

COMPARISON BETWEEN BETAMETHASONE GEL APPLIED OVER ENDOTRACHEAL TUBE AND KETAMINE GARGLE FOR ATTENUATING POSTOPERATIVE SORE THROAT, COUGH AND HOARSENESS OF VOICE

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Abstract

Background: Tracheal intubation for general anesthesia often leads to trauma of the airway mucosa resulting in postoperative sore throat, hoarseness of voice and cough. The aim of this study was to evaluate two different methods as regard their efficacy for controlling the postoperative pharyngo-laryngo-tracheal sequelae (sore throat, cough, hoarseness of voice) after general anesthesia with laryngoscopy and tracheal intubation. We compared between the effects of betamethasone gel applied over the endotracheal tube and gargling with ketamine solution in reducing these complications during the first 24 postoperative hours after elective surgical procedures in a prospective randomized controlled single blind clinical trial.

Methods: Seventy five patients ASA physical status I and II, undergoing elective surgery under general anesthesia using endotracheal intubation were enrolled in this prospective, randomized, single-blind study. Patients were randomly divided into 3 groups of 25 patients each: Group (K): (n: 25) Patients in this group were asked to gargle with ketamine 40 mg in 30 ml saline for 60 seconds as repeated smaller attempts, 5 minutes before induction of anesthesia. Group (B) (n: 25): Endotracheal tubes were lubricated with 0.05% betamethasone gel. Group(C) (n: 25): Control group: patients did not receive ketamine gargle nor betamethasone gel. The incidence and the severity of Postoperative sore throat, cough, and hoarseness of voice were graded at 0, 2, 4, and 24 h after operation by a blinded investigator.

Results: The incidence and severity of sore throat were significantly lower in group (K) and group (B) than group (C) ($p < 0.05$) at all time intervals. While there was no significant difference between group (K) and group (B) ($p > 0.05$). The incidence and severity of cough and hoarseness of voice were significantly lower in group (B) than group (C) and group (k) ($p < 0.05$) at all time intervals.

Conclusion: Gargling with ketamine before induction of anesthesia is comparable with application of 0.05% betamethasone gel over the Endotracheal tubes in decreasing postoperative sore throat. In addition, Betmethasone application decreased the incidence and severity of postoperative cough and hoarsness of voice.

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Introduction

Postoperative sore throat, cough, and hoarseness of voice are common, uncomfortable, sequelae after tracheal intubation. Even though they are minor complications, But still contribute to postoperative morbidity and patient dissatisfaction and may decrease patient satisfaction with their anesthetic and surgical experience¹⁻³. These effects are likely to be due to irritation and inflammation of the airway as a result from the trauma occurs to the airway mucosa^{4,5}.

Numerous non pharmacological and pharmacological measures have been used for attenuating Postoperative sore throat, cough, and hoarseness of voice 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, minimizing intracuff pressure, gentle oropharyngeal suctioning, and extubation when the tracheal tube cuff is fully deflated^{6,7}. Numerous pharmacological methods have been tried like, Aspirin gargles, gargling with azulene sulphonate, and beclomethasone inhalation^{8,9}.

It was postulated that postoperative airway complications are most likely due to local irritation and inflammation of the airway⁶.

Betamethasone gel applied over the endotracheal tube might reduce the incidence of postoperative sore throat, cough, and hoarseness of voice due to its anti-inflammatory effect¹⁴.

As regard the role of gargling with ketamine, there is an increasing amount of experimental data showing that NMDA receptors are not found only in the central nervous system but also in the peripheral nerves. Moreover, experimental studies point out that peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade¹⁰. Therefore ketamine gargle was evaluated in this study.

The purpose of this study is to compare the role of extensive application of betamethasone gel on the tracheal tube and cuff with another method which is gargling with ketamine for reducing the incidence of post operative sore throat, cough, and hoarseness of voice.

Patients and Methods

After approval from the hospital Ethics Committee and written informed consent, 75 patients were enrolled in this prospective randomized single blind controlled clinical study. Patients were of either sex, aged between 20 and 50 year, belonging to ASA physical status class I or II, scheduled for elective surgery (likely to last between half an hour and four hours) under general anesthesia with orotracheal intubation. Operations included gynecological, lower abdominal, and orthopedic surgeries in the supine position with expected extubation immediately after the operation.

