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A prospective study to evaluate the role of ketamine hydrochloride gargles for attenuating postoperative sore throat in patients undergoing general anaesthesia with endotracheal intubation

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Abstract

Aim and Objective:: To determine the role of ketamine hydrochloride gargles for attenuating postoperative sore throat in patients undergoing general anaesthesia with endotracheal intubation.

Material and Method: 100 patients of ASA grade 1&2 undergoing general anaesthesia with endotracheal intubation were included in this study. Patients were randomly divided into two groups of 50 each. Group A received normal saline gargle before surgery. Group B received ketamine gargles before surgery. Surgeries were done under routine general anaesthesia with endotracheal intubation. Postoperative pain was assessed by a four pointer scale.

Results: Incidence of sore throat is significantly low (32%) in ketamine group in comparison to placebo group (46%)

Conclusion: As per our study ketamine gargles are effective in attenuating postoperative sore throat in comparison to control group.

Keywords: Ketamine, postoperative sore throat

INTRODUCTION

Postoperative sore throat (POST) is a well-recognized minor complication after general anaesthesia (1,2). Although most of the times symptoms resolve spontaneously without any treatment but prophylactic management for decreasing its frequency and severity is still recommended to improve the quality of post anaesthesia care. POST representing a broad constellation of signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia (3). The reporting of a sore throat is also affected by the method of interview, that is, whether the questions regarding sore throat are asked directly or indirectly (4). Incidence of POST varies with the method of airway management. The incidence is the highest after tracheal intubation and varies from 14.4% to 100% (2,3) while after laryngeal mask airway insertion, the incidence has been found to vary from 5.8% to 34% and it is much less when a face mask - 3.3% (3) is used for the maintenance of anaesthesia (2). Significantly higher incidence of sore throat in women than in men is attributed to the tube fitting tighter in women (5).The use of uncuffed tubes is associated with a significantly higher incidence of sore throat than the use of cuffed tubes (7). Patients who were placed in lithotomy position reported a higher rate of POST than those who were supine during surgery. The use of succinylcholine was associated with an increased incidence of POST. It is suggested that a difficult intubation does not significantly increase the likelihood of POST (6). Younger patients, gynaecological surgery, large tracheal tube, cuff design, intracuff pressure, throat packs and the use of succinylcholine also seem to increase the incidence. It is less well recognized that uneventful intubation for routine surgical procedures can cause pathological changes that may provide an organic basis for patients' postoperative throat symptoms. 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). Pathological changes in the laryngotracheal area, such as epithelial loss, glottis hematoma, glottic edema, sub mucosal tears and contact ulcer granuloma, can occur after even uneventful intubation for routine surgery as a contributing factor to the postoperative hoarseness(8). The injuries took longer to resolve were thought to be due to inadequate relaxation of patients during intubation or to poor or careless technique.(2) Possible causes include neuropraxia of recurrent laryngeal nerve due to high intracuff pressure and nerve demyelination due to gas sterilization of the tubes(9). Virtually all tracheal intubations are associated with laryngeal

changes that affect the voice-frequency histogram (10) even if they do not cause blatant hoarseness. Research indicates that POST can be attenuated using a multi modal approach consisting of non-pharmacological and pharmacological interventions.

Non Pharmacological Interventions

The use of a smaller endotracheal tube has consistently been shown to significantly reduce the incidence of POST without resulting in problems ventilating the patient.

Determination and maintenance of the minimum pressure < 20 mm Hg (millimetres mercury) for an effective cuff seal during positive pressure ventilation is an effective way to decrease POST. Following manufacturer's recommendations for sizing laryngeal mask airway, use of water-soluble lubricants on laryngeal mask airway facilitating insertion and limiting laryngeal mask airway cuff pressure < 60 cm H2O will decrease the incidence of POST. Filling the cuff with an anesthetic gas mixture, saline, or lignocaine (endotracheal tube only) have been shown to be effective methods of eliminating diffusion of N2O increasing intracuff pressures.

Pharmacological interventions

There are many studies evaluating medications in an effort to reduce the incidence of POST. Most of these studies involve the use of steroids and non-steroidal anti-inflammatory drugs, both aimed at reducing the irritation and inflammation believed to be a causative factor in the development of POST. Betamethasone dipropionate, dexamethasone, methyl prednisolone, clonidine hydrochloride, diclofenac sodium, magnesium sulphate, lignocaine hydrochloride, ketamine hydrochloride, etc. are included in this group.

