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Ketamine gargle for attenuating postoperative sore throat

O. Canbay*, N. Celebi, A. Sahin, V. Celiker, S. Ozgen and U. Aypar

Faculty of Medicine, Department of Anaesthesiology, Hacettepe University, 06100 Sıhhıye/Ankara, Turkey
**Corresponding authors. E-mail: ozgurcanbay@yahoo.com*

Background. Tracheal intubation is a foremost cause of trauma to the airway mucosa, resulting in postoperative sore throat (POST) with reported incidences of 21–65%. We compared the effectiveness of ketamine gargles with placebo in preventing POST after endotracheal intubation.

Methods. Forty-six, ASA I–II, patients undergoing elective surgery for septorhinoplasty under general anaesthesia were enrolled in this prospective, randomized, placebo-controlled, single-blind study. Patients were randomly allocated into two groups of 23 subjects each: Group C, saline 30 ml; Group K, ketamine 40 mg in saline 30 ml. Patients were asked to gargle this mixture for 30 s, 5 min before induction of anaesthesia. POST was graded at 0, 2, 4, and 24 h after operation on a four-point scale (0–3).

Results. POST occurred more frequently in Group C, when compared with Group K, at 0, 2, and 24 h and significantly more patients suffered severe POST in Group C at 4 and 24 h compared with Group K ($P<0.05$).

Conclusions. Ketamine gargle significantly reduced the incidence and severity of POST.

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Tracheal intubation is a foremost cause of trauma to the airway mucosa, resulting in postoperative sore throat (POST) with reported incidence of 21–65%.[1 2] Even though 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.[3] 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 intracuff pressure, and extubation when the tracheal tube cuff is fully deflated have been reported to decrease the incidence of POST.[4] The pharmacological methods include beclomethasone inhalation and gargling with azulene sulphonate.[5 6]

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.[7 8] Moreover, experimental studies point out that peripherally administered NMDA receptor antagonists are involved with antinociception[9] and anti-inflammatory cascade.[10]

The present study compared the effectiveness of ketamine gargles with placebo for prevention of POST after oral endotracheal intubation.

Methods

The study was approved by the institutional ethics committee and performed at Hacettepe University Anesthesiology Department. A written informed consent was received from 46 ASA I–II, elective patients undergoing surgery for septorhinoplasty under general anaesthesia. The study was conducted in a prospective, randomized, placebo-controlled, and single-blinded manner. Patients with a history of preoperative sore throat and asthma, Mallampati grade >2, known allergies to study drug, recent NSAID medication, and those who required more than one attempt at intubation were excluded from the study. It took 6 months to complete this study. The same surgeon operated on all the patients.

Presuming the incidence of POST to be 65%, the power analysis[11] (taking α=0.05 and β=0.90) calculated a sample size of 22 patients in each of the two groups to show a 50% reduction in the incidence. Thus, we chose to enrol 23 patients in each group.

Patients were randomized into the two groups with the help of a computer-generated table of random numbers. Group C received saline 30 ml and Group K received ketamine 40 mg in saline 30 ml. The preparations of 30 ml each were placed in an opaque container by a staff nurse who also asked patients to gargle with the preparation for 30 s after their arrival in the operation room. This nurse did not participate in the subsequent management of these patients. Anaesthesia was induced 5 min later. The patients could not be blinded because of the different tastes of the two preparations.

