
**“EFFICACY OF KETAMINE GARGLE IN PREVENTION
OF POSTOPERATIVE SORE THROAT IN PATIENTS
UNDERGOING GENERAL ANESTHESIA WITH
ENDOTRACHEAL INTUBATION, A 1 YEAR DOUBLE
BLINDED PLACEBO CONTROLLED
RANDOMIZED TRIAL”**

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ENDORSEMENT

This is to certify that the dissertation entitled “**EFFICACY OF KETAMINE GARGLE IN PREVENTION OF POSTOPERATIVE SORE THROAT IN PATIENTS UNDERGOING GENERAL ANESTHESIA WITH ENDOTRACHEAL INTUBATION, A 1 YEAR DOUBLE BLINDED PLACEBO CONTROLLED RANDOMIZED TRIAL**” is a bonafide research work done by **REG NO.BA0113004.**

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LIST OF ABBREVIATIONS USED

ASA	– American society of Anaesthesiologists
BMI	– Body mass index
cm	– Centimeter
CNS	– Central nervous system
CO ₂	– Carbon dioxide
CVS	– Cardiovascular system
ECG	– Electrocardiogram
GIT	– Gastrointestinal tract
H ₂ O	– Water
Hb	– Haemoglobin
Inj.	– Injection
IV	– Intravenous
Kgs	– Kilograms
mcg	–Micrograms
mg	– Milligrams
Min	– Minute
ml	– Millilitre

- NMDA – N-methyl D aspartate
- PR – Pulse rate
- POST – Post operative sore thraot
- RBS – Random blood sugar
- RR – Respiratory rate
- SPO₂ – Saturation percentage of oxygen
- Alpha
- Beta

ABSTRACT

Background: Postoperative sore throat (POST) following extubation after general anaesthesia is one of the most distressing side effect of endotracheal intubation during the immediate postoperative period. Ketamine, a NMDA antagonist, has anti-nociceptive and anti-inflammatory properties. Through its action on the peripherally located NMDA receptors it reduces inflammation and pain.

Objective: To assess the efficacy of ketamine gargle in prevention of postoperative sore throat in patients undergoing endotracheal intubation for general anaesthesia.

Methodology: One year double blinded randomized controlled trial was conducted at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi between January 2014 and December 2014. 106 patients undergoing general anaesthesia with endotracheal intubation were included in our study and were randomised using computer generated randomisation table into Group A and B with 53 patients each. Group A received 50mg(1ml) of Ketamine diluted with 29 ml of normal saline in the form of a gargle and Group B received 30 ml normal saline 5 minutes before induction. Patients had to gargle for a period of 30 seconds. 4 patients were excluded from the study as they were unable to gargle for a period of 30 seconds.

Results: Age, Gender distribution, Duration of procedure was comparable between the two groups. Gargling with 50 mg (1 ml) of ketamine diluted with 29 ml of normal saline 5 minutes before induction successfully reduces the incidence

and severity of POST (post-operative sore throat). When compared the difference in the incidence of sore throat at 0, 4, 8, 12, 24 hours post extubation was found to be statistically significant ($p < 0.001$)

Conclusion: Ketamine gargle significantly reduces the incidence and severity of postoperative operative sore throat.

Keywords: Postoperative sore throat, Ketamine gargle.

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INTRODUCTION

Management of airway is central to the practice of anaesthesia & it encompasses the whole range of airway manipulations required during the course of anaesthesia. Endotracheal intubation forms an integral part of airway management. Cuffed endotracheal tubes prevent aspiration and hence are commonly used. However local irritation, inflammation of the airway is a common sequelae to cuffed endotracheal intubation, which leads to post extubation morbidities like sore throat, cough & hoarseness of voice which is extremely distressing to the patient.

A number of different measures both pharmacological & non pharmacological have been studied to reduce the incidence & the severity of post extubation sore throat. Smaller sized tubes¹, high volume low pressure endotracheal tubes², careful instrumentation of the airway, adequate intracuff pressure, fully deflating the cuff before extubation, lubricating with lignocaine jelly³, betamethasone gel³, IV dexamethasone⁴, beclomethasone inhalation⁵ are some of strategies used to reduce postoperative sore throat. However each intervention is associated with side-effects which may not be desirable. Hence there is a need for an intervention which would prevent rather than treat post-operative sore throat which is effective, patient friendly and reliable.