MATERIALS AND METHODS

A study titled "EFFECT OF KETAMINE HYDROCHLORIDE GARGLES FOR ATTENUATING POST OPRATIVE SORE THROAT IN PATIENTS UNDERGOING GENERAL ANESTHESIA WITH ENDOTRACHEAL INTUBATION" was undertaken at Gujarat Cancer and research Institute, Ahmedabad, during the period January 2013 to December 2013.The study was undertaken after obtaining ethical committee clearance as well as written informed consent from all patients.100 patients aged 18 - 70 years belonging to ASA class I - II scheduled to undergo an elective surgical(abdominal, lower limb, breast, pelvic) procedure in supine position under general anaesthesia with endotracheal intubation (lasting between 60 and 300 minutes) were included in the study.

INCLUSION CRITERIA

1. Patients aged between 18 - 70 years of both sex.
2. Patients belonging to ASA I- II
3. Patients undergoing an elective surgical procedure under general anaesthesia with endotracheal intubation.
4. Anaesthesia duration: 60 to 300 minutes.

EXCLUSION CRITERIA

1. Surgical duration of >300 minutes & < 45 minutes.
2. More than two attempts at intubation.
3. Use of nasogastric tube / throat packs.
4. Patients with recent upper respiratory tract infection within 1 week of scheduled surgery.
5. Known allergy to ketamine.
6. Patients on steroid therapy > 2 weeks
7. Patients with history of bronchial asthma.
8. MPG 4.

100 patients were randomized into two groups of 50 each.

- Group A : Normal saline gargle (placebo) and topical 2% Lignocaine jelly on the tracheal tube
- Group B: Ketamine hydrochloride gargle and topical 2% Lignocaine jelly on the tracheal tube.

Preparation of gargle;

Material required: Ketamine hydrochloride vial(with preservative) having concentration 50mg/ml, 20cc sterile syringe and needle, normal saline, sterile plastic container.

Procedure: For group A, 20 ml of normal saline, measured with the help of syringe, given to patient in a plastic container.

For group B – 1ml (50mg) of inj. ketamine hydrochloride is taken into 20 cc syringe and mixed with 19 ml of normal saline and given to patient in sterile plastic container.

A routine pre anaesthetic examination was conducted before the surgery assessing, General condition, Airway assessment and Systemic examination of the patient.
Appropriate investigations were done according to the condition of the patient and surgery requirements. All the patients included in the study were premedicated with inj. ranitidine hydrochloride1mg/kg iv and inj. Ondansetron 0.1mg/kg on the day of surgery with 8 hours of fasting period.
The patients allocated to Group A and B were asked to gargle with normal saline (20 ml) and a preparation of ketamine hydrochloride (50 mg/mL) 1ml (50mg) in 19ml of normal saline respectively for 30 seconds, 5 minutes before induction of anaesthesia. The patient was then shifted to the operation theatre and recording of vital parameters was done like, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, electrocardiograph, oxygen saturation, respiratory rate, end tidal carbon dioxide.
Anaesthesia was induced with inj. Fentanyl citrate 2mcg/ kg and inj. Propofol 1.5 mg/kg or inj. Thiopentone sodium 5mg/kg. Tracheal intubation was facilitated by inj. Vecuronium bromide 0.1 mg/ kg or inj. Atracurium besylate 5mg/kg, and the trachea was intubated with a soft seal cuffed sterile portex endotracheal tube with a standard cuff and internal diameter of 7millimetre for women and 8/9millimetres for men. 2% lignocaine jelly was applied on the external surface of tracheal tube as a part of institutional protocol. Immediately after intubation, the tracheal tube cuff was inflated. Anaesthesia was maintained with oxygen 50% in N20, supplemented with isoflurane/sevoflurane. Towards the end of the surgery, inj. paracetamol 15 mg/kg IV was administered. After completion of surgery administration of appropriate doses of Neostigmine methyl sulphate 0.05mg/kg and inj. Glycopyrrolate 0.4mg and oropharyngeal suction was performed under direct vision. Deflation of the cuff was done when the patient was fully awake. Patient was then shifted to the post operative room. On arrival at the post operative ward, assessment of patients for postoperative sore throat at 1/2, 4, 24 h. after surgery was graded on a **four-point scale** (0–3) (6):
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)
3: severe sore throat (change of voice or hoarseness, associated with throat pain).
Rescue protocol:
For POST score 1 - Observation and reassurance.
For POST score 2 - Lozenges and nebulization.
For POST score 3 - Indirect laryngoscopy to assess vocal cord edema, if present iv steroid given followed by viscous lignocaine gargles and nebulization.

