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Efficacy of Ketamine Gargle for Attenuating Post-Operative Sore Throat in Patient Undergoing General Anaesthesia with Endotracheal Intubation

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Abstract

Background and Objective: Postoperative sore throat (POST) is a common complication of general anaesthesia with endotracheal intubation that affects patient satisfaction after surgery. Postoperative sore throat following tracheal intubation is due to trauma to the airway mucosa. The reported incidence of postoperative sore throat varies from 21-65%. Various pharmacological and nonpharmacological agents have been used for attenuating postoperative sore throat with variable success. Ketamine, a NMDA antagonist, is involved with antinociception and anti-inflammatory cascade with "anti-hyperalgesic',' anti-allodynic' and possibly opioid 'tolerance-protective' effect due to an additive effect with opioids reducing wind up and central sensitization by postsynaptic NMDA blockade. *Methodology*: 64 patients aged between 18 to 59 years, scheduled for various elective surgical procedures undergoing endotracheal intubation belonging to ASA I-II satisfying the criteria were randomly assigned into 2 groups of 32 each. Group C: Drinking water gargle- 30ml (placebo) for 40 seconds, 5 minutes before induction. Group K: Ketamine gargle (1mL=50 mg in 29 mL drinking water) for 40 seconds, 5 minutes before induction. *Results:* The overall incidence of post-operative sore throat in the control group (Group C) of our study population was 96.9%. The overall incidence of post-operative sore throat was positively less in Ketamine gargle group (Group K) with 53.1% when compared to 96.9% in the control group (Group C). There was a significant decrease in the incidence of post-operative sore throat seen in the Ketamine gargle group at 4, 8 and 24 hours after extubation. *Conclusion:* Ketamine gargle (50 mg ketamine =1 mL in 29 mL of drinking water) for 40 seconds, 5 minutes before induction of anaesthesia is a useful adjunct to decrease post-operative sore throat after endotracheal intubation.

Keywords: Post-Operative Sore Throat; Endotracheal Intubation; Ketamine Gargle.

Introduction

Postoperative sore throat is a common complication of anaesthesia with endotracheal intubation that affects patient satisfaction after surgery. Recently quality assurance of anaesthesia has become increasingly important for improving postoperative outcome [1].

Tracheal intubation is a foremost cause of trauma to the airway mucosa, resulting in postoperative sore throat (POST) and reported incidence varies from 14.4% to 100% [2,3]. The high variability of incidence is due to a large number of factors implicated in POST such as type of airway device, technique of insertion, type of lubricant used, airway design, cuff pressure, length of procedure, anaesthesia administered, evaluation techniques and a multitude of patient features.

Postoperative sore throat was recently ranked by American Society of Anaesthesiologist as the eighth most important problem of current anaesthesiology practice [4]. Although the symptoms resolve spontaneously without any treatment, prophylactic management for decreasing its frequency and severity is still recommended [5].

Lack of airway humidity, trauma during airway insertion, suctioning, high anaesthetic air flow rates and surgical manipulation of airway and adjacent tissue are possibly the causative factors for POST [2].

Various pharmacological and non-pharmacological agents have been used for

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attenuating postoperative sore throat with variable success. Identification of the factors associated with an increased risk of POST will allow anaesthesia providers to avoid combinations of controllable factors, decrease the incidence of POST and improve patient anaesthetic outcomes [2].

Ketamine gargle is shown to be a promising agent to reduce post-operative sore throat by a few authors [4,6,7,8,9]. Ketamine is a noncompetitive inhibitor at the N-methyl D-aspartate (NMDA) receptor. It has been shown that NMDA receptors are present not only in the CNS but also in peripheral nerves. It has been further reported that peripherally administered NMDA receptor antagonist are involved with antinociception and antiinflammatory cascade [4,10,11].

Objective

1. To assess the efficacy of preoperative gargling with ketamine for attenuating postoperative sore throat in patient undergoing general anaesthesia with endotracheal intubation compared with placebo
2. Incidence of POST in surgeries under general anaesthesia.
3. To evaluate the effect of ketamine gargle on the incidence of POST at 4, 8, and 24 hours after extubation in the post-operative period.

Methodology

The present study was conducted in the Department of Anaesthesiology, Government Medical College Kottayam during the period of November 2013 to November 2014.

Study Population

64 patients belonging to ASA. PS 1 and II category undergoing elective surgery.