N-methyl D aspartate (NMDA) receptors are present not only in the central nervous system but also in the peripheral nervous system⁶. These receptors contribute in inflammatory pain. Ketamine is a NMDA antagonist with anti-nociceptive and anti-inflammatory properties, which may be the possible mechanism in prevention of post-operative sore throat (POST)⁶.

Hence we undertook a study on the effect of ketamine gargle and compared it with normal saline gargle in prevention of post-operative sore throat.

OBJECTIVES

To assess the efficacy of ketamine gargle in prevention of postoperative sore throat in patients undergoing endotracheal intubation for general anaesthesia.

REVIEW OF LITERATURE

Tracheostomy procedure has been described in Egyptian tablets dating back to as early as 3600 BC. Since then airway management has come a long way. John Snow in 1858 intubated an anesthetized animal through a tracheostomy wound. Friedrich Trendelenberg in the year 1871 applied this in human beings, and occluded the trachea using an inflatable cuff. In 1878 William Mc Even passed the tube from mouth into the trachea in a conscious patient. Ralph Waters & Arthur Guedel introduced inflatable cuff to rubber tube in 1928 thus paving way for true airway isolation & closed circuit anaesthesia⁷. Pilot balloon was introduced by Victor Eisenmenger in 1893 & was re-introduced by Langton Hewer in 1939⁸. Alfred Kirsten 1895 and Gustav Kellian 1912 were the pioneers of direct laryngoscopy to aid tracheal intubation.

Many studies have been done to recognize & evaluate the complications associated with endotracheal intubation. Among the complications reported, post extubation sore throat, hoarseness & cough account for problems with high incidence(21-65%)⁹.

A number of studies have been conducted to propose measures in reducing post extubation morbidities.

Loeser E A. et al¹⁰(1978) investigated the effect of using low volume high pressure and high volume low pressure endotracheal tubes on post-operative sore throat and demonstrated that low volume high pressure endotracheal tube cuffs were associated with higher incidence of postoperative sore throat. They suggested that cuff tracheal surface contact area is probably a causative factor.

Incidence of sore throat is affected by the method of questioning, this was recognised by Harding C J et al¹¹(1987). They studied 242 patients who had undergone general anaesthesia. Patients were questioned either directly or indirectly. Significantly higher incidence was obtained when patients were questioned directly.

A study conducted by Navarro RM et al¹² (1997) studied the effect of intra-cuff lidocaine in reduction of post-operative sore throat. 106 patients were studied, In 53 patients the cuff was inflated using air, while remaining 53 patients received intracuff 2% lidocaine solution. It was concluded that inflating the cuff with lidocaine instead of air reduced both the incidence & severity postoperative sore throat.

Ayoub CM et al¹³ (1998) studied application of steroids to decrease sore throat hoarseness & cough after tracheal intubation. Endotracheal tubes were lubricated uniformly from the cuff to the 15-cm mark with 3 mL of a water-soluble gel containing chlorhexidine gluconate alone or with the addition of betamethasone 0.05% (equivalent to 3 mg of prednisone). Significant reduction in post-operative sore throat by application of steroid to the cuff was concluded.

Dexamethasone given intravenously prior to tracheal intubation was studied by Thomas et al⁴(2007). Patients in the control group received normal saline 2 mL IV and patients in study group received dexamethasone 8 mg iv. Visual analogue scale (VAS) scores at rest and with effort (swallowing movement) for postoperative sore throat were recorded after the surgery. They found that incidence of sore throat was significantly reduced in the study population compared to the control population who received normal saline

Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice, was conducted by Sumathi PA et al³ (2008). ASA grade I to III patients were divided into 3 groups randomly. The endotracheal tube was lubricated with either with 2.5 ml of 0.05% betamethasone gel or 2.5ml of 2% lignocaine jelly. The third group was control where no jelly was applied. The study showed that application of betamethasone gel is more effective in reduction of postoperative sore throat than lidocaine gel.

