Efficacy of Ketamine Gargles in the Prevalence of Postoperative Sore Throat after Endotracheal Intubation

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ABSTRACT

Background: *Postoperative sore throat is a common and disturbing complication after endotracheal intubation, leading to patient discomfort and dissatisfaction.*

Objective: *To find out the efficacy of ketamine gargles in reducing the incidence and severity of postoperative sore throat after endotracheal intubation.*

Material and method: *We studied the role of pre-operative ketamine gargles for reducing postoperative sore throat. Patients undergoing elective abdominal and pelvic surgery under general anaesthesia with endotracheal tube were included in the study. They were randomly allocated in two groups, each group comprising of 30 patients. Group 1(K) received preservative free ketamine 50mg in 29 ml distilled water. Group 2(C) gargled with 30 ml distilled water. Patients were asked to gargle for 30 seconds, 5minutes before induction of anaesthesia. Postoperatively sore throat was assessed at 0, 4, 8 and 24 hours after extubation. The severity of sore throat was assessed from mild to severe.*

Results: *Immediately after extubation, 90% patients in group C had sore throat compared to 66.7% in group K. 24 hours after extubation, the incidence decreased to 50% in group C and 13.3% in group K. Similar decrease incidence was noted at 4 and 8 hours post extubation in group K. No patient in group K complained of change in voice or hoarseness of voice.*

Conclusion: *We found that preoperative gargling with ketamine is a simple and cost effective way to reduce the incidence and severity of postoperative sore throat.*

Key words: *Abdominal and pelvic surgery, endotracheal intubation, ketamine gargles, postoperative sore throat.*

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-4994.2015.00039.6

BACKGROUND

Airway maintenance in an anaesthetized patient is of vital importance. Securing the airway with an endotracheal tube provides an opportunity for positive pressure ventilation with minimal risk of aspiration. Amongst the various complications of endotracheal intubation, postoperative sore throat (POST) and postoperative hoarseness is the most common.[1, 2] The incidence of postoperative sore throat varies in different studies. In most studies it is reported as 40% to 60%.[1, 3, 4] These symptoms are so common that the patients and the anaesthesia staff believe that they are a natural consequence of endotracheal intubation. As per the ranking and relative value of anaesthesia outcomes, postoperative sore throat is rated as the 8th most undesirable outcome in the postoperative period.[5] Postoperative sore throat is at its peak 2 to 6 hours after extubation. [6, 7] In majority of patients it is relieved within 24 hours. It has been reported that 11% can have residual symptoms 96 hours post extubation.[6]

The cause of postoperative sore throat could be mucosal injury in the trachea[8] or vocal cord injury. [9] Other factors that may contribute to postoperative sore throat are trauma due to oropharyngeal suctioning, irritant effect of unhumidified gases, use of throat pack. Previously female gender, size of the endotracheal tube, grade of difficulty in intubation and duration of surgery were recognized as the risk factors for postoperative sore throat.[1, 2, 10]

Various pharmacological and non-pharmacological methods to prevent postoperative sore throat have been studied. Ketamine is a N-methyl D-aspartate (NMDA) receptor antagonist. It is involved in the anti-nociception and anti-inflammatory cascade. Considering this we studied whether pre-operative gargling with ketamine helps to decrease the incidence and severity of postoperative sore throat.

MATERIAL AND METHODS

The present study was conducted after approval from the institutional ethical committee. In a prospective randomized double blind study 60 patients among the age group 20-40 years were studied. They were randomly divided into two groups using closed envelope technique. Each group had 30 patients; Group 1(K), the ketamine group and Group 2(C), the placebo group. Group K patients gargled with preservative free ketamine 50mg in 29ml distilled water while Group C patients gargled with 30 ml distilled water. Inclusion

criteria were both male and female patients aged 20-40 years undergoing elective abdominal and pelvic surgery, American Society of Anaesthesiologists (ASA) physical status I and II and those who were willing to give informed consent. Patients refusing to participate in the study and patients with ongoing sore throat or upper respiratory tract infection were excluded from the study. Other exclusion criteria were patients with history of bronchial asthma, patients with anticipated airway difficulty (Mallampati grade III / IV), patients on ongoing treatment with anti-inflammatory medications and patients with known allergy to the study drug.