Sample Size

Total sample size of 64 cases, 32 cases in each group

Sample Size Calculation

Calculated by following formula

$$\frac{C \times {}_1(1-{}_1)+{}_2(1-{}_2)}{({}_1-{}_2)2}$$

C = 7.9 for 80% power

$_1$ = Proportion of control

$_2$ =Proportion of cases

Study Tools

Interview Schedule

Inclusion Criteria

- Patient belongs to categoryASA PS1 & ASAPS II.
- Patients aged between 18-59 years of both sex.
- Patients undergoing elective surgery under general anaesthesia with endotracheal intubation.

Exclusion Criteria

- Anticipated airway difficulty.
- Cardiac disease, Bronchial asthma.
- H/O pre-operative Sore throat.
- H/O recent anti-inflammatory medication
- Patient requiring more than one attempt for passage of tracheal tube
- Patients undergoing oral-surgeries, surgeries requiring throat packing and ryles tube insertion.
- Known allergy to ketamine.
- Patients on steroid therapy > 2 weeks.

Study Procedure

The study was undertaken after obtaining ethical committee clearance. The protocol was explained to all patients in detail and an informed written consent for participation in study was obtained. The study was conducted in a prospective, randomized, placebo-controlled, and single-blinded manner. Patients satisfying the inclusion criteria are selected and were randomly assigned (by means of a random number table) in a single-blind manner into one of two groups, group C (control) and K (ketamine), each group having 32 members.

A routine pre anaesthetic examination was conducted before the surgery assessing:

- General condition.
- Airway assessment.
- Systemic examination of the patient, presence of any exclusion factors.

Appropriate investigations were done according to the condition of the patient.

All selected patient were pre-medicated on the previous night and on the morning of day of surgery at 6 am with T. Ranitidine 150mg + T.metoclopramide10mg+ T.alprazolam 0.25mg. On arrival at the pre-operative ward, an 18/20 gauge intravenous cannula was inserted and an infusion of normal saline was started.

Group C received drinking water 30 ml and Group K received Ketamine 1ml (50mg) in 29 ml of drinking water. 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 40 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 consists of ECG, Noninvasive blood pressure and Pulse oxymetry following preoxygenation, Anaesthesia was induced with pethidine 1 mg/kg and thiopentone 5 mg/ kg. Tracheal intubation was facilitated by vecuronium bromide 0.1 mg/kg and the trachea was intubated with a soft seal cuffed sterile polyvinyl chloride endotracheal tube with a standard cuff internal diameter of 7/ 7.5 millimetre for women and 8/8.5 millimetres for men.

Tracheal intubation was performed by an experienced anaesthesiologist having experience of >3 years. Immediately after intubation, the cuff of the endotracheal tube was filled with a volume of room air to prevent an audible air leak. Anaesthesia was maintained with oxygen 33% in nitrousoxide and supplemented with isoflurane. At the end of the procedure residual neuromuscular blockade was reversed with neostigmine and glycopyrrolate. Oropharyngeal suctioning was performed under direct vision before extubation.

The patient was interviewed by a blind investigator at 4, 8 and 24 hour after the procedure. Postoperative sore throat was graded on a four point scale (0-3).

1. No sore throat
2. Mild sore throat (complaints of sore throat only on asking)
3. Moderate sore throat (Complaints of sore throat on his / her own)
4. Severe sore throat (change in voice associated with throat pain)

Other side effect if any, also will be noted like head *ache,* vomiting, blurred vision/diplopia, and emergence phenomena.

Data Management and Analysis

Data was coded and entered in Microsoft Excel sheet and analysed using statistical software package SPSS software. Data was analysed by appropriate statistical methods. To compare patient characteristics, including age, height, body weight and duration of endotracheal intubation student's t-test was performed. Quantitative variables were expressed as mean and standard variation. The chi-square test was used for multiple paired comparisons of counts in patients with POST. $P< 0.05$ was considered statistically significant.

Results

Age Distribution of Patients

The minimum age in group K and C were 20 and 21 years respectively. The maximum age in groups K and C were 56 years. The mean age in group K and C were 39.1 and 41.6 years. Age distribution was statistically similar in both groups with p = 0.324.

Table 1: Age distribution of patients studied

Group	N	Age in years		T	P
		Mean	SD		
Ketamine	32	39.1	11.0	.995	.324
Control	32	41.6	9.0		

χ^2 =1.121 df = 2 p=0.571

Table 2: Showing the body weight distribution of the patients

Group	N	Weight in Kg		t	p
		Mean	SD		
Ketamine	32	57.81	8.078	0.357	0.688
Control	32	58.50	7.291		

χ^2 =1.299 df =2 p=0.522

Table 3: Height distribution of patients studied

Table 3a:

Group	N	Height in cm	
		Mean	sd
Ketamine	32	156.28	5.372
Control	32	153.53	3.716

Table 3b:

Height in cm	Group				Total	
	Ketamine		Control			
	N	%	N	%	N	%
<155	15	46.9	22	68.8	37	57.8
155-160	9	28.1	9	28.1	18	28.1
>160	8	25.0	1	3.1	9	14.1
Total	32	100.0	32	100.0	64	100.0

Body Weight Distribution

The minimum body weight in groups K and C were 46kg and 45 kg respectively. The maximum body weight in groups K and C were 74 and 70 kg respectively. Weight distribution was statistically similar in two groups with p = 0.688

Height distribution of patients

The minimum Height in cm. in groups K and C were 148 cm. The maximum Height in groups K and C were 166 and 163 respectively. Height distribution was statistically similar in two groups.