Calculation of sample size was based on the presumption that these studied drugs would reduce the incidence of post operative sore throat by 50%, For the results to be of clinical significance with power analysis ($\alpha = 0.5$, $\beta = 0.5$), one needed to recruit 19 patients in each group.

Patients were excluded who were smokers or with a history of preoperative sore throat, upper respiratory tract infection, common cold or asthma, known allergies to the study drugs, Patients undergoing surgeries of the oral, nasal cavity or pharynx, use of nasogastric tube, oesophageal temperature probe or throat packs, patients with anticipated difficult airway (Mallampati grade >2), and more than two attempts at intubation.

After exclusion, Patients were randomly allocated to one of three groups using a computer-generated randomization list (n = 25 for each group).

- **Group (K)** (n = 25): Patients were asked to gargle with a mixture of ketamine 40 mg in 30 ml saline for 60 seconds as repeated smaller attempts, 5 min before induction of anaesthesia.

- **Group (B)** (n = 25): The external surface of tracheal tubes were lubricated with 2.5 ml of betamethasone gel 0.05% from the distal end of the cuff to a distance of 15 cm from the tip with sterile precautions

- **Group (C)** (n = 25): Control group. No ketamine gargle. nor betamethasone gel applied.

The patients and the staff providing postoperative scoring were blinded to the group. After the patients arrival in the operating room, standard monitoring

(electrocardiogram, noninvasive arterial blood pressure, end tidal co2, and arterial oxygen saturation) was initiated.

Anesthesia was induced with intravenous fentanyl 2 µg/kg and propofol 2.5 mg/kg IV over 15-20 s. Rocuronium, 0.6 mg/kg IV, to facilitate tracheal intubation. Tracheal intubation was performed by an experienced anaesthesiologist after ensuring maximum neuromuscular blocking effect as assessed by TOF guard. Direct laryngoscopy was done with the use of a Macintosh laryngoscope blade by applying minimal pressure, The endotracheal tubes used were Single use PVC tracheal tubes (Portex ® Profile tracheal tube), having low-pressure-high-volume cuffs, of size 8.0 mm and 7.0 mm internal diameter were used for male and female patients, respectively.

The tracheal tube cuff was inflated with just enough room air to prevent an audible leak. With a peak airway pressure at 20 cm H2O, and cuff pressure was maintained between 18 and 22 cm H2O using handheld pressure gauge in which the transducer was connected to the pilot balloon of the endotracheal tube to provide digital display of the intra-cuff pressure on the screen of the monitor (Endotest; Rüsch, Kernen, Germany). Anaesthesia was maintained with oxygen 33% in air, supplemented with sevoflurane and bolus doses of rocuronium guided by TOF (maintain one to two twitches on train-of-four stimulation of ulnar nerve). A heat and moist exchanger was used to provide humidification of the anesthetic gases.

At the end of the surgery, oxygen 100% was administered and residual neuromuscular block was antagonized with by a combination of neostigmine 0.05 mg/kg and glycopyrolate 0.01 mg/kg. Oral suctioning by a 12 F suction catheter was done gently just before extubation only under direct vision to avoid trauma to the tissues and to confirm that the clearance of secretions was complete. The trachea was extubated after deflating the cuff when the TOF ratio was at least 70% and patient fully awake. All patients received oxygen by a facemask after operation.

Assessment of patients for the incidence and the severity of postoperative sore throat, cough, and hoarseness of voice, and any side effect was done on arrival in the post-anesthesia care unit (o h) and at 2, 4, and 24 h after operation by the anesthetist in charge

of the post-anesthesia care unit, blinded to the group allocation, using the questionnaire shown in Table (1). (By providing direct questions, as suggested by Harding and McVey⁷.

