

# An Evaluation of the Efficacy of Ketamine Gargle and Benzydamine Hydrochloride Gargle for Attenuating Post Operative Sore Throat: A Prospective Randomized, Placebo Controlled Single- Blind Study

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## ABSTRACT

**Background:** Post-operative sorethroat (POST) is a well-recognized complication in patients with endotracheal intubation for general anaesthesia. Many pharmacological measures for attenuating POST are being used during anaesthesia. In our study we compared the effectiveness of ketamine and benzydamine hydrochloride versus a placebo as preoperative gargle in decreasing the incidence and severity of POST in patients undergoing endotracheal intubation for general anaesthesia. **Methods:** A total of 90 patients aged between 18-60 years of ASA I-II of either sex were randomly assigned into three groups of 30 patients each . Group 1(C) received distilled water, group 2(BH) received 15 ml of benzydamine hcl(0.15%) and group 3(K) received preservative free ketamine 40 mg as preoperative gargle 10 min before induction. The incidence of POST was recorded at 2, 4 and 24 hr post operatively. **Results:** The three groups were comparable in term of demographic characteristics. The incidence and severity of POST is much more in group 1(C) i.e control group (30%) after 24 hr compared to group 2 (BH) 0% and group 3(K) 3.5%. There was no significant difference of POST in group 2(BH) and group 3(K). **Conclusion:** From our study it can be concluded that both benzydamine and ketamine gargle significantly reduces the incidence and severity of POST compared to distilled water gargle up to 24 hr in the patients undergoing general anaesthesia with endotracheal intubation. Both the Benzydamine and ketamine gargles are safe, simple and equally effective in reducing POST.

**Keywords:** Benzydamine Hcl, Endotracheal tube (ET tube), Ketamine and Post-operative sorethroat (POST).

## INTRODUCTION

Post-operative sorethroat (POST) is well recognized complication that remains unresolved in patients undergoing endotracheal intubation for general anaesthesia with reported incidence of 28% to 80% 1-5. POST had been rated by patients as the 8th most undesirable outcome in postoperative period. It also increases the duration of hospital stay and delays discharge, especially in day care surgeries. Routine tracheal intubation for elective surgeries can result in advent trauma to the airway which accounts for POST symptoms. Numerous non-pharmacological and pharmacological measures have been used for attenuating POST with variable success.

Among the non-pharmacological methods, smaller sized ET tubes, lubricating the ET tubes with water soluble jelly, careful airway instrumentation, minimizing the number of laryngoscopy attempts, experienced laryngoscopist, intubation after full relaxation of larynx, gentle oropharyngeal suctioning, minimizing in tracuff pressure and extubation after fully deflation of tracheal cuff have been reported to decrease the incidence of POST. Pharmacological attempts for attenuating POST are inhalation of beclomethasone, fluticasone and gargling with azune sulfonate, aspirin and licorice, local spray of benzydamine hcl and intracuff administration of alkanizes lignocaine. In this regards Ketamine (phencyclidine derivative) and Benzydamine hcl (topical NSAID) have been used independently as preoperative gargle and have been noted to decrease the incidence and severity of POST.

In our study we plan to compare the effectiveness of these two agents vs a placebo in decreasing the incidence and severity of POST. Both the drugs are

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easily available and a gargle may be simple, cost-effective method to decrease POST symptoms.

## MATERIALS AND METHODS

The present study was conducted at M.K.C.G MEDICAL COLLEGE AND HOSPITAL, after obtaining clearance from the institutional ethical committee & scientific committee 90 adult patients between 18-60 years of ASA grade I-II of either sex undergoing elective abdominal surgery under general anaesthesia were enrolled in this study. We excluded patients with a recent H/O preoperative sore throat, more than two attempts at intubation, Mallampati grade >2, use of gum elastic bougie or stylet to facilitate intubation, history of bronchial asthma and known allergies to ketamine and benzylamine HCl.