BMI Distribution of Patients Studied

The mean body mass index in group K was 23.6 ± 2.58 and in group C was 24.81 ± 2.74. BMI distribution was statistically similar in two groups with p =0.208

Gender Distribution

Group K had 16 males and 16 females. Group C had 14 males and 18 females. Samples are gender matched with p=0.616

Type of surgery

In Group k, 23(71.9%), 4(12.5%) and 5 (15.6%) and in Group C, 22(68.8%), 3(9.4%) and 7(21.9%) patients underwent general surgery, orthopedics surgery and urosurgery respectively. Distribution of surgery type is statistically similar in both groups with p=0.779.

ASA Grading

In Group K, 22(68.8%) and 10(31.3%) patients belonged to ASA category 1 and 11 respectively. In Group C, 24(75%) and 8(25%) patients belonged to ASA category 1 and 11 respectively. Samples are ASA grade matched with p=0.578.

Table 4: BMI Distribution of Patients Studied

Group	N	BMI		t	p
		Mean	sd		
Ketamine	32	23.6	2.5	1.835	.071
Control	32	24.8	2.7		

df =2 p=0.208 χ^2 =3.141

Table 5: Gender distribution of patients studied

Sex	Group				Total	
	Ketamine		Control			
	N	%	N	%	N	%
Male	16	50	14	43.8	30	46.9
Female	16	50	18	56.3	34	53.1
Total	32	100	32	100	64	100

χ^2 =0.251 df =1 p=0.616

Table 6: ASA grade of the two groups of patients studied

ASAPS	Group				Total	
	Ketamine		Control			
	N	%	N	%	N	%
Category 1	22	68.8	24	75	46	71.9
Category 2	10	31.3	8	25	18	28.1
Total	32	100	32	100	64	100

X^2 =0.309 df =1 p=0.578

Table 7: Comparison of duration of endotracheal intubation in two groups studied

Group	N	DOEI		t	p
		Mean	sd		
Ketamine	32	137.2	20.9	1.542	.128
Control	32	145.8	23.6		

Table 8: Distribution of postoperative sore throat

Post	Ketamine group	Control group
YES	17[53.1%]	31[96.9%]
NO	15[46.9%]	1[3.1%]

Duration of Endotracheal Intubation

Duration of endotracheal intubation was statistically similar in two groups with p=0.128 and mean ± SD of 137.2±20.9 and 145.8±23.6 minutes in Group A and Group B respectively.

Incidence of Post-Operative Sore Throat

The overall post-operative sore throat was positively less in Group K with 17 (53.1%) patients when compared to Group C with 31(96.9%).

46.9% of patient among the ketamine group did not develop sore throat while only 3.1% of the control group were free of sore throat. This difference is statistically significant with Pearson chi-square value of 16.33 and p value of< 0.001

Incidence of Post at 4 hour, 8 hours and 24 hours after Extubation

The incidence of POST in Group K was lesser compared to Group C at 4, 8 and 24 hours after extubation.

Table 9: Post at 4 hour

Grading of post	Ketamine group	Control group
Grade 0	21	5
Grade1	9	18
Grade 2	2	7
Grade3	0	2

χ^2 =17.624 df =3 p=0.001

Table 10: Post at 8 hour

Grading of post	Ketamine group	Control group
Grade 0	26	10
Grade 1	5	12
Grade 2	1	4
Grade 3	0	6

Table 11: Post At 24 Hours

POST grading	Ketamine group	Control group
Grade 0	30	17
Grade 1	2	5
Grade 2	0	2
Grade 3	0	8

Post at 4 hour

At 4 hour after extubation, reduction in mild, moderate and severe post-operative sore throat is seen in Group 1 compared to Group 2.

65.6% of patient among the ketamine group did not develop sore throat while only 15.6% of the control group were free of sore throat. This difference is statistically significant with Pearson chi-square value of 17.624 and p value of 0.001.