Table 1
Scoring System for Sore Throat, Cough, and Hoarseness⁷

Please grade any sore throat you may have according to the following scale:

- 0: No sore throat at any time since your operation (until now).
- 1: Minimal sore throat, less severe than with a cold, occurring at any time since your operation.
- 2: Moderate sore throat, similar to that noted with a cold, occurring at any time since your operation.
- 3: Severe sore throat, more severe than noted with a cold, occurring at any time since your operation.

Please grade any cough that you may have according to the following scale:

- 0: No cough or scratchy throat occurring at any time since your operation.
- 1: Minimal scratchy throat or cough, less than noted with a cold, occurring at any time since your operation.
- 2: Moderate cough, as would be noted with a cold, occurring at any time since your operation.
- 3: Severe cough, greater than would be noted with a cold, occurring at any time since your operation.

Please grade any hoarseness that you have according to the following scale:

- 0: No evidence of hoarseness occurring at any time since your operation.
- 1: No evidence of hoarseness at the time of interview, but hoarseness was present previously
- 2: Hoarseness at the time of interview that is noted by the patient only.
- 3: Hoarseness that is easily noted at the time of interview

The method of analysis was decided prospectively. Demographic data were analyzed with one way analysis of variance (ANOVA) for continuous variables and χ^2 test for categorical variables. The incidence of postoperative symptoms was analyzed by Chi-square test and Fisher's exact test, whereas the severity of symptoms was analyzed by the Kruskal-Wallis and Mann-Whitney U tests. The incidence of side effects if present was analyzed with Fisher's exact test. All statistical analysis were performed with SPSS 14.0 (SPSS, Chicago, IL). Probability values (P) <0.05 was considered significant.

Results

Eighty one patients were evaluated in this study, of which four patients were excluded from the study because of a history of preoperative common cold and anticipated difficult intubation. Two other patients were excluded from the ketamine group as they could not gargle properly. There were no significant differences between the groups in terms of age, body weight, gender distribution, or duration of surgery, (Table 2).

Table 2

Patients characteristics and and duration of surgery. Data Presented Either as Mean \pm SD or Absolute Numbers. No significant differences between the groups by one way analysis of variance (ANOVA) for continuous variables and χ^2 test for categorical variables

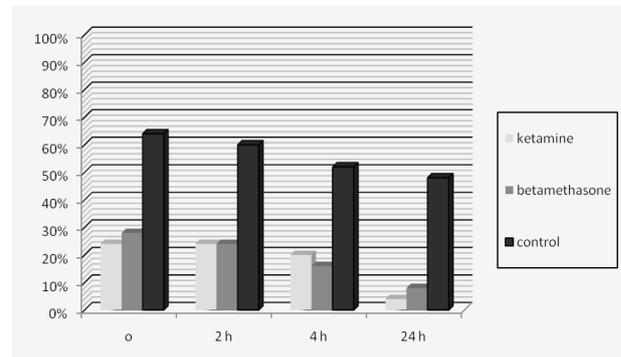
variable	Group		
	Ketamine (n = 25)	Betamethasone (n = 25)	Control (n = 25)
Age (years)	35.2 \pm 11.6	31.9 \pm 12.2	32.7 \pm 11.9
Sex (male\female)	12/13	13/12	12/13
Weight (kg)	59.2 \pm 7.2	57 \pm 6.2	58.3 \pm 7.7
Duration of surgery (min)	71 \pm 22.2	89 \pm 36.6	79 \pm 30.9

The incidence of sore throat was significantly higher in the control group in all time points in comparison with the other two groups ($p < 0.05$). While there was no significant difference between the ketamine group and the betamethason group ($p > 0.05$) (Fig. 1).

The severity of postoperative sore throat was significantly high in the control group when compared

Fig. 1

Incidence of postoperative sore throat, Data presented as percentage of patients. $P < 0.05$ during intergroup comparison between control (C) versus ketamine (k) and $P < 0.05$ between control (C) versus betamethasone (B)



with the other 2 groups ($p < 0.05$). Four patients from the control group suffered from severe postoperative sore throat. The severity of postoperative sore throat was similar between the ketamine and the betamethasone group ($p > 0.05$) (Table 3).

