

EFFICACY OF KETAMINE GARGLE FOR ATTENUATING POSTOPERATIVE SORE THROAT IN PATIENTS UNDERGOING GENERAL ANAESTHESIA WITH ENDOTRACHEAL INTUBATION

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ABSTRACT

BACKGROUND

Postoperative sore throat is ranked by American Society of Anesthesiologists as eighth most important problem of current clinical anaesthesiology. This study is to evaluate whether preoperative gargling with ketamine reduce postoperative sore throat after endotracheal intubation when compared with gargling with saline.

MATERIALS AND METHODS

130 patients of either sex in the age group 20 - 60 years scheduled for elective surgery under general anaesthesia with endotracheal intubation were included in the study. The duration of surgeries was taken as less than or equal to 3 hours. Patients were asked to gargle with preparation for 30 seconds. Anaesthesia was induced 5 minutes later. Patients were interviewed by a blinded investigator at 4, 8, 24 hours after the procedure for postoperative sore throat. Postoperative sore throat was graded on a four point scale. Group 1 will receive preservative free ketamine 50 mg in 29 mL 0.9% saline. Group 2 will receive 30 mL 0.9% saline.

RESULTS

The groups were comparable with respect to age, sex, weight, height, ASA grading, type of surgery and duration of surgery. There was no statistically significant difference in comparison of pulse rate or blood pressure between the two groups at specific time intervals. The overall incidence of sore throat in control group and study group at 4 hrs., 8 hrs. and 24 hrs. intervals was analysed with Mann-Whitney U test, which showed p value of less than 0.05 and difference was statistically significant. Incidence of severe sore throat was significantly higher in control group than study group. There were no adverse reactions noted in ketamine group.

CONCLUSION

In conclusion, gargling with ketamine for 30 seconds five minutes prior to induction reduces postoperative sore throat.

KEYWORDS

Sore Throat, Ketamine Gargle, Endotracheal Intubation.

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BACKGROUND

Postoperative sore throat is ranked by American Society of Anesthesiologists as eighth most important problem of current clinical anaesthesiology.¹

Postoperative sore throat following tracheal intubation is due to mucosal erosion caused by cuff of endotracheal tube,² trauma from intubation and mucosal dehydration.³ The prevalence of postoperative sore throat also varies with diameter, type of endotracheal tube⁴ and cuff pressure used. It may be helpful to give drugs prophylactically to alleviate postoperative sore throat. Pharmacological methods include beclomethasone inhalation and gargling with azulene sulfonate.⁵ Among 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, minimising intra cuff pressure and extubation when tracheal tube cuff is fully deflated have been reported to decrease incidence of postoperative sore throat. The reported incidence of postoperative sore throat is 30% to 70%.⁶ Postoperative sore throat contributes to postoperative morbidity and patient dissatisfaction.

N Methyl D aspartate receptors are members of glutamate receptor channel superfamily, which mediate most of the fast excitatory synaptic transmissions in the central nervous system. The superfamily consists of 3 subtypes: kainate receptors, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors and N-methyl-D-aspartate (NMDA) receptors.

NMDA receptors possess 4 transmembrane (TM) helical domains in the C-terminal half of the sequence and require both glycine and glutamate for activation, resulting in influx of calcium ions into the cell.⁷ The receptors can also be activated by polyamine. They can be blocked by magnesium ions, inhibited by zinc ions and modulated by arachidonic acid.

There is an increasing amount of experimental data showing that N-methyl D aspartate receptors are present also in peripheral nerve.⁸ It is reported that peripherally

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administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade.

Ketamine hydrochloride is 2-(2-chlorophenyl)-2-methylamine cyclohexanone chloride. Ketamine is a non-competitive inhibitor of NMDA receptor. This study is to evaluate whether preoperative gargling with ketamine reduce postoperative sore throat after endotracheal intubation when compared with gargling with saline.

Incidence of sore throat was measured on a four point scale.⁹

MATERIALS AND METHODS

Design

Randomised clinical trial.

Setting

Department of Anaesthesiology, Govt. Medical College, Thiruvananthapuram.

Study Population

Patients scheduled for elective surgery of duration less than or equal to 3 hours under general anaesthesia in Govt. Medical College, Thiruvananthapuram. All of them belong to ASA 1 or ASA 2.

Inclusion Criteria

1. ASA PS 1 and 2.
2. Age group 20 - 60 years.
3. Mallampati grading 1 and 2.
4. Patients posted for elective surgery who will need endotracheal intubation.

