



COMPARATIVE STUDY OF THE EFFECT OF PREOPERATIVE KETAMINE, ASPIRIN AND NORMAL SALINE GARGLES ON POST OPERATIVE SORE THROAT AFTER ORAL ENDOTRACHEAL INTUBATION

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(ABSTRACT) **Background:** Post-Operative Sore Throat (POST) is a common complication after general anaesthesia. We compared the effectiveness of Aspirin and Ketamine gargles in attenuating post-operative sore throat after oral endotracheal intubation.

Study design: Prospective randomized double blind study

Material and method: After ethical committee approval, 75 patients of ASA grade 1, 2, 3, between 18-70 years receiving general anaesthesia with oral endotracheal intubation were randomly allotted to three groups, Group N (Normal Saline), Group K (Ketamine), Group A (Aspirin). Patients were asked to gargle for 30 seconds with normal saline (20ml), preservative free ketamine 1mg/kg in 19ml NS, or 325mg dispersible Tab. Aspirin in 20ml NS respectively; 15 minutes before induction. Post-operatively, incidence and severity of sore throat were assessed using 4-point scale at 4, 8, 12, and 24 hours.

Results: Group K showed least whereas Group N showed highest incidence of sore throat. The difference in incidence of sore throat between Groups A and N was statistically insignificant ($p > 0.05$) whereas that between groups N & K and A & K was statistically highly significant ($p < 0.001$). Post operatively at 4 and 8 hours, 4% and 0% patients in Ketamine group, 68% and 4% in Aspirin group and 96% and 68% patients in Normal Saline group had mild sore throat respectively ($p < 0.001$), the difference being statistically highly significant. None of the patients in any group had POST at 12 and 24 hrs.

Conclusion: Incidence and severity of Post-Operative Sore Throat after oral endotracheal intubation is greatly reduced by preoperative Ketamine (1mg/Kg) gargles compared to Aspirin (325 mg) and Normal saline gargles.

KEYWORDS : Aspirin, Ketamine, Post operative sore throat

INTRODUCTION:

Post-Operative Sore Throat (POST) is a common complication after general anaesthesia that can cause patients a lot of discomfort (Kim, Lee, & Park, 2011). It is found to be the highest after endotracheal intubation (Kim et al., 2011). Incidence of POST in various studies ranges from 18 to 65% (Hartsell and Stephen, 1964; Chandler, 2002; Jaansson, Nilsson, & Olowsson, 2010).

Various pharmacological measures that have been tried to decrease POST include beclomethasone inhalation, gargling with Aspirin, Ketamine, IV steroids, Magnesium lozenges and local spray with Lidocaine, nebulisation with Ketamine (Chandler, 2002; Aypar et al., 2008; Agarwal, Goswami, & Nath, 2006; Jung, Kim, 2013).

This study compared the efficacy of Ketamine and aspirin gargles given 15 minutes before induction of anaesthesia on reduction of POST. We hypothesised that Ketamine and Aspirin are equally effective in decreasing incidence and severity of POST.

MATERIALS AND METHODS:

After approval from the ethical committee, this prospective randomized double blinded study was conducted in a tertiary care teaching hospital over a period of 2 years. Power analysis (α value of 0.95 and β value of 0.80) indicated that the minimum sample size required was 24. Seventy-five patients of both sexes between the age group of 18 – 70 years with ASA physical status of 1, 2 and 3, undergoing any elective surgery requiring general anaesthesia with oral endotracheal intubation were divided in 3 groups of 25 each. Patients with upper respiratory tract infections, sore throat, bleeding diathesis, psychiatric disorders, known sensitivity to study drugs, patients requiring Ryle's tube insertion, procedures taking place in prone position and surgery lasting > 3 hours were excluded from the study.

Informed written consent of the patient was taken. Patients included in the study were given Cap. Omeprazole 40 mg on the night before surgery. Patients were kept nil by mouth for 8 hrs before the surgery. On the day of surgery, 20 G intravenous cannula was inserted and an infusion of ringer lactate started in the preoperative room. Patients

were randomly allocated to 3 groups using sealed envelope method. Patients allocated to Group N were asked to gargle for 30 seconds with normal saline (20ml), Group K patients received a preparation of preservative free Ketamine (50mg/ml) 1mg/kg in 19ml of normal saline for gargle and those in Group A received 325 mg dispersible Tab. Aspirin in 20ml NS for gargle; 15 minutes before induction of anaesthesia. The person administering the gargles did not take part in the further study. Both the observer and patient were unaware of the study drug used making the study double blind.