Prior to surgery pre-anaesthetic evaluation was done of all patients. Thorough systemic and general examination was done to rule out associated systemic disease. Investigations like complete blood count, urine routine and microscopy, liver function test, kidney function test, blood sugar, electrocardiogram and chest X-ray PA view was done. Height and weight of patients was recorded. Written, valid and informed consent was taken from the patients. Nil by mouth status was confirmed. All the equipment and drugs necessary for resuscitation and general anaesthesia were kept ready. On operating table baseline vital parameters were recorded. Intraoperative monitoring included non-invasive blood pressure monitor, pulse oximeter and continuous ECG monitor. An intravenous line was secured with 20G angiocath. In order to maintain the blind nature of the study, the studied drugs were prepared by the anaesthesia technician unaware of the study drugs, as per the instructions written in a sealed envelope. Procedure of gargling was explained to the patients. They were asked to gargle with the preparation for 30seconds. Anaesthesia was induced 5 minutes after gargling.

Patients were pre-medicated with injection glycopyrrolate 4µg/kg IV, injection midazolam 0.03 mg/kg IV and injection fentanyl 2 µg/kg IV. Pre-oxygenation was done with 100% oxygen for 3 minutes following which anaesthesia was induced with injection propofol 2mg/kg IV. After assuring that the patient is adequately ventilated, injection atracurium 0.5 mg/kg IV was given. Patient was ventilated with 100% oxygen for 3-4 minutes for adequate muscle relaxation. Patient was intubated with sterile portex cuffed endotracheal tube 7.0 mm internal diameter for females and 8.5 mm internal diameter for males. All patients were intubated by senior anaesthesiologist. Tracheal tube cuff was inflated with volume of air required to prevent an audible leak. Anaesthesia was maintained with 50% oxygen, 50% nitrous oxide, isoflurane and maintenance doses of injection atracurium IV (1/5th of induction dose). For post operative analgesia injection paracetamol 1gm 6 hourly IV was given.

After completion of surgery residual neuromuscular blockade was reversed with injection neostigmine 50 µg/kg IV and injection glycopyrrolate 10 µg/kg IV. Oropharyngeal secretions were suctioned under direct vision to avoid trauma to tissues. Patients were extubated after they fulfil the criteria for adequate reversal (audible cough reflex, sustained head lift and hand grip for 5 seconds). Patients who required more than one attempt of intubation and duration of laryngoscopy more than 20 seconds were excluded from the study. Duration of surgery was noted in both groups.

Post operatively patients were asked about sore throat by blinded observer. Sore throat was assessed at 0, 4, 8 and 24 hours after extubation and graded on 0 -3 scale.

Side effects if any were also noted.
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 or her own).
3-Severe sore throat (complains of change in voice or hoarseness of voice associated with throat pain).

Statistical analysis was done by using unpaired t-test and chi square test.

RESULTS

The two groups were comparable in terms of demographic data, mean pulse rate and mean arterial pressure (Table1).

Table 1: Demographics and hemodynamic parameters

Parameters	Group C	Group K	P value
Age (years)	32.03 ± 7.015	31.07 ± 7.168	p = 0.599
Height (cms)	158.8 ± 10.05	160.2 ± 9.817	p =0.596
Weight (Kgs)	59.23 ± 7.113	58.30 ± 8.665	p = 0.649
Mean pulse rate	82.73 ± 10.71	73.10 ± 4.901	p = 0.764
Mean arterial pressure	81.87 ± 11.60	75.13 ± 5.476	p =0.135

Table 2 shows the duration of laryngoscopy and duration of surgery in both groups. The p value for duration of laryngoscopy (p =0.668) and duration of surgery (p=0.646) was comparable in both groups.

Table 2: Duration of laryngoscopy and duration of surgery

Particulars	Group C Mean +SD	Group K Mean +SD	P value
Duration of laryngoscopy (sec)	13 + 1.77	13 + 1.80	0.668
Duration of surgery (min)	124.4 + 26.50	121.3 ± 26.09	0.646

Table 3 shows the number of patients in Group C, complaining postoperative sore throat at 0, 4, 8 and 24 hours after surgery. In Group C, 27 patients complained of postoperative sore throat at '0 hour'. At '4 hours' postoperative sore throat was present in 26 patients. This decreased to 20 patients at '8 hours' and 15 patients at '24 hours' postoperatively. Severe sore throat means change in voice or hoarseness of voice, was reported in 4 patients 24 hours postoperatively.

Table 3: Post Operative Sore Throat: Group C

TIME (hours)	0	4	8	24
NO SORE THROAT	3	4	10	15
MILD SORE THROAT	19	18	12	8
MODERATE SORETHROAT	6	6	5	3
SEVERE SORE THROAT	2	2	3	4
TOTAL SORE THROAT	27	26	20	15

Table 4 shows the number of patients in Group K reporting postoperative sore throat at 0, 4, 8 and 24 hours after surgery. In Group K 20 patients complained of postoperative sore throat at '0 hours'. This decreased to 14 patients at '4 hours', 7 patients at '8 hours' and 4 patients at '24 hours'. There was not a single patient who reported severe sore throat at any time after surgery.