Exclusion Criteria

1. History of preoperative sore throat, asthma.
2. Known sensitivity to drug.
3. History of upper respiratory tract infection within past 2 weeks.
4. Recent anti-inflammatory medication.
5. More than one attempt of passage of endotracheal tube.
6. Patients in whom extubation provoked coughing or bucking.
7. Patients undergoing surgeries of neck, nose, oral cavity.
8. Patients not accepting taste.

Duration of Study

3 months.

Sample Selection and Size

Sample size is calculated using formula:

$$n = c^2 \left[\frac{P1 \times (1 - P1) + P2 \times (1 - P2)}{(P1 - P2)^2} \right]$$

n= Sample size.

P1= Incidence of postoperative sore throat in control population.

P2= Incidence of postoperative sore throat in study population.

C= Constant, 7.9 if alpha error= 5% and beta error is 20%.

With an error of 20%, power of the study was 80% and sample size required for the present study was calculated as 124, which was rounded off to 130 patients in total study population. Hence, 65 patients per group will be selected for the study considering the inclusion as well as the exclusion criteria stipulated for the study.

Statistical Analysis

Data was analysed using suitable computer software (SPSS) and appropriate statistical tools were used for analysis. Data was expressed in frequency and percentages. Following statistical tests were used for analysing the data.

1. Chi-square analysis.
2. Mann-Whitney U test.
3. Student's 't' test.

Outcome Variables

Incidence of sore throat was measured using a four-point scale.

Data Collection

The present study was carried out in Govt. Medical College Hospital, Thiruvananthapuram, after obtaining ethical committee clearance. One hundred and thirty patients, of either sex in the age group of 20 - 60 years scheduled for elective surgery under general anaesthesia were included in the study. The duration of surgeries was taken as less than or equal to 3 hours. All the patients belonged to ASA 1 or ASA 2.

Methodology

All patients included in the study underwent a detailed pre-anaesthetic check-up. Patients and nearest relatives were explained about the procedures and written informed consent was taken. Age, weight and height were recorded. Heart rate and blood pressure were recorded 30 minutes before surgery.

Patients are randomly allocated into two groups as per a computer generated random number table. Patients satisfying the criteria were allocated into two groups by choosing particular order from the table.

Pre-Operative Orders

Patients were asked to keep nil orally 8 hours prior to procedure.

All were given Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg preoperative day and night and on morning of surgery.

Monitors

- ECG.
- Pulse oximeter.
- Non-invasive blood pressure monitor.
- End-tidal carbon dioxide monitor.

Premedication

On morning of surgery after securing IV access, Inj. Glycopyrrolate (0.004 mg per kg) and Inj. Midazolam (0.02 mg per kg), Inj. Ondansetron (0.15 mg per kg) were given 15 mins prior to induction. Fentanyl 2 mcg/kg was given 5 mins prior to induction.

Procedure

Group 1- Will receive preservative free ketamine 50 mg in 29 mL of 0.9% saline.

Group 2- Will receive 30 mL of 0.9% saline.

Patients were asked to gargle with preparation for 30 seconds. Procedure of gargling was explained to the patient on pre-operative day. 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 seconds. The nurse did not participate in the subsequent management of these patients. Anaesthesia was induced 5 minutes later. The patients could not be blinded because of different tastes of two preparations.

Anaesthesia

After 3 minutes of pre-oxygenation, induction of anaesthesia with 2 mg/kg propofol followed by 0.1 mg/kg vecuronium bromide followed by bag and mask ventilation for 3 minutes and after adequate relaxation was achieved direct laryngoscopy and endotracheal intubation with sterile polyvinyl chloride orotracheal tube with an internal diameter of 7 - 7.5 mm for women and 8 - 8.5 mm for men. Cuff was filled with a volume of room air required to prevent audible air leak. Heart rate and blood pressure were recorded intraoperatively at specific time intervals. Anaesthesia was maintained with oxygen 33% in nitrous oxide and supplemented with Isoflurane (0.6% - 0.8%). Supplemental analgesia was provided by small doses of intravenous fentanyl. Residual neuromuscular blockade was antagonised by neostigmine (50 mcg/kg) and glycopyrrolate (10 mcg/kg) at end of surgery. Oropharyngeal suction before extubation was done under direct vision to avoid trauma to the tissues confirming that secretion clearance was complete.