Canbay O¹⁴ (2008) studied ketamine gargle for attenuation of postoperative sorethroat. 56 patients were included & randomly divided into 2 groups. One group received normal saline gargle 5 min before induction & the other received 40mg of ketamine diluted in normal saline 5 min before induction. Incidence & severity of sore throat was more in the group that received normal saline gargle. Hence this study concluded that ketamine gargle was effective in reducing the incidence as well as the severity of postoperative sore throat.

Honarmand A et al⁵(2008) studied Beclomethasone inhaler versus intravenous lidocaine in the prevention of postoperative airway and throat complaints. 2 doses of lignocaine 1 mg/kg & 1.5mg/kg IV, 50 mcg beclomethasone inhalation & normal saline were compared. It was found that Beclomethasone inhaler is comparable with intravenous lidocaine given prior to intubation in decreasing post-operative sore throat and cough. In addition, beclomethasone inhaler decreases the incidence and severity of postoperative sputum production.

Rudra A et al¹⁵(2009) conducted a study to evaluate whether gargling with ketamine reduced postoperative sore throat caused by endotracheal intubation.

Control group received normal saline & study group received 50mg of ketamine as gargle solution. Both the groups were followed up for a period of 24 hrs post operatively. Ketamine effectively reduced the incidence & severity of post operative sore throat without producing any drug related side effects.

Liu MD et al¹⁶(2010) studied the correlation between endotracheal cuff pressure & postoperative sore throat. They found that cuff pressure decided by means of palpation was higher than optimal. Proper control of endotracheal cuff pressure by a manometer helped reduce complications such as cough, sore throat, hoarseness.

A study on the prophylactic use of ketamine gargle to reduce post operative sore throat following endotracheal intubation was conducted by Rajkumar G et al⁹ (2012). 90 patients were included in the study between the age group of 18-65 years, belonging to ASA status I & II. Group S received 30 ml of normal saline & Group K received 40mg of ketamine in 30 ml of normal saline before being shifted to the operating room. The patients were followed up for 24 hours. The incidence of hoarseness significantly reduced in the group that received ketamine.

Shaaban AR et al¹⁷ (2012) conducted a study to compare the effects of betamethasone gel applied over endotracheal tube and ketamine gargle for attenuating POST, cough, and hoarseness of voice. One group of patients were asked to gargle with a mixture of ketamine 40 mg in 30 ml saline for 60 seconds. In another group of patients tracheal tubes were lubricated with 2.5 ml of betamethasone gel 0.05% from the distal end of the cuff and the control group did not receive either of the above. The incidence and severity of sore throat was significantly higher in the control group in all time points in comparison with the other two groups. Hence it was concluded that gargling with ketamine prior to intubation is comparable with betamethasone gel

when applied over the endotracheal tube in reducing postoperative sore throat. In addition, using betamethasone gel decreased the incidence and the severity of postoperative cough and hoarseness of voice more than gargling with ketamine.

Although a number of measures are available for the prevention of post-operative sore throat, this complication still remains widely unresolved. Ketamine gargle can be used for the attenuation of post-operative sore throat, although its efficacy has been studied, data pertaining to Indian population is certainly lacking. Hence we have undertaken this study to evaluate the efficacy of ketamine gargle for prevention of sore throat in adult patients undergoing general anaesthesia with endotracheal intubation.

BASIC SCIENCES

POSTOPERATIVE SORE THROAT

Postoperative sore throat (POST) is one of the most common side effect associated with general anaesthesia with endotracheal intubation.¹⁸ Prophylactic management for decreasing its frequency and severity is recommended to improve the quality of post anaesthesia care.

POST includes signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia.¹⁹

Incidence of POST varies with the method of airway management. The incidence is the highest after tracheal intubation and varies from (21-65%)⁹ 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%)²⁰ is used for the maintenance of anaesthesia. Significantly higher incidence of sore throat in women (17%) than in men (9%) is attributed to the tube fitting tighter in women.²¹ The incidence of postoperative complications is known to vary among different races.²² The use of cuffed tubes is associated with a significantly higher incidence of sore throat than the use of uncuffed tubes, even when the patients breathed warmed and humidified gases.¹⁰ It is suggested that a difficult intubation does not significantly increase the likelihood of POST. Younger patients¹⁸, gynaecological surgery¹⁸, large tracheal tube¹, cuff design, intracuff pressure¹⁴, throat packs²³ and the use of succinylcholine also seem to increase the incidence¹⁸.