Table 4: Post Operative Sore Throat: Group K

TIME (Hours)	0	4	8	24
NO SORE THROAT	10	16	23	26
MILD SORE THROAT	15	10	5	3
MODERATE SORE THROAT	5	4	2	1
SEVERE SORE THROAT	0	0	0	0
TOTAL SORE THROAT	20	14	07	04

By applying Chi-Square test to data in table 3 and table 4, mean and standard deviation of the incidence of postoperative sore throat was calculated (table 5). At all observation time point, it was noted that $p < 0.05$. Thus it proved that preoperative ketamine gargles help in preventing postoperative sore throat.

Table 5: Mean and standard deviation of the incidence of postoperative sore throat

TIME (hours)	GROUP C MEAN + SD	GROUP K MEAN + SD	p VALUE
0	1.233 +0.727	0.833 + 0.698	0.034
4	1.200 + 0.761	0.600 + 0.724	0.002
8	1.033 + 0.964	0.300 + 0.596	0.0008
24	0.866 + 1.07	0.166 + 0.461	0.0018

The incidence of postoperative sore throat was more in Group C compared to Group K. In Group C the incidence of postoperative sore throat at 0, 4, 8 and 24 hours was 90%, 86.7%, 66.7% and 50% respectively. At corresponding time point in Group K it was 66.7%, 46.7%, 23.3% and 13.3% (as shown in table 6).

Table 6: Comparison of postoperative sore throat in Group C and Group K

TIME (hours)	0		4		8		24	
GROUP	C	K	C	K	C	K	C	K
No sore Throat	3 (10%)	10 (33.3%)	4 (13.3%)	16 (53.3%)	10 (33.3%)	23 (76.6%)	15 (50%)	26 (86.7%)
Mild sore throat	19 (63%)	15 (50%)	18 (60%)	10 (33.3%)	12 (40%)	5 (16.6%)	8 (26.7%)	3 (10%)
Mod sore throat	6 (20%)	5 (16.6%)	6 (20%)	4 (13.3%)	5 (16.6%)	2 (6.6%)	3 (10%)	1 (3.3%)
Severe sore throat	2 (6.6%)	0	2 (6.6%)	0	3 (10%)	0	4 (13.3%)	0
Total sore Throat	27 (90%)	20 (66.7%)	26 (86.7%)	14 (46.7%)	20 (66.7%)	7 (23.3%)	15 (50%)	4 (13.3%)

DISCUSSION

After general anaesthesia with endotracheal intubation, sore throat is a common postoperative complication. It is usually self-limiting but is an important measure of quality of patients care. Patients with postoperative sore throat had a 14-minute longer stay in the post anaesthesia care unit and a 25-minute longer stay in the ambulatory care unit, and were discharged 51 minutes later from the facility compared with those who did not complain of postoperative sore throat.[11] Therefore, identification of risk factors and prevention of these symptoms would add to patient satisfaction and decrease the cost of care. Literature shows number of risk factors implicated in postoperative sore throat. They are age and gender of patient, duration of surgery, surgical positioning, type and size of airway device, intra-cuff pressure, use of anaesthetic spray or lubricant, use of succinylcholine, concurrent use of nasogastric tube, throat packing, oropharyngeal suctioning.

In the present study, we found no association between the age and gender of patient and postoperative sore throat. Few studies report postoperative sore throat to be more common in younger age group[11] while others found it to be more common in elderly.[10] The reason for postoperative sore throat to be common in a particular age group is not known. It is said that, in women, hormonal changes after menopause result in dryness of upper airway mucosa. This dry mucosal lining is more susceptible to injury during laryngoscopy, intubation, throat packing and suctioning. Many authors report female gender to be at risk for developing postoperative sore throat.[1,10,11] Biro et al, Ahmed et al and Higgins PP found sore throat to be more common in females. The reason is not known but it has been suggested that there might be a gender difference in reporting adverse outcomes to hospital staff.[12]

Duration of surgery more than 60 minutes increases the incidence of postoperative sore throat.[1, 10,13] In our study duration of surgery was comparable in both groups (p=0.664). No anaesthesia trainee was allowed to intubate patients included in the study. It is assumed that in the inexperienced hands of trainee the duration of laryngoscopy will be more, more important is that the chances of mucosal injury during laryngoscopy is increased leading to more sore throat. The experience of the person performing the intubation was considered significant for the development of postoperative sore throat in the study of Jaensson et al.[6] On the other hand, Monroe et al and Edomwonyi et al found no relation between postoperative sore throat and the experience or skill of anaesthesiologist in their study.[4, 13] Duration of laryngoscopy was comparable in both groups (p=0.668).