Patients were interviewed by a blinded investigator at 4, 8 and 24 hours after the procedure for postoperative sore throat. Postoperative sore throat was graded on a four-point scale.⁹

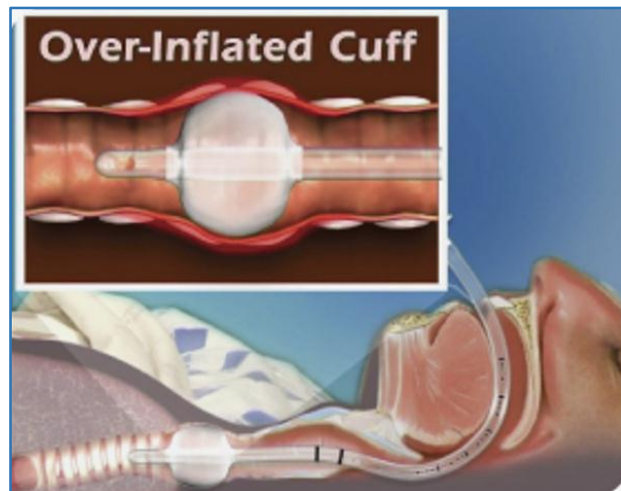
- 0- Nil.
- 1- Mild (Only on asking).
- 2- Moderate (Complains on their own).
- 3- Severe (Change of voice associated with throat pain).



Figure 1. Endotracheal Tube made of different Materials



Figure 2. Endotracheal Tube made of different Materials

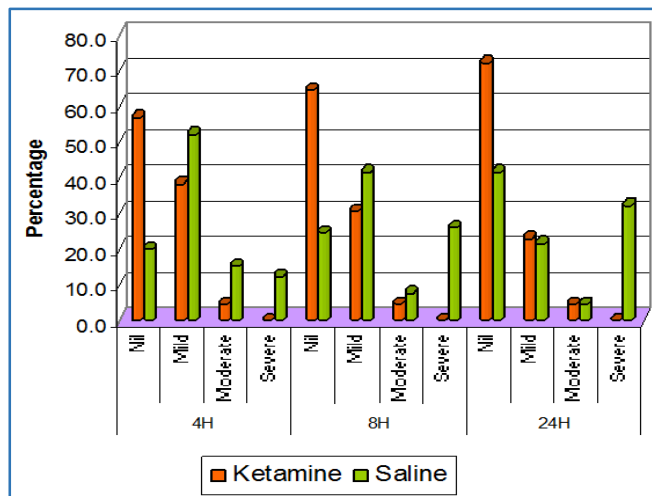


RESULTS

Sore Throat	Ketamine		Saline		Z#	P	
	Count	%	Count	%			
4H	Nil	37	56.9	13	20.0	4.88**	0.000
	Mild	25	38.5	34	52.3		
	Moderate	3	4.6	10	15.4		
	Severe	0	0.0	8	12.3		
8H	Nil	42	64.6	16	24.6	5.27**	0.000
	Mild	20	30.8	27	41.5		
	Moderate	3	4.6	5	7.7		
	Severe	0	0.0	17	26.2		
24H	Nil	47	72.3	27	41.5	4.38**	0.000
	Mild	15	23.1	14	21.5		
	Moderate	3	4.6	3	4.6		
	Severe	0	0.0	21	32.3		

Comparison of Sore Throat at different Time Intervals based on Group

Mann-Whitney U-Test



The overall incidence of sore throat in control group and study group at 4 hrs., 8 hrs. and 24 hrs. interval was analysed with Mann-Whitney U-test, which showed $p < 0.05$ and difference was statistically significant.

DISCUSSION

A general anaesthetic technique that would allow patients to have comfortable postoperative period is highly beneficial. Sore throat is a frequent side effect of general anaesthesia and is reported between 30% - 70% of patients after extubation.^{3,6} Postoperative sore throat is ranked by American Society of Anesthesiologists as eighth most important problem of current clinical anaesthesiology.¹ Postoperative sore throat following tracheal intubation is due to mucosal erosion caused by cuff of endotracheal tube,² trauma from intubation and mucosal dehydration.³ The prevalence of postoperative sore throat also varies with diameter, type of endotracheal tube⁴ and cuff pressure used. Postoperative sore throat contributes to postoperative morbidity and patient dissatisfaction.

The present study was carried out in Govt. Medical College Hospital, Thiruvananthapuram, after obtaining Ethical Committee clearance. One hundred and thirty patients of either sex in the age group of 20 - 60 years scheduled for elective surgery under general anaesthesia were included in the study. The duration of surgeries was taken as less than or equal to 3 hours.

Those excluded from the study included patients with history of preoperative sore throat or asthma with known sensitivity to drug with history of upper respiratory tract infection within past 2 weeks, on recent anti-inflammatory medication, more than one attempt of passage of endotracheal tube, patients in whom extubation provoked coughing or bucking, patients undergoing surgeries of neck, nose, oral cavity and patients not accepting taste.

