly encountered minor complications.

Various causes have been attributed to the occurrence of POST such as trauma to the mucosa during laryngoscopy, repeated attempts at intubation, mechanical irritation of the airway with inflammation, and high intracuff pressures.^[17] Different pharmacological trials and non-pharmacological techniques have been tried previously for the prevention of POST. Although various drugs were used through different routes to alleviate POST in earlier studies, some are associated with unwanted side effects and need for acceptance and cooperation from the patient. We chose the inhalational route for administering drugs in our study due to its ease of administration, low cost, rapid action, safety, convenience, need of a minimal dose of the drug, and topical effects avoiding systemic adverse effects.

The present study was undertaken to evaluate and compare the effectiveness of nebulized dexamethasone versus ketamine in alleviating POST following GA with endotracheal intubation.

The past literature supports the use of topical, intravenous, and inhaled steroids such as betamethasone gel and IV dexamethasone for the treatment of POST.^[18] Due to the concerns associated with the use of IV steroids, we used nebulized dexamethasone as the route of choice in our study.

The total incidence of POST in our study was 19%, of which 5 persons (10%) in Group D and 14 persons (28%) in Group K developed POST.

Tabari *et al.*,^[19] in their study, compared the effects of the application of betamethasone gel to the endotracheal tube cuff with intravenous dexamethasone and concluded that the topical application of betamethasone gel effectively reduced POST. These findings are in accordance with our study, wherein we used nebulized dexamethasone for its topical effects on the upper airway.

Lee *et al.*^[20] found that the incidence of POST was reduced to 27% in their study on the effects of topical dexamethasone on a POST, whereas in our study, nebulized dexamethasone resulted in a much lower incidence of 10% due to its topical effects.

Ashwini *et al.*^[21] have reported an incidence of 27.5% of POST in the dexamethasone group in their study on nebulized dexamethasone versus $MgSO_4$ in the prevention of POST. When compared to their study, our study showed an incidence of 10% in the dexamethasone group which was much lower.

Atef K. Salama *et al.*^[22] demonstrated that a single dose of 8 mg of nebulized dexamethasone reduced the incidence and severity of POST at 0, 2, 4, 6, and 12 h post-extubation of post-operative assessment. These observations are similar to the findings of our study, except for the immediate post-operative period.

Zhu *et al.*^[23] demonstrated in their experimental study on animals that, ketamine an NMDA receptor antagonist, by its topical effect, attenuated the local inflammation induced by trauma and showed a protective effect on airway through nebulization route. In our study also, we preferred ketamine by inhalational route for a similar reason.

Chan *et al.*^[24] evaluated the topical action of ketamine gargle in reducing the incidence and severity of POST by observing low intraoperative serum levels of ketamine. The observations of Chan *et al.* study correlated with our study, except that we used nebulized ketamine for abating POST by its topical effects.

Shaaban *et al.*^[25] in their comparative study between betamethasone gel applied over endotracheal tube and ketamine gargle for attenuating POST, proved that both were effective in reducing POST but betamethasone use being superior. These effects are in agreement with our study, wherein nebulized steroids proved superior to nebulized ketamine in preventing POST.

We fulfilled all the inclusion and exclusion criteria and tracheal intubation was performed by an experienced anesthesiologist.

There are few limitations of our study. First, we were unable to measure serum concentrations of the study drugs, dexamethasone and ketamine to monitor drug levels during the study period due to lack of feasibility in our institute. The concern with ketamine is its effect on the recovery profile of the patients at the end of the surgery. In this study, the dose of nebulized ketamine administered is a single dose of 50 mg and its overall effect on the recovery of patients was negligible. At the end of the surgery, all the patients in both the groups had good recovery according to the modified Aldrete's recovery score. Second, the scale used to assess the POST score was a subjective scale and may be associated with bias.

CONCLUSION

We conclude from our study that the pre-operative single dose of nebulized dexamethasone 8 mg effectively attenuates the incidence and severity of POST following

GA with endotracheal intubation than nebulized ketamine 50 mg with no adverse effects.