Using a prospective, randomized, placebo-controlled, single-blind study, these patients were divided into three groups of 30 patients each as group 1 (C) received distilled water, group 2 (BH) received 15 ml of benzylamine HCl (0.15%) and group 3 (K) received preservative free ketamine 40 mg as preoperative gargle 10 min before induction.

Depending upon the results of randomization, all the medications were made to a final volume of 25 ml after adding required amount of distilled water. It was placed in an opaque container by a staff nurse who asked these patients to gargle this mixture for 30 sec in a preinduction room. Patients were strictly instructed not to swallow the medication. This nurse was not involved in the subsequent management of these patients. Induction of anaesthesia was commenced 10 min later.

Valid informed written consent was taken from each patient and all patients were kept fasting overnight. On arrival in the OT, the routine monitoring devices (pulse oximetry, NIBP, ECG) were placed and baseline HR, BP, SPO<sub>2</sub> were recorded. An I.V line was secured. Anaesthesia was induced with inj. Fentanyl 2 µg/kg and inj. Thiopentone 5 mg/kg. Tracheal intubation was facilitated by inj. Vecurium bromide 0.1 mg/kg and the trachea intubated with a soft seal cuffed sterile PVC (Portex Ltd, CT 21, UK) ET tube with 7 mm ID for female and 8 mm ID for male patients. The ET tube cuff was lubricated with distilled water. The ET tube cuff was inflated with air until no air leakage could be heard with peak airway pressure with 20 cm of H<sub>2</sub>O. The cuff pressure was checked using cuff pressure monitor (Portex cuff inflator/pressure gauge, SIMS Portex, Hythe, Kent, UK) every half hourly till end of surgery and maintained between 18 to 22 cm of H<sub>2</sub>O. Anaesthesia was maintained with

N<sub>2</sub>O:O<sub>2</sub> (60%:40%), Isoflurane 1% and intermittent dose of inj. vecuronium as required. No nasogastric tube was inserted. At the end of surgery residual neuromuscular blockage was antagonized using i.v inj. Glycopyrrolate and inj. Neostigmine and trachea was extubated following a gentle oral suction by a 12F soft suction catheter after signs of adequate neuromuscular reversal. Patients were transferred to PACU and postop analgesia was maintained with inj. Tramadol 75 mg IV B.D for next 24 hrs.

At arrival of patients in PACU (0h) and thereafter at 2, 4 and 24h POST was assessed by an investigator who was unaware of group allocation. POST was graded on a 4 point verbal analogue scale (VAS) pain score (0-3) with 0 = no sore throat, 1 = mild sore throat (complaints of sore throat only on asking), 2 = moderate sore throat (complaints of sore throat only on his/her own), 3 = severe sore throat (change of voice or hoarseness, associated with throat pain).

### Statistical Analysis

Data were expressed as mean 95% confidence interval of mean for height, weight, age, duration. Categorical data (sex, ASA grade, POST score) were expressed as frequency of occurrence. Comparison of continuous data between groups were done using ANOVA of means. P value of < 0.05 was considered statistically significant. Comparisons of categorical data between groups were done using Chi-square test, P value of < 0.05 considered statistically significant. SPSS 13.0 (SPSS Inc, Chicago, IL) was used for statistical analysis.

## RESULTS

Out of 90 patients, 88 completed the study. Two patients (1 each from the group BH & K) could not gargle properly and were therefore excluded. There was no significant difference among the groups in terms of age, gender, height, weight, ASA grade and duration of intubation [Table 1]. The mean duration of intubation was 146.60, 138.86 and 148.28 mins in group C, group BH and group K respectively. No statistical correlation was observed between the incidence of POST at different time intervals and age, gender, height, weight and duration of intubation [Table 2]. The incidence of POST in the control group was more frequent compared to group BH and group K at all the times (P < 0.05). There was no difference in the incidence of POST between group BH and group K at any time (P > 0.05) [Table 3]. Regarding severity of POST, moderate POST was significantly high in group C at 0 hr & 2 hr compared to group BH & group K (P < 0.05). Mild POST was significantly more in group C compared to group BH at 24 hr. The severity of POST was similar between group BH & group K at all the times (P > 0.05) [Table 4].