In our study, all female patients were intubated with 7.0 mm internal diameter ETT while all male patients were intubated with 8.5 mm internal diameter ETT. Both McHardy and Chung[3] and Edomwonyi et al[13] have shown that the small sized ETT reduces the incidence of postoperative sore throat. In addition to the size of ETT, another important factor is the intra-cuff pressure of ETT. Ratnaraj et al concluded that maintaining the ETT cuff pressure to 20 mm of Hg helps in decreasing the incidence of postoperative sore throat and hoarseness.[14] High cuff inflation pressure leads to decrease tracheal mucosal blood flow. Due to non availability of pressure manometer in our institute intra-cuff pressure was not monitored in our study. Use of succinylcholine was avoided in our study. Intravenous succinylcholine causes post operative skeletal muscle pain .This may be due to sarcolemmal tears during fasciculations or widening of sarcolemmal pores and / or membrane bound vacuole formation within the muscle fibres following succinylcholine treatment. As peripharyngeal muscles are striated it is possible that succinylcholine can induce muscle pain at this site which presents clinically as sore throat. Higgins et al reported an increase in the incidence of POST with use of succinylcholine.[11] Ketamine is absorbed both via the oral and transmucosal routes. Gargling with ketamine would keep the drug in contact with oral mucosa leading to systemic absorption of ketamine. Also some amount of drug is swallowed along with saliva. Even though the quantity of absorbed ketamine is small it may have significant analgesic effect. NMDA receptors are present in the central nervous system and in the peripheral nerves. Ketamine, an NMDA receptor antagonist, is involved in pain pathway and anti-inflammatory cascade.

Chan et al[15] studied whether the beneficial effect of ketamine gargles on postoperative sore throat was due to the systemic effects of ketamine. In their study, subjects gargled with 40 mg of ketamine for 30 seconds, and serum ketamine and nor-ketamine levels were measured in 5 subjects after gargling at intervals up to 103 minutes. After oral administration the plasma concentration of ketamine at which analgesic effect is seen is 40 ng/ml [16]. In their study, the highest average ketamine and norketamine concentrations during surgery was 16.16 ng/ml and 11.43 ng/ml respectively. These levels would have decreased after surgery suggesting that systemic absorption was unlikely to play a major role in reduction of post operative sore throat and a topical effect is a possibility. The pharmacokinetics of ketamine in analgesic doses after intravenous, intramuscular and oral administration was investigated in healthy volunteers by Clements et al[17]. Elevation of pain threshold was noted in an ischemic exercise test. After intramuscular injection the pain threshold was increased for 15-60 minutes while after the oral solution there was no effect. Pain threshold elevation occurred at plasma ketamine concentration above 160ng/ml.

The anti-inflammatory effects of ketamine have been studied in various models including

endotoxemia, sepsis, ischemia and burns[18,19,20]. These effects involve modulation of the molecular mediators of inflammatory response, including transcription factors such as nuclear factor- kB (NF-kB) and peroxisome proliferator- activated receptor-gamma (PPAR-gamma) and proteins such as heme oxygenase-1 (HO-1), inducible nitric oxide synthase (i NOS) and cyclooxygenase-2 (COX-2)[18,21,22]. When ketamine is given either before or after various pro-inflammatory insults it diminishes systemic production of cytokines, such as interleukins -1 alpha, -1 beta and -6, tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) thus improves survival[19, 20]. Recent evidence suggests that ketamine in sub-anaesthetic doses improves end-organ dysfunction and has anti-inflammatory effects[23,24].

In Group C, the incidence of POST at 0, 4, 8 and 24 hours after surgery was 90%, 86.7%, 66.7% and 50% respectively. At the same observation time point, the incidence in Group K was 66.7%, 46.7%, 23.3% and 13.3%. In ketamine group not a single patient reported severe sore throat at any point of time. The difference in the incidence and severity of postoperative sore throat was statistically significant ($p<0.05$). In our study we did not measure serum ketamine and norketamine levels. However a central action due to systemic absorption cannot be ruled out. Reduction in the incidence of postoperative sore throat was thought to be due to the anti-inflammatory property of ketamine.

CONCLUSION

We found that preoperative gargling with ketamine is a simple and effective means in reducing the incidence and severity of postoperative sore throat up to 24 hours post extubation. Though it involves an additional step of gargling prior to induction of anaesthesia, it goes a long way to improve patient satisfaction and comfort after general anesthesia with endotracheal tube.

Abbreviations

ETT: Endotracheal Tube, POST: Postoperative sore throat

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