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REFERENCES

- Higgins PP, Chung F, Mezei G. Postoperative sore throat after ambulatory surgery. *Br J Anaesth* 2002;88:582-4.
- Loeser EA, Bennett GM, Orr DL, Stanley TH. Reduction of postoperative sore throat with new endotracheal tube cuffs. *Anesthesiology* 1980;52:257-9.
- Macario A, Weinger M, Carney S, Kim A. Which clinical anesthesia outcomes are important to avoid? The perspective of patients. *Anesth Analg* 1999;89:652-8.
- Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice. *Br J Anaesth* 2008;100:215-8.
- Stenqvist O, Nilsson K. Postoperative sore throat related to tracheal tube cuff design. *Can Anaesth Soc J* 1982;29:384-6.
- Ratnaraj J, Todorov A, McHugh T, Cheng MA, Laurysen C. Effects of decreasing endotracheal tube cuff pressures during neck retraction for anterior cervical spine surgery. *J Neurosurg* 2002;97:176-9.
- Kalil DM, Silvestro LS, Austin PN. Novel preoperative pharmacologic methods of preventing postoperative sore throat due to tracheal intubation. *AANA J* 2014;82:188-97.
- Banihashem N, Alijanpour E, Hasannasab B, Zarei A. Prophylactic effects of lidocaine or beclomethasone spray on post-operative sore throat and cough after orotracheal intubation. *Iran J Otorhinolaryngol* 2015;27:179-84.
- Canbay O, Celebi N, Sahin A, Celiker V, Ozgen S, Aypar U. Ketamine gargle for attenuating postoperative sore throat. *Br J Anaesth* 2008;100:490-3.
- Teymourian H, Mohajerani SA, Farahbod A. Magnesium and ketamine gargle and postoperative sore throat. *Anesth Pain Med* 2015;5:e22367.
- Ahuja V, Mitra S, Sarna R. Nebulized ketamine decreases incidence and severity of post-operative sore throat. *Indian J Anaesth* 2015;59:37-42.
- Yadav M, Chalumuru N, Gopinath R. Effect of magnesium sulfate nebulization on the incidence of postoperative sore throat. *J Anaesthesiol Clin Pharmacol* 2016;32:168-71.
- Rajan S, Malayil GJ, Varghese R, Kumar L. Comparison of usefulness of ketamine and magnesium sulfate nebulizations for attenuating postoperative sore throat, hoarseness of voice, and cough. *Anesth Essays Res* 2017;11:287-93.
- Borzan H, Kececioglu A, Okesli S, Otelcioglu S. Oral magnesium lozenges reduces postoperative sore throat: A randomized prospective, placebo-controlled study. *Surv Anesthesiol* 2013;57:36.
- el Hakim M. Beclomethasone prevents postoperative sore throat. *Acta Anaesthesiol Scand* 1993;37:250-2.
- Zhao X, Cao X, Li Q. Dexamethasone for the prevention of postoperative sore throat: A systematic review and meta-analysis. *J Clin Anesth* 2015;27:45-50.
- McHardy FE, Chung F. Postoperative sore throat causes, prevention, and treatment. *Anesthesia* 1999;54:444-53.
- Bagchi D, Mandal MC, Das S, Sahoo T, Basu SR, Sarkar S. Efficacy of intravenous dexamethasone to reduce the incidence of postoperative sore throat: A prospective randomized controlled trial. *J Anaesthesiol Clin Pharmacol* 2012;28:477-80.
- Tabari M, Soltani G, Zirak N. Comparison of the effectiveness of betamethasone gel applied to the tracheal tube and IV dexamethasone on postoperative sore throat: A randomized controlled trial. *Iran J*

- Otorhinolaryngol 2013;25:215-20.
20. Lee JH, Kim SB, Lee W, Ki S, Kim MH, Cho K, *et al.* Effects of topical dexamethasone in postoperative sore throat. *Korean J Anesthesiol* 2017;70:58-63.
 21. Ashwini H, Kumari SK, Lavanya R. Comparative study of dexamethasone nebulisation with magnesium sulphate nebulisation in preventing post operative sore throat following endotracheal intubation. *Indian J Clin Anaesth* 2018;5:341-7.
 22. Salama AK, El-badawy AM. Does nebulized dexamethasone decrease the incidence of a postextubation sore throat? A randomized controlled study. *Ains Shams J Anaesthesiol* 2016;9:104-7.
 23. 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.
 24. Chan L, Lee ML, Lo YL. Postoperative sore throat and ketamine gargle. *Br J Anaesth* 2010;105:97.
 25. Shaaban AR, Kamal SM. Comparison between betamethasone gel applied over the endotracheal tube and ketamine gargle for attenuating postoperative sore throat, cough and hoarseness of voice. *Middle East J Anaesthesiol* 2012;21:513-9.

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