The incidence of hoarseness and cough were significantly high in the control group in comparison with the ketamine and the betamethasone group ($p < 0.05$) while it was comparable between the ketamine and the betamethone group. None of the patients suffered from sever cough or sever hoarsness of voice in any group. (Fig. 2, 3). There were no complications related to administration of betamethasone gel or ketamine gargle.

Discussion

This study confirms the relatively high incidence of pharyngo-laryngotracheal sequelae (sore throat, cough, hoarseness of voice) after general anesthesia with laryngoscopy and tracheal intubation, which ranges from 44.2 to 50.9%, and these results consistent

Table 3
grades of sore throat in the three groups (Data ae presented as number of patients and percentage)

Group	Number of patients			
	Score 0	Score 1	Score 2	Score 3
ketamine	12 (48%)	10 (40%)	3 (12%)	0 (0%)
Betamethasone	13 (52%)	9 (36%)	3 (12%)	0 (0%)
control	2 (8%)	11 (44%)	8 (32%)	4 (16%)

Fig. 2
incidence of postoperative cough, data presented as percentage of patients. $P < 0.05$ during intergroup comparison between control (C) versus ketamine (k) and $P < 0.05$ between control (C) versus betamethasone (B)

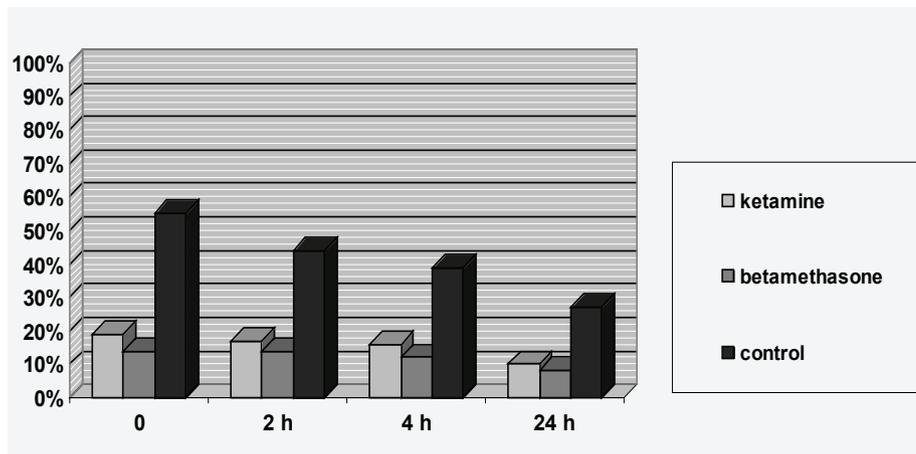
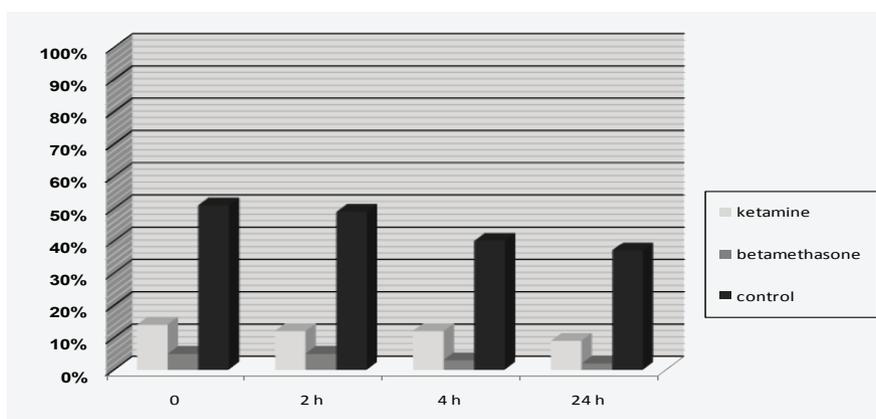


Fig. 3
incidence of postoperative hoarseness of voice, data presented as percentage of patients. $P < 0.05$ during intergroup comparison between control (C) versus ketamine (k) and $P < 0.05$ between control (C) versus betamethasone (B)



with other studies^{1,3,6}.