**Table 1: Demographic data presented as either mean with 95% confidence interval for mean or as number**

Variables	Group-C(n=30)	Group-BH(n=29)	Group-K(n=29)	P-value
Age(yr) mean&95% C.I	37.67	42.38	38.93	0.22
Gender(M/F)	17/13	16/13	18/11	0.85
Weight(kg)mean&95% C.I	58.43	58.24	59.28	0.85
Height(cm)mean&95% C.I	161.73	160.69	161.90	0.71
Duration Intubation (min) mean&95% C.I	146.60	138.86	148.28	0.25
ASA grade (I/II)	24/6	20/9	21/8	0.61

**Table 2: Specimen's coefficients(r) for age, gender, height, weight and duration of intubation with POST.**

Variables	0Hr	2Hr	4Hr	24Hr
Age	0.042	0.062	0.016	0.018
Gender	0.048	0.040	0.032	0.058
Height	-0.058	-0.046	0.002	0.015
Weight	-0.026	-0.062	0.082	-0.011
Duration of intubation	-0.042	-0.090	-0.111	0.015

**Table 3: Incidence of POST in the groups at various time intervals.**

Time interval	Groups			p- values(inter group comparison)		
	C n=30	BH n=29	K n=29	Between C & BH	Between C & K	Between BH & K
0Hr	23(76.6%)	7(24.2%)	8(27.6%)	0.000	0.000	0.764
2Hr	19(63.4%)	4(13.8%)	6(20.7%)	0.000	0.001	0.487
4Hr	14(46.7%)	2(6.9%)	4(13.8%)	0.001	0.006	0.389
24Hr	9(30%)	0	1(3.5%)	0.001	0.007	0.313

**Table 4: Severity.**

Groups	0Hr			2Hr			4Hr			24Hr		
	C	BH	K	C	BH	K	C	BH	K	C	BH	K
Groups	30	29	29	30	29	29	30	29	29	30	29	29
Mild	14	7	8	11	4	6	8	2	4	6	0*	1
Moderate	7	0*	0*	6	0*	0*	5	0	0	2	0	0
Severe	2	0	0	2	0	0	1	0	0	1	0	0

Severity POST.\* denotes  $P < 0.005$  during inter group comparison between group C vs BH, \*\* denotes  $P < 0.05$  during inter group comparison between group C vs K.

## DISCUSSION

The present study compared the effectiveness of preoperative gargle of the study drugs (either benzydamine hydrochloride or ketamine) versus a placebo (distilled water) in reducing the incidence and severity of post-operative sore throat following general anaesthesia with endotracheal tube for elective abdominal surgery.

In our study we did not find any significant difference between the groups in terms of age, gender, height, weight, duration of intubation and ASA grade [Table 1]. Several contributing factors for POST after surgery have been reported, including patient sex, age, gynecological surgery, use of succinylcholine, large tracheal tube cuff design, and intracuff pressure.<sup>[3,11,13]</sup> No correlation was observed between incidence of POST, age, gender, height, weight and duration of intubation. [Table 2] Similar results were found by studies of Canbay et al.<sup>[6]</sup> They observed no correlation between POST and age, gender, smoking habit,

duration of surgery and intubation. Rudra et al,<sup>[26]</sup> also did not find any correlation between the incidence of POST and age, gender, duration of surgery, duration of intubation in their study.

In the control group the incidence of POST at 0 hr was 76.7% and 30% at 24 hr. the reported incidence of POST is between 28% to 80%.<sup>[1-5]</sup> Our results in the control group was consistent with previous findings. Agarwal et al<sup>7</sup> observed the incidence of POST in the control group at 0 hr and 24 hr to be 80% (16/20) and 20% (4/20) respectively.