After gargling, the patients were shifted to the operation theatre and monitors were attached. ECG, Pulse rate, Blood pressure, oxygen saturation and respiratory rate were monitored. Patients were pre-oxygenated with 100% O₂ at 8L/minute for 3-5 minutes. Patients were premedicated with Inj. Glycopyrrolate 0.01mg/kg, Inj. Midazolam 0.3mg/kg, Inj. Pentazocine 0.5mg/kg. Anaesthesia was induced by administering Inj. Propofol 2mg/kg and Inj. Succinylcholine 1.5mg/kg. Trachea was intubated with appropriately sized cuffed sterile portex endotracheal tube by an experienced anaesthesiologist. Patients who required more than one attempt or more than 15 seconds for endotracheal intubation and patients who had trauma to oral structures during intubation were excluded from the study. Anaesthesia was maintained using Isoflurane and Inj. Atracurium. Gentle oropharyngeal suctioning was done after completion of surgery. After completion of surgery reversal was done using 0.5mg/kg neostigmine and 0.01 mg/kg glycopyrrolate followed by extubation. Patients who had coughing and bucking on the endotracheal tube were also excluded from the study. Assessment of patient for POST at 4, 8, 12 and 24 hrs were done after surgery and graded on a 4-point scale from 0-3 (Hartsell and Stephen, 1964; Hurley Murphy, & Wu, 2015). 0- No sore throat 1- Mild sore throat (patient mentions about it only if asked) 2- Moderate sore throat (patient mentions about it himself) 3- severe (associated with throat pain, change in voice)

Statistical analysis:

All data was presented as Mean \pm Standard Deviation (SD). Demographic data was analyzed using Chi-square test and statistical significance in mean difference was done using student's t test. P value of < 0.05 was regarded as statistically significant and $p < 0.001$ was

taken as highly significant.

RESULTS:

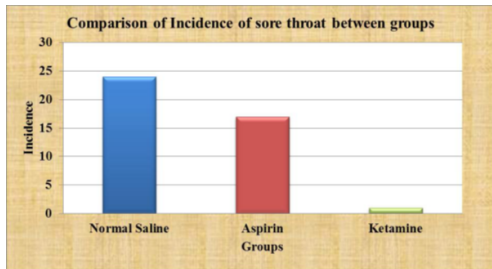
Demographic data (age, weight, gender distribution and duration of surgery) was comparable in all the study groups ($p > 0.05$)

Table 1: Demographic data. Results are given as mean \pm SD.

Parameters	Group N (N=25)	Group A (N=25)	Group K (N=25)	P Value	
Age (in years)	31.28 \pm 11.26	35.40 \pm 15.51	35.08 \pm 11.41	0.468 NS	
Weight (in Kilograms)	54.12 \pm 10.46	59.48 \pm 10.70	56.48 \pm 7.67	0.155 NS	
Gender distribution (as percentage)	Male	07 (28 %)	05 (20 %)	09 (36%)	0.4521 NS
	Female	18 (72 %)	20 (80 %)	16 (64%)	
Duration of surgery (in minutes)	113.80 \pm 32.38	119.6 \pm 33.51	119.6 \pm 33.51	0.831 NS	

NS = Not significant

The difference in incidence of sore throat between Aspirin and Normal Saline groups was not statistically significant ($p > 0.05$) whereas that between Normal Saline and Ketamine groups and Aspirin and Ketamine groups was statistically highly significant ($p < 0.001$). Amongst all groups, Ketamine group showed least incidence and Normal saline group showed highest incidence of sore throat.



Graph 1: Comparison of Incidence of sore throat between the three groups

Post operatively at 4 hours, only 4% patients in Ketamine group showed Mild sore throat while 68% patients in Aspirin group and 96% in Normal Saline group had mild sore throat ($p < 0.001$) making the difference highly significant. At 8 hours post operatively, 0% patients in Ketamine group, 4% in Aspirin group and 68% in Normal Saline group had Mild sore throat ($p < 0.001$) the difference being statistically highly significant. None of the patient in any group complained of sore throat at 12 & 24 hours in the post operative period. No patient had moderate or severe degree of sore throat at any given time throughout the study.

Table 2: Distribution of patients according to Severity of sore throat at different time intervals

Sore throat at	Grade	Normal saline N (%)	Aspirin N (%)	Ketamine N (%)	P value
4 hours	No	01 (04)	08 (32)	24 (96)	0.0000 HS
	Mild	24 (96)	17 (68)	01 (04)	
8 hours	No	08 (32)	24 (96)	25 (100)	0.0000 HS
	Mild	17 (68)	01 (04)	00 (00)	
12 hours	No	25 (100)	25 (100)	25 (100)	
	Mild	00 (00)	00 (00)	00 (00)	
24 hours	No	25 (100)	25 (100)	25 (100)	
	Mild	00 (00)	00 (00)	00 (00)	

HS = Highly significant

DISCUSSION:

Post-Operative Sore Throat (POST) is a common adverse effect of general anaesthesia with endotracheal intubation. Age $>$ 60 years, female gender, use of throat pack, large sized endotracheal tube, higher intracuff pressure, multiple attempts at intubation, pre-existing sore throat, Ryle's tube insertion, prone position and prolonged surgery are some of the predisposing factors for development of POST (Gupta, Jaansson, & Nilsson, 2012).