Monitoring consisted of ECG, non-invasive arterial pressure, pulse oximetry, and end-tidal carbon dioxide. Anaesthesia was induced with fentanyl 2 $\mu g\ kg^{-1}$ and propofol 2 mg kg^{-1}. Tracheal intubation was facilitated by vecuronium bromide 0.1 mg kg^{-1}, and the trachea was intubated with a soft seal cuffed sterile polyvinyl chloride endotracheal tube with a standard cuff (Bıçakcılar, İstanbul, Turkey) and an internal diameter of 7–8 mm for women and 8–9 mm for men. Tracheal intubation was performed by an experienced anaesthesiologist after ensuring maximum neuromuscular blocking effect as assessed by TOF guard. All the patients received i.v. acetaminophen 500 mg 30 min after tracheal intubation. Anaesthesia was maintained with oxygen 33% in air, supplemented with sevoflurane. Remifentanil i.v. infusion was started in all the patients at a dose of 0.1–0.2 $\mu g\ kg^{-1}$.The tracheal tube cuff was inflated until no air leakage could be heard with a peak airway pressure at 20 cm H_2O, and cuff pressure was maintained between 18 and 22 cm H_2O using handheld pressure gauge (Endotest; Rüsch, Kernen, Germany). Those patients who required more than one attempt for passage of the tube were excluded from the study.

Gauze packs were used to occlude the posterior nasopharynx, thus isolating the nasal passage in order to allow suctioning of blood and debris from the operative field and prevent soiling of the pharynx, oesophagus, and trachea. The nose was packed at the end of operation by a small nasal packing. Residual vecuronium relaxation was reversed with neostigmine and atropine on completion of surgery. Oropharyngeal suction was performed under direct vision to avoid trauma to the tissues before extubation and to confirm that the clearance of secretions was complete.[12]

The patients were interviewed in a standard fashion by a blinded investigator. On arrival in the post-anaesthesia care unit (0 h), and at 2, 4, and 24 h thereafter, 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); and 3, severe sore throat (change of voice or hoarseness, associated with throat pain). Other side-effects, if any, were also noted.

Differences in the age and weight among the groups were compared by one-way analysis of variance. Differences in the incidence of POST among the groups were compared with the help of Mann–Whitney *U*-test. Severity of POST was analysed by Fisher's exact test. SPSS 11.5 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. $P<0.05$ was considered as significant.

Results

Age, height, weight, smoking habit, duration of surgery and intubation, and total remifentanil consumption were similar among the groups (Table 1) ($P>0.05$). Two patients in the ketamine group could not gargle properly and one patient in the same group required two attempts for the intubation; these patients were excluded. The incidence of POST was higher in Group C (control) compared with Group K at 0, 2, and 24 h as shown in Figure 1 ($P<0.01$). Significantly more patients suffered severe POST in Group C at 4 and 24 h compared with Group K ($P<0.05$) (Table 2). Gender, age, duration of intubation, and smoking habit did not correlate with sore throat (Table 3). No local or systemic side-effects were observed.

Discussion

We found that the incidence and severity of POST were reduced after preoperative gargling with ketamine compared with saline gargling in patients undergoing septorhinoplasty operation, during general anaesthesia with endotracheal intubation for up to 24 h.

Several contributing factors for sore throat after surgery have been reported, including patient sex, age, gynaecological surgery, use of succinylcholine, large tracheal tube, cuff design, and intracuff pressure.[13–15] In this study, no correlation was observed between pain, age, gender, smoking habits, duration of surgery and intubation.

The cause of sore throat related to pharyngeal pack might be a consequence of localized trauma, leading to

Table 1 Patient characteristics and data related to the surgery. Data are given as mean (range), mean (SD) or absolute numbers. There were no significant differences between the groups

Groups	Control (n=23)	Ketamine (n=20)
Age (yr)	23.6 (18–30)	25.6 (19–38)
Height (cm)	162.3 (8.5)	164.5 (9.2)
Weight (kg)	62.8 (91)	60.0 (11.3)
Duration of surgery (min)	54.1 (14.4)	55.8 (14.8)
Time taken for tracheal intubation (min)	55.0 (25.3)	61.2 (12.3)
Smoking habit (+/−)	16/7	10/10
Total remifentanil consumption (mg)	1.61 (1.37)	1.53 (1.03)