Several factors have been described to influence the incidence of this sequelae like the diameter of the endotracheal tube used, the intra-cuff pressure, coughing on the tube, and excessive pharyngeal suction¹².

We found that the incidence and severity of sore throat, was significantly reduced after preoperative gargling with ketamine and also in the group when betamethasone gel was widely applied over the tracheal tube with no significant inter group difference compared with the control group. But the incidence of postoperative cough, and hoarseness of voice was less when betamethasone gel was widely applied over the tracheal tube compared with the ketamine gargle group. While it was significantly high in the control group.

The potential role of aseptic inflammation in these postoperative airway sequelae due to localized trauma of the tracheopharyngeal mucosa have

been recognized^{12,16}. So many agents acting on the inflammatory cascade have been tried to alleviate these sequelae^{12,13,14,16}.

Locally administered steroids have been tried; Topical application of 1% hydrocortisone near the endotracheal tube cuff was not beneficial¹³. Whereas one puff of a beclomethasone inhaler (50 µg) effectively reduced the incidence of sore throat from 55% to 10%⁸. In our study, the widespread application of betamethasone gel to cover the major points of contact with the pharynx, larynx, and trachea may account for the greater benefit compared with those achieved by **Stride** when he applied topical hydrocortisone 1% from the distal tip of the endotracheal tube to 5 cm above the cuff. Our study confirms the findings of studies by **Sumathi** and colleagues¹⁵ and the study done by **George Allen**¹⁶ proving that widespread application of betamethasone gel significantly reduces the incidence of postoperative sore throat, cough, and hoarseness of voice. However, both **Sumathi**

and colleagues¹⁵ and **George Allen**¹⁶, compared the betamethasone gel group versus lidocaine gelly group. We included another method which is gargling with ketamine, 5 minutes prior to the operation.

In recent years, studies have shown that ketamine has its anti-inflammatory properties and it plays a protective role against lung injury¹⁵. In addition, ketamine has been shown to attenuate symptoms of endo-toxemia in a lipopolysaccharide (LPS)-induced rat model of sepsis, by reducing NF-kappa B activity and TNF-alpha production and decreasing the expression of inducible nitric oxide synthase which has been implicated in endotoxin-induced tissue injury¹⁶. Taken together, these results suggest that ketamine has anti-inflammatory and anti-hyperresponsiveness effects. The effect of nebulized ketamine inhalation on allergen-induced rats have been examined in the study done by **Zhu et al.** and they concluded that Ketamine administration by local route appears to inhibit the inflammatory cascade response as there is a growing amount of experimental data presenting that NMDA receptors are present in the CNS and in the peripheral nerves¹⁹.

Besides, experimental studies point out that peripherally administered NMDA receptor antagonists are implicated with antinociception^{20,21}. Our results for the effect of gargling with ketamine in reducing the postoperative sore throat confines with study done by O. Canbay and his colleagues²¹, Who studied the effect of ketamine gargle for attenuating postoperative sore

throat, but unlike our study, they did not study its effect on postoperative cough or hoarseness of voice.

The dose of betamethasone gel used in our study was equivalent to 4 mg of prednisone and that of ketamine was 40 mg, which is in the safe clinical range for both drugs. Although flaring up of local subtle infection is a possibility with topical steroid application, there are no reports of adverse effects secondary to betamethasone gel application over the tracheal tube. Also Comparing with the previous reports with topical ketamine with higher doses²², our doses were relatively low and we did not observe any CNS side-effects.

The drawbacks of this study are that it could not evaluate the effect on prolonged intubation period. And it did not measure the plasma level of ketamine or betamethasone, so it did not rule out the effect of possible systemic absorption.

In conclusion, We found that gargling with ketamine prior to intubation is comparable with betamethasone gel when applied over the endotracheal tube in reducing postoperative sore throat. In addition, using betamethasone gel decreased the incidence and the severity of postoperative cough and hoarseness of voice more than gargling with ketamine. Also, this study suggests that airway inflammation is an important causative factor in eliciting the postoperative laryngopharyngeal sequelae in adult patients undergoing laryngoscopy and tracheal intubation under general anesthesia.

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