Post at 8 hour

At 8 hours after extubation, reduction in mild and moderate and severe post-operative sore throat is seen in Group K compared to Group C.

81.3% of patient among the ketamine group did not develop sore throat while only 31.3% of the control group were free of sore throat. This difference is statistically significant with pearson chi-square value of 16.254 and p value of < 0.001.

Post at 24 Hours

93.8% of patient among the ketamine group did not develop sore throat while only 53.1% of the control group were free of sore throat. This difference is statistically significant with Pearson chi-square value of 14.196 and p value of 0.003

Discussion

In the modern anaesthetic practice many of the general anaesthetic procedures are carried out with endotracheal intubation. Postoperative sore throat (POST) is a well-recognized minor complication after general anaesthesia [2] rated by ASA as the 8th most common outcome in the postoperative period.[4] Though the symptoms resolve spontaneously without any treatment[5] prophylactic management for decreasing its frequency and severity is still recommended to improve the quality of post anesthesia care.

POST is a description representing a broad constellation of signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia [4] with incidence varying from 14.4% to 100% after endotracheal intubation [2]. 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 intra-cuff pressure [12,13].

Various pharmacological and non-pharmacological agents have been used for attenuating postoperative sore throat with variable success. Identification of the factors associated with an increased risk of POST will allow anaesthesia providers to avoid combinations of controllable factors, decrease the incidence of POST and improve patient anaesthetic outcomes.

Many pharmacological interventions like steroids, non-steroidal anti-inflammatory drugs, lignocaine, etc. have been used to attenuate POST by various authors. But all such manoeuvres had their own limitations.

Hence, in this study, patients in Group C were asked to gargle with drinking water 30 mL for 40 seconds 5 minutes prior to induction and in Group K were asked to gargle with Ketamine 1 mL=50mg in 29 mL of drinking water for 40 seconds, 5 minutes prior to induction.

Post Severity Grading Scale

In this study, a four point scale similar to the scale used in the above mentioned studies was used.

Post Assessment Interval

In this study, POST was assessed at 4 hour after arrival at the post anaesthetic care unit, 8 hours and 24 hours later.

Incidence of POST

In our study, the overall incidence of POST was positively less in group K (ketamine) with 53.1% when compared to Group C (controls) [96.9%] which is statistically significant with Pearson chi-square value of 16.583 and p value of < 0.001.

Ketamine a noncompetitive NMDA antagonist has been found to attenuate POST by various authors [4,6,7,8,9].

Sore throat might be a consequence of localized trauma, leading to aseptic inflammation of pharyngeal mucosa. It may also be associated with oedema, congestion, and pain [14]. 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.

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.

Post at 4 Hour after Extubation

In our study, the incidence of POST was lesser in group K (ketamine) with 34.4%compared to 84.4% in group C.

The incidence of mild, moderate and severe POST in Group K was 28.1%, 6.3% and 0% respectively compared to Group C which was 56.3%, 21.9% and 6.3% respectively. This difference is statistically significant with Pearson chi-square value of 16.583 and p value of <0.001 [4,6,8].

Our study results did show a decrease in the incidence of POST at 4 hours after extubation after ketamine gargle similar to the above mentioned.

Post at 8 Hours after Extubation

In our study, the incidence of POST was lesser in group K (ketamine) with 18.8% compared to 68.8% in group C. The incidence of mild, moderate and severe POST in Group K was 15.6%, 3.1% and 0% respectively which was lesser compared to Group C which was 37.5%, 12.5% and 18.8% respectively. This difference is statistically significant with Pearson chi-square value of 16.254 and p value of < 0.001 [6,8].

Our study results did show a decrease in the incidence of POST at 8 hours after extubation after ketamine gargle similar to the above mentioned.

Post at 24 Hours after Extubation

In our study, the incidence of POST was lesser in group K (ketamine) with 6.3% compared to 46.9% in group C. The incidence of mild, moderate and severe POST in Group K was 6.3%, 0% and 0% respectively compared to Group C which was 25%, 6.3% and 15.6%. This difference is statistically significant with Pearson chi-square value of 13.537 and p value of < 0.001)

Comparing with the previous reports with topical ketamine with higher doses, our doses were relatively low and we did not observe any CNS side-effects.

Limitation of Study

1. 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.
2. Intracuff pressure was not monitored during our study.

Conclusion

We conclude that the overall incidence of post-operative sore throat in the control group (Group C) of our study population was 96.9%. The overall incidence of post-operative sore throat was positively less in Ketamine gargle group (Group K) with 53.1% when compared to 96.9% in the control group. There was a significant decrease in the incidence of post-operative sore throat seen in the Ketamine gargle group at 4, 8 and 24 hours after extubation.

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