In the BH group the incidence of POST at 0 hr was 24.2% and 0% at 24 hr. similar results were found by Agarwal et al.<sup>[7]</sup> In the K group the incidence of POST was 27.6% at 0 hr and 3.5% at 24 hr. Rudra et al<sup>26</sup> (2009) found a similar result, they observed a small reduction in the incidence of POST in K gargle group at 24 hr which was 30% compared to 0 hr where it was 35%.

We observed that the incidence of POST was significantly more frequent in the control group compared to both the study groups at all-time points ( $P < 0.05$ ). Agarwal et al,<sup>[7]</sup> also noticed the incidence compared to BH gargle group, for 24 hr. Huang et al,<sup>[24]</sup> observed the control group at 0,2,4 and 24 hr, postextubation. Similarly Hung et al,<sup>[23]</sup> noticed a significant reduction in the incidence of POST at

1,6,12 and 24 hr postextubation in BH group compared to normal saline.

Canbay et al,<sup>[6]</sup> noticed the incidence of POST to be significantly more in the normal saline gargle group compared to K gargle group at 0, 2 and 24 hr, but there was no difference at 4 hr. Rudra et al,<sup>[26]</sup> also observed a significant increased of incidence of POST in the control group compared to ketamine group at 4,8 and 24 hr. We did not find any difference in the incidence of POST between the BH and K group at any time [Table 3], (P>0.05).

In our study significantly more number of patients suffered from moderate POST in the control group at 0 and 2 hr compared to both the study groups (P<0.05) and more number patients in control group complained of mild POST compared to BH group at 24 hr (P<0.05) [Table 4]. There was no significant difference between severity of POST between BH and K group. Agarwal et al,<sup>[7]</sup> noticed that significantly more number of patients had severe POST in group C at 0 and 2 hr compared to BH and aspirin group. The severity of POST was similar between aspirin and BH group. In Canbay et al,<sup>[6]</sup> study, the incidence of severe POST in the control group was 21.7% (5/23) at 4 hr and 26.1% (6/23) at 24 hr which was significantly more compared to the ketamine group. But in this study, we observed the incidence of severe POST in the control group to be 3.4% at both 4 and 24 hr which was not significantly high compared to group BH and group K.

Sore throat related to orotracheal tube might be consequence of localized trauma, leading to aseptic inflammation of pharyngeal mucosa. It may also be associated with edema, congestion, and pain.<sup>[11,20]</sup>

Reduction of this inflammation by benzydamine as well as by ketamine gargling may be the reason for decrease in the incidence and severity of POST in our study. In Agarwal et al,<sup>[7]</sup> (2006) study, 2 patients out of 19 complained of numbness of mouth and dysgeusia following BH gargle. Similar side effects were observed by Kati et al,<sup>[8]</sup> when they applied Bh spray to posterior pharyngeal wall before introducing LMA. But no serious complications were noticed. In our study none of the patients complained of such side effect in BH group.

Erhan et al,<sup>[25]</sup> infiltrated the tonsillar region with ketamine which reduced the postoperative pain score without any systemic side effects of ketamine. In our study 2 patints complained of bitterness of the ketamine gargle. Out of these two patients one could not gargle properly and hence was excluded from the study group. No systemic side effects of ketamine were noticed. Park et al,<sup>[27]</sup> (2010) suggested that topical application of ketamine, and not systemic ketamine, may influence POST, reduce local inflammation, and mediate the peripheral anti-nociceptive effect. The systemic effect of BH in reducing POST was ruled as systemic absorption of the durg is very low when it is used as a topical application<sup>51</sup>.

## CONCLUSION

To conclude, the result of the present study indicates the fact that the incidence of POST in the patients undergoing GA with endotracheal intubation for routine surgical cases is quite common and this throat discomfort remains for next 24 hrs.Both Benzydamine and Ketamine gargle significantly reduces the incidence and severity of POST compared to distilled water gargle, up to 24 hrs.Both BH and K gargles are safe, simple and equally effective in reducing POST symptoms. However BH has an added advantage of better taste thank K, which has slight bitter taste.

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