The aim was to study the efficacy of ketamine gargle for attenuating postoperative sore throat in patients undergoing general anaesthesia with endotracheal intubation. After getting Ethical Committee clearance and informed consent from the patients study was started. Preoperatively, the procedure was explained to the patient and consent was taken. They were randomly allocated to study group and control group based on computer generated random number table. After premedication patients in study group were given ketamine gargle with 50 mg (1 mL) of preservative free ketamine in 29 mL of saline. Patients in control group were given 30 mL of saline. They were asked to gargle the preparation for 30 seconds. Anaesthesia was induced 5 minutes later. Patients were intubated with sterile polyvinyl chloride endotracheal tube with an internal diameter of 7 - 7.5 mm for women and 8 - 8.5 mm for men. Cuff was filled with a volume of room air required to prevent an audible air leak. Heart rate and blood pressure were recorded intraoperatively at specific time intervals. Anaesthesia was maintained with oxygen 33% in nitrous oxide and supplemented with Isoflurane (0.6 - 0.8). Postoperatively, severity of sore throat was assessed on a four-point scale.⁹

0- Nil.

1- Mild (only on asking).

2- Moderate (Complains on their own).

3- Severe (Change of voice associated with throat pain).

The groups were comparable with respect to age, sex, weight, height, ASA grading, type of surgery and duration of surgery. There was no statistically significant difference in comparison of pulse rate or blood pressure between the two groups at specific time intervals.

In the present study, the incidence of mild sore throat at 4 hrs, 8 hrs, and 24 hrs. in ketamine group was 25%, 20% and 15% respectively, where that of control group was 34%, 27% and 41.5% respectively. The incidence of moderate sore throat at 4 hrs., 8 hrs. and 24 hrs. in ketamine group was 4.6%, whereas in control group it was 15.4%, 7.7% and 4.6%. The incidence of severe sore throat at 4 hrs., 8 hrs. and 24 hrs. in ketamine group was 0%, whereas in control group it was 12.3%, 26.2% and 32.3% respectively. In study group 28 (43%) patients complained of sore throat at 4 hours, out of which 23 (35%) had sore throat at 8 hours and 18 (27%) had sore throat at 24 hours. In control group 52 (80%) patients had sore throat at 4 hours, out of which 49 (75%) had sore throat at 8 hours and 39 (60%) had sore throat at 24 hours. The overall incidence of sore throat in control group and study group at 4 hrs., 8 hrs. and 24 hrs. interval was analysed with Mann-Whitney U-test, which showed p value of less than 0.05 and difference was statistically significant. Incidence of severe sore throat was significantly higher in control group than study group. There were no adverse reactions noted in ketamine group.

The results were comparable with the studies conducted by Rudra et al,⁹ Canbay et al¹⁰ and Sherstha et al.¹¹

N-Methyl D aspartate receptors are members of glutamate receptor channel superfamily, which mediate most of the fast excitatory synaptic transmissions in the central nervous system. There is an increasing amount of experimental data showing that N-methyl D aspartate receptors are present also in peripheral nerve.^{12,13} It is reported that peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory¹⁴ cascade. Ketamine hydrochloride is 2-(2-chlorophenyl)-2-methylamine cyclohexanone chloride. Ketamine is a non-competitive inhibitor of NMDA receptor.

In the present study, the overall incidence of postoperative sore throat was significantly reduced in study group compared to control group at 4 hours, 8 hours and 24 hours.

CONCLUSION

The aim of the study was to evaluate efficacy of ketamine gargle for attenuating postoperative sore throat in patients undergoing general anaesthesia with endotracheal intubation. Post-intubation sore throat was assessed with a four-point scale.

One hundred and thirty patients of ASA 1 and ASA 2 patients were taken up for study. They were divided into 2 groups by computer generated random number tables. Control group was given saline gargle; and study group was given ketamine gargle for 30 seconds five minutes prior to intubation.

Demographic profile in both study and control groups were comparable. Vital parameters in both groups were comparable. Overall incidence in postoperative sore throat at 4 hours, 8 hours and 24 hours was significantly reduced in study group compared to control group. Incidence of severe sore throat was significantly reduced in ketamine group.

There is an increasing amount of experimental data showing that N-methyl D aspartate receptors are present also in peripheral nerve. It is reported that peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade. Ketamine is a non-competitive inhibitor of NMDA receptor.

In conclusion, gargling with ketamine for 30 seconds five minutes prior to induction reduces postoperative sore throat. There were no side effects due to ketamine like tachycardia or hypertension. There were no complications noted in the study.

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