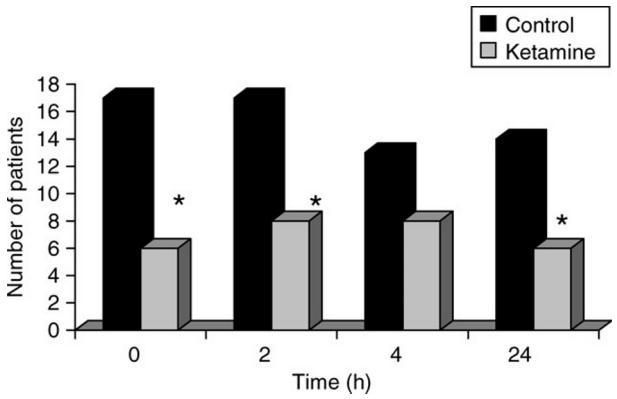

Fig 1 Incidence of POST, data presented as number of patients. *$P<0.05$ during comparison between control (C) *vs* ketamine (K).

aseptic inflammation of pharyngeal mucosa. It may also be associated with oedema, congestion, and pain.[16] Kempe and colleagues[17] reported that patients who underwent surgery of nasal septum suffered from dryness and inflammation of the oral cavity due to mouth breathing. We presume that late onset of severe pain in the control group reflects a more gradually developing local inflammation. Reduction of this inflammation by ketamine gargling may be the reason for decrease in POST in our study.

In recent years, studies have shown that ketamine plays a protective role against lung injury, by means of its anti-inflammatory properties.[18 19] Additionally, ketamine has been shown to attenuate symptoms of endotoxaemia in a lipopolysaccharide (LPS)-induced rat model of sepsis, by reducing NFkappa B activity and TNF-alpha production[20] and diminishing the expression of inducible nitric oxide synthase.[21] In a recent animal study for asthma, Zhu and colleagues[10] have indicated that nebulized ketamine attenuated many of the central components of inflammatory changes. In another study, Zhu and colleagues[22] have proposed a protective effect of ketamine on allergen-induced airway inflammatory injury and high airway reactivity in asthma in an experimental model with rats. With respect to this potential protective effect, we propose that ketamine gargle might be effective in reducing the incidence and severity of POST due to its anti-inflammatory effects. Studies into the nasal, oral, and rectal administration of ketamine also suggest that local use of this drug is both effective and conceivable.[23–25]

Table 2 Severity of POST in control (C) and ketamine (K) groups. Data are presented as number of patients. *$P<0.05$ on between-group comparison

	0 h		2 h		4 h		24 h	
Groups	**K**	**C**	**K**	**C**	**K**	**C**	**K**	**C**
n	20	23	20	23	20	23	20	23
Grading of discomfort								
Mild	5	13	8	11	8	5	6	5
Moderate	2	4	0	3	0	3	0	3
Severe	0	0	0	3	0	5*	0	6*

Table 3 Spearman's coefficients for correlation (*r*) for gender, age, duration of intubation, and smoking habit with POST. None of these was statistically significant

	POST			
	0 h	**2 h**	**4 h**	**24 h**
Gender	−0.234	−0.080	−0.009	0.139
Age	−0.058	0.071	0.084	−0.114
Smoking habit	−0.072	0.237	0.181	0.127
Duration of intubation	−0.074	−0.152	−0.092	−0.184

There is a growing amount of experimental data presenting that NMDA receptors are present in the CNS and in the peripheral nerves.[7 8] Besides, experimental studies point out that peripherally administered NMDA receptor antagonists are implicated with antinociception.[26 27]

A drawback of our study was the absence of the measurements of plasma ketamine levels. So we cannot rule out the contribution of the systemic effect of ketamine in our results. As a result, either systemic or topical anti-inflammatory and antihyperalgesic effect of ketamine might contribute to this outcome. Comparing with the previous reports with topical ketamine with higher doses,[23] our doses were relatively low and we did not observe any CNS side-effects.

In conclusion, gargling with ketamine decreases the incidence and severity of POST in patients undergoing septorhinoplasty operation under general anaesthesia.

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