Non-pharmacological methods for attenuating POST include use of small size endotracheal tubes, lubricating the endotracheal tube with water soluble jelly, careful airway instrumentation; intubation after full relaxation, gentle oropharyngeal suctioning and extubation when the tracheal tube cuff is fully deflated (Chung and McHardy, 1999).

Many pharmacological measures have been suggested to reduce the incidence as well as severity of POST through different routes of administration such as oral tablets, IV injection, gargles, nebulisation, spray etc. The drugs those have been tried for prevention of POST include application of triamcinolone acetonide paste to endotracheal tube, ketamine gargles, aspirin gargles, magnesium sulphate gargles, liquorice gargles, benzydamine hydrochloride gargles, intravenous use of dexamethasone, magnesium sulphate, opioids, local anaesthetic agents, non-steroidal anti-inflammatory drugs, alpha 2 agonists and ketamine, nebulised ketamine, nebulised magnesium sulphate and lignocaine spray. However, no single drug has been found to be superior over all others.

In our study we used normal saline gargles as the control group. The incidence of post-operative sore throat was 96% in control group with 96% and 68% patients having mild sore throat at 4 hours and 8 hours respectively. None of the patients complained of sore throat at 12 and 24 hours. Other studies have used various agents as control groups, such as normal saline, mineral water, dextrose water, distilled water and drinking water. The incidence of post-operative sore throat in these studies was 73% for Normal Saline, 80% for Mineral water, 50% for Dextrose water, 90% for Distilled water and 85% for drinking water. Our observations in control group are similar to these studies.

Aspirin is a drug which has analgesic, antipyretic and anti-inflammatory properties. It works by causing inhibition of the prostaglandin system (Levy, 2015; Hurley et al., 2015). Multiple studies have shown a positive result of aspirin's efficacy in reducing incidence and severity of POST. Aspirin (325 mg or 350 mg) in the form of gargles has been used in prevention of POST with various control groups like 20-30ml of mineral water, distilled water and normal saline. Ketamine, an intravenous anaesthetic, acts on N-methyl D-aspartate receptors causing inhibition of these receptors. Since these receptors are involved with antinociception and also have anti-inflammatory action, ketamine can help in attenuating sore throat (Trevor, Way, & White 1982; Clement, Grant, & Nimmo, 1981; Rathmell and Rosow, 2015; Reekers, Sitsen & Vuyk, 2015). Ketamine by various routes has been used in a number of studies which demonstrated its efficacy in decreasing the incidence and severity of POST with a positive response. Studies have been conducted using Ketamine gargles in the dose of 40-50 mg in 20-30ml of various solvents like normal saline, distilled water and mineral water. Nebulized ketamine has also been tried in the dose of 1mg/kg body weight in the prevention of POST with success. We compared efficacy of preoperative Ketamine (1 mg/kg) gargles and aspirin (325 mg) gargles in decreasing the incidence and severity of POST.

Our study demonstrated that the incidence of POST was least in Ketamine group (4%) as compared to Aspirin group (68%) and highest in Normal saline group (96%).

Altiparmak and Turan (2018) conducted a retrospective study to compare the efficacy of Benzydamine Hydrochloride and Ketamine gargles preoperatively to attenuate POST. Chan, Lee, & Lo (2011) also evaluated the effectiveness of preoperative Ketamine gargles in attenuating POST. Both the studies found preoperative gargles with Ketamine to be effective in reducing POST. Our results are in agreement with these studies.

Anis and Ibrahim (2016) evaluated the efficacy of Liquorice and Ketamine gargles preoperatively in reducing POST. They observed a decrease in the incidence and severity of POST after preoperative Ketamine gargles. At 4 and 24 hours, their study found 3.3% and 0% patients respectively who complained of POST. Our results coincide with their study.