Calculation and graphs made through software Microsoft excel and using website www.graphpad.com.

OBSERVATIONS AND RESULTS

Age distribution:
The minimum age in group A and B were 18 and 20 years respectively. The maximum age in groups A and B were 70 and 65 years respectively. The mean age in group A and B were 44.7±12.6 and 45.6±11.2.

Gender Distribution
Group A had 28 males(56%) with 22(44%) females, and Group B had 26 males(52%) with 24 (48%) females.

ASA Grading:
In Group A, 6 (8%) and 44 (42%) patients belonged to ASA Grade I and II respectively. In Group B, 5(1%) and 45 (49%) patients belonged to ASA Grade I and II respectively.

Mallampatti grading:
In Group A,18%, 74%, and 8% had Mallampatti grade 1, 2 and 3. respectively. In Group B, 7%, 40%, and 3% patients had Mallampatti grade 1, 2 and 3 respectively. Distribution of patients according to Mallampatti grade in two groups was statistically similar.

Table 4: Mallampatti grade in two groups of patients studied
Mallampatti grade

MALLAMPATTI GRADE	GROUP A		GROUP B	
	No.	%	No.	%
1	9	18	7	14
2	37	74	40	80
3	4	8	3	6

4	0	0	0	0
TOTAL	50	100	50	100

Endotracheal intubation attempts:
In Group A,47 (96%) and 3(4%) patients were intubated in first and second attempts respectively. In Group B,46 (92%) and 4 (8%) patients were intubated in 1 and 2 attempts respectively.

Table 5: Endotracheal intubation attempts in two groups of patients.

INTUBATION ATTEMPTS	GROUP A		GROUP B	
	No.	%	No.	%
ONE	47	96	46	92
TWO	3	4	4	8
TOTAL	50	100	50	100

Endotracheal tube size:
In Group A, 50%, 34%, 16%, patients were intubated with 7 ,8 and 9 mm (internal diameter) endotracheal cuffed tubes respectively. In Group B, 50%, 30%, 20% patients were intubated with 7 ,8 and 9mm (internal diameter) endotracheal portex cuffed tubes respectively. Mean endotracheal tube size used was statistically similar in two groups.

Table 6: Endotracheal tube size in two groups of patients studied

TUBE SIZE IN MILIMETERS	GROUP A		GROUP B	
	No.	%	No.	%
7	25	50	25	50
8	17	34	15	30
9	8	16	10	20
TOTAL	50	100	50	100

Duration of surgery:
Mean ± SD of 147.66 ± 51.8 and147.36±53.21 minutes in Group A and Group B respectively.

Table 7: Comparison of duration of surgery in two groups studied

DURATION OF SURGERY(in minutes)	GROUP A		GROUP B	
	No.	%	No.	%
60- 120	22	44	16	32
121-180	17	34	24	48
181-240	10	20	8	16
241-300	1	2	2	4
TOTAL	50	100	50	100
MEAN± SD	147.66 ± 51.8		147.36±53.21	

Incidence of smoking:
Number of smokers was nearly same in both groups. 30% study population associated with smoking in group A and 24% in group B.

Incidence of post-operative sore throat:
The overall post-operative sore throat was positively less in Group B with 16 (32%) patients when compared to Group A with 23 (46%) patients complaining of it with.

Table 9: Comparison of Incidence of overall sore throat at any point of time in two groups of patients studied

OVER ALL SORE THROAT	GROUP A		GROUP B	
	No.	%	No.	%
YES	23	46	16	32
NO	27	54	34	68

Table 10: Incidence of severity of post-operative sore throat at ½ hour, 4 hours and 24 hours after extubation

POST	GROUP A (n = 50)		GROUP B (n = 50)		p VALUE
	No.	%	No.	%	
POST AT ½ HOUR					
GRADE 0	27	54	37	74	0.0745
GRADE 1	17	34	13	26	
GRADE 2	5	10	2	4	
GRADE 3	1	2	0	0	
POST AT 4 HOUR					
GRADE 0	32	64	45	90	0.0705
GRADE 1	12	24	4	8	
GRADE 2	3	6	1	2	
GRADE 3	0	0	0	0	
POST AT 24 HOUR					
GRADE 0	45	90	46	92	0.550
GRADE 1	4	8	4	8	
GRADE 2	1	2	0	0	
GRADE 3	0	0	0	0	

Correlation of age, gender, duration of surgery, Mallampatti grading, tube size no of attempt, smoking and ASA grading with overall incidence of POST

Table 11: Showing correlation of variables with POST

P: Number of patients with POST in the subgroup, N: Number of patients in the subgroup:

VARIABLES	OVERALL INCIDENCES OF POST					
	GROUP A			GROUP B		
	N	P	%	N	P	%
AGE						
18 – 30	7	2	28	12	4	33
31 – 50	28	14	50	22	8	36
51 – 70	15	8	53	16	4	25
GENDER						
FEMALE	22	15	68	24	8	33
MALE	28	8	28	26	8	30
ASA GRADE						
I	6	3	50	5	2	40
II	44	20	45	45	14	31
MPG GRADE						
1	9	4	44	7	2	28
2	37	17	45	40	12	30
3	4	2	50	3	2	66
DURATION OF SURGERY						
60 – 120	22	7	31	16	1	6
121 – 180	17	10	59	24	5	21
181 – 240	10	6	60	8	8	100
241 – 300	1	0	0	2	2	100
SMOKING						

YES	15	5	33	12	5	41
NO	35	18	51	38	11	29
INTUBATION ATTEMP						
ONE	47	20	42	46	13	28
TWO	3	3	100	4	3	75
TUBE SIZE						
7	25	16	64	25	9	36
8	17	3	17	15	3	20
9	8	4	50	10	4	40

DISCUSSION

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

Ketamine is in the middle of the affinity range of uncompetitive NMDA antagonists which has been found by various authors to attenuate POST (11,12,13). An increasing amount of experimental data shows that NMDA receptors are found not only in the central nervous system but also in the peripheral nerves. Peripherally administered NMDA receptor antagonists are involved with antinociception and anti-inflammatory cascade (8, 14,15,16) by reducing NFκβ activity, TNF-α (tumour necrosis factor α) production, expression of inducible nitric oxide synthase serum C-reactive protein, IL-6 and IL-10. Pharmacological studies reveal that low dose ketamine especially in the 'sub-psychotomimetic' range (blood concentration < 50 nanogram/ml) has 'anti-hyperalgesic',' anti-allodynic' and possibly opioid 'tolerance-protective' effect due to an additive effect with opioids which is attributed to presynaptic opioid inhibition reducing afferent transmission by diminished transmitter release, and postsynaptic NMDA blockade which reduces wind up and central sensitization.

In a study conducted by Chan et al(14), blood samples were obtained intra operatively, but POST was assessed post-surgery when ketamine concentrations are likely to be lower. Systemic absorption and the possibility of swallowing the residual solution would contribute to the ketamine in the blood. The highest average ketamine and nor ketamine concentrations, 16.16 and 11.43 ng/ml respectively, were detected during surgery but would have decreased after the surgery. These low levels suggested that it was unlikely that systemic absorption played a major role for the reduction of POST. A topical effect is possible.

CONCLUSION

From the present study it can be concluded that:

- The overall incidence of POST in the control group (Group A) of our study population was 46%.
- The overall incidence of POST was positively less in Ketamine gargle group (Group B) with 32%
- Ketamine gargle contributed to 14% in the reduction of POST in the study population.(Although p value is > than .05)
- There was a decrease in the incidence of POST seen in the Ketamine gargle group at ½, 4 and 24 hours after extubation.
- At ½ hour after extubation, the incidence of mild, moderate and severe POST was lesser in the Ketamine gargle group.
- At 4 hours after extubation, the incidence of mild and moderate POST was lesser in the Ketamine gargle group.
- At 24 hours after extubation, the incidence of mild POST was lesser in the Ketamine gargle group.
- Females, ASA II, MPG 2, Age group 31 – 50 years, duration of surgery between 121 – 180 minutes, tube with internal diameter 7mm and single attempt intubation was associated with more number of POST in study population.
- Hence, it is concluded that Ketamine gargle (1 mL=50 mg in 20 mL normal saline) for 30 seconds, 5 minutes before induction of anesthesia is a useful adjunct to decrease post-operative sore throat after oral endotracheal intubation.

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