Aypar et al., (2008) while evaluating the efficacy of preoperative Ketamine gargles in attenuating POST observed that Ketamine gargle decreased incidence and severity of POST. In their study, ketamine group at 4 and 24 hours found 40% and 30% patients having mild POST as opposed to 4% and 0% respectively in our study. Although both studies demonstrate reduced severity of POST after preoperative

ketamine gargles, our study shows better results in Ketamine group. Ahmed, Chatterjee, Ghosh, Ray, & Rudra, (2009) conducted a study to compare the effectiveness of preoperative ketamine gargles with a placebo in attenuating POST. The incidence of POST in their study at 4, 8 and 24 hours was 40%, 35% and 25% respectively as opposed to 4%, 0% and 0% in our study. Their Ketamine group showed mild and moderate POST in 35%/ 5% patients at 4 hours, 30%/ 5% patients at 8 hours and 20%/ 5% patients at 24 hours. None of the patients had severe POST. We observed only mild POST at 4 hours in 4% patients. Our patients in Ketamine group did not complain of POST at 8 & 24 hours showing a lesser incidence and severity of POST.

Eshwori et al., (2012) observed that preoperative Ketamine gargles decreased the incidence and severity of POST. At 4 and 24 hours, their incidence of POST was 8.8% as compared to 4% at 4 hours and 0% in 24 hours in our study. Severity of POST in their study at 4 hours was 17.7% with mild POST as compared to 4% in our study. At 24 hours their study showed 15.5% patients with mild POST and 2% with moderate POST whereas none of the patients in our Ketamine group had POST at 24 hours.

Gajbhare and Kamble (2015) after their study came to a conclusion that preoperative Ketamine gargles caused a reduction in severity and incidence of POST for up to 24 hours after extubation. The incidence of POST at 4, 8 and 24 hours in their study was 46.7%, 23.3% and 13.3% as compared to 4%, 0% and 0% respectively in our study. At 4 hours their study showed 33.3% patients having mild and 13.3% having moderate POST as compared to our 4% with mild POST. At 8 hours, their study group had 16.6% with mild POST and 6.6% with moderate POST as compared to 0% in our study group. At 24 hours, they found 10% with mild and 3.3% with moderate POST while our study showed 0% showing more favourable results.

Chand, Sharma & Vaidya, (2015) observed that preoperative Ketamine gargles were safe and effective in reducing POST with 12.1% and 6% patients complaining of POST at 4 and 24 hours, as compared to 4% and 0% respectively in our study.

All the above studies have used fixed dose of Ketamine (either 40 or 50 mg) whereas we have used Ketamine in the dose of 1mg/kg. The higher dose of ketamine may have contributed to more favourable results in attenuation of POST in our patients.

Agarwal et al., (2006) conducted a study comparing the efficacy of preoperative Aspirin gargles with Benzylamine Hydrochloride gargles in attenuating POST. They observed that at 4 hours and 24 hours, aspirin group had 21% and 5% patients with mild POST respectively as compared to 68% and 0% in our study. None of the patient in aspirin group had severe POST. In their study at 4 hours, the mineral water group showed 45% patients with mild and 5% patients with severe POST as compared to our study which showed 96% patients with mild and 0% with severe POST. At 24 hours, their mineral water group had 10% patients with mild, 5% with moderate and 5% with severe POST while none of our patients in saline group had POST at 24 hours. Both these studies showed that preoperative Aspirin gargles reduced incidence and severity of POST. The differences in the incidence and severity of POST maybe attributed to the different doses of Aspirin (350 vs. 325mg) used in both the studies and use of two different agents i.e. mineral water vs. normal saline as control group.

Chattopadhyay et al., (2017) conducted a study to compare the effectiveness of preoperative Aspirin gargles and Magnesium Sulphate (MgSO₄) in attenuating POST. At 4 and 12 hours, incidence of POST in their aspirin group was 25% and 17.8% as compared to 4% and 0% respectively in our study. At 4 hours, their study showed 17.8% patients with mild and 7.1% with moderate POST while we observed only 4% patients with mild POST. At 12 hours, they observed 14.2% patients with mild and 3.5% with moderate POST whereas none of our patients complained of POST.

In our study, an experienced anaesthesiologist did the endotracheal intubation and the time allowed for doing intubation was less than 15 seconds. If there was trauma to oral structures during intubation, those patients were not included in the study. The patients who had episode of coughing or bucking on the tube at the time of extubation were also excluded from the study. All these factors might have contributed to the decrease in the severity of the POST so that no patients in our study had moderate or severe sore throat at any point in the study period.

CONCLUSION:

Incidence and severity of post-operative sore throat after oral endotracheal intubation is greatly reduced using preoperative Ketamine gargles (1 mg/ Kg in 19 ml NS) compared to Aspirin (325 mg in 20 ml NS) and Normal saline (20 ml) gargles. Thus, Ketamine can be effectively used for reducing incidence and severity of Post-Operative Sore Throat.

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