Lack of airway humidity, trauma during airway insertion, suctioning, high anaesthetic air flow rates and surgical manipulation of airway¹⁸ and adjacent tissue are possibly the causative factors for POST. Laryngeal trauma²⁴ with mucosal

dehydration most commonly occurred posteriorly over the cricoid plate and also over the vocal processes of the arytenoids, as a result of forces exerted by the rigid tubes. Trauma over the cartilaginous rings of the trachea, tending to occur only along the anterior tracheal wall; resulted presumably from the insertion or removal of the tube.¹⁸ Pathological changes in the laryngotracheal area, such as epithelial loss, glottic 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.⁵

Glottic hematomas on the left cord are more often seen possibly because of the fact that the tube is turned to the left by the anaesthetist during intubation. The injuries resolve within 4 weeks and were thought to be due to inadequate relaxation of patients during intubation or due to poor or careless technique. Possible causes include neuropraxia of recurrent laryngeal nerve due to high intracuff pressure¹⁸ and nerve demyelination due to gas sterilization of the tubes²⁵.

Decreased elasticity of the trachea and surrounding tissues in older people may also increase the likelihood of damage occurring during laryngoscopy and intubation lesions were seen more frequently in the interarytenoid and subglottic area when the standard polyvinylchloride tube was used. This was presumably due to the elastic recoil of the polyvinylchloride tube, which exerted more pressure against the posterior wall of the larynx.¹⁸ The standard endotracheal tube acts as a curved lever and the posterior larynx especially cricoid and arytenoid acts as fulcrum.^{26,27}

Although these lesions are only superficial ulcerations of the mucous membrane comprising less than one-third of the circumference of the airway, it is thought that they constitute a very efficient barrier against mucus flow. Virtually all

tracheal intubations are associated with laryngeal changes that affect the voice-frequency histogram^{28,29,13}, even if they do not cause blatant hoarseness.

CLINICAL ANATOMY

ANATOMY OF UPPER AIRWAY AND LARYNX³⁰

Pharynx

The pharynx extends from posterior aspect of the nose at the base of the skull down to the level of lower border of cricoid cartilage where it becomes continuous with esophagus, and the respiratory tract through larynx. The soft palate partially divides the pharynx into upper nasopharyngeal portion and lower oropharyngeal portion. Hence pharynx is divided into 3 parts:

1) Nasopharynx 2) Oropharynx and 3) Laryngopharynx

Nasopharynx

This is the upper part of the pharynx situated behind the nose, and above the lower border of soft palate. The roof and posterior wall form a continuous slope, opposite the posterior part of body of sphenoid, basiocciput and anterior arch of atlas. Under the mucous membrane, opposite the basiocciput is a collection of lymphoid tissue called nasopharyngeal tonsil or adenoids.

Oropharynx

It is the middle part of the pharynx, starts below the soft palate and extends to hyoid bone to continue as laryngopharynx at the level of upper border of the epiglottis. Behind, it is supported by the body of the axis vertebra. In the lateral walls of oropharynx are situated the tonsillar pillars or fauces. The anterior pillar contains glossopharyngeal muscle and the posterior pillar contains palatoglossus muscle.

Laryngopharynx

It is also called hypopharynx. It is situated behind the larynx. It extends from upper border of the epiglottis to lower border of the cricoid cartilage. The lateral wall presents a depression called pyriform fossa, one on each side of the inlet of larynx.

The fossa is bounded medially by aryepiglottic fold, and laterally by thyroid cartilage and thyrohyoid membrane. Beneath the mucosa of the fossa, lies the internal laryngeal nerve.

Tongue

Tongue is a muscular organ situated in the floor of the mouth. It has an oral part that lies in the mouth and a pharyngeal part that lies in the pharynx. The oral and the pharyngeal parts are separated by a V shaped sulcus, the sulcus terminalis.

Oral Part

It is placed on the floor of the mouth. The margins are free and in contact with gums and teeth.

Pharyngeal Part

The posterior part of the tongue is connected to epiglottis by folds of mucous membrane. These are median glossoepiglottic fold, the right and the left glossoepiglottic folds. On the either side of the median fold there is a pouch called vallecula. The lateral folds separate the vallecula from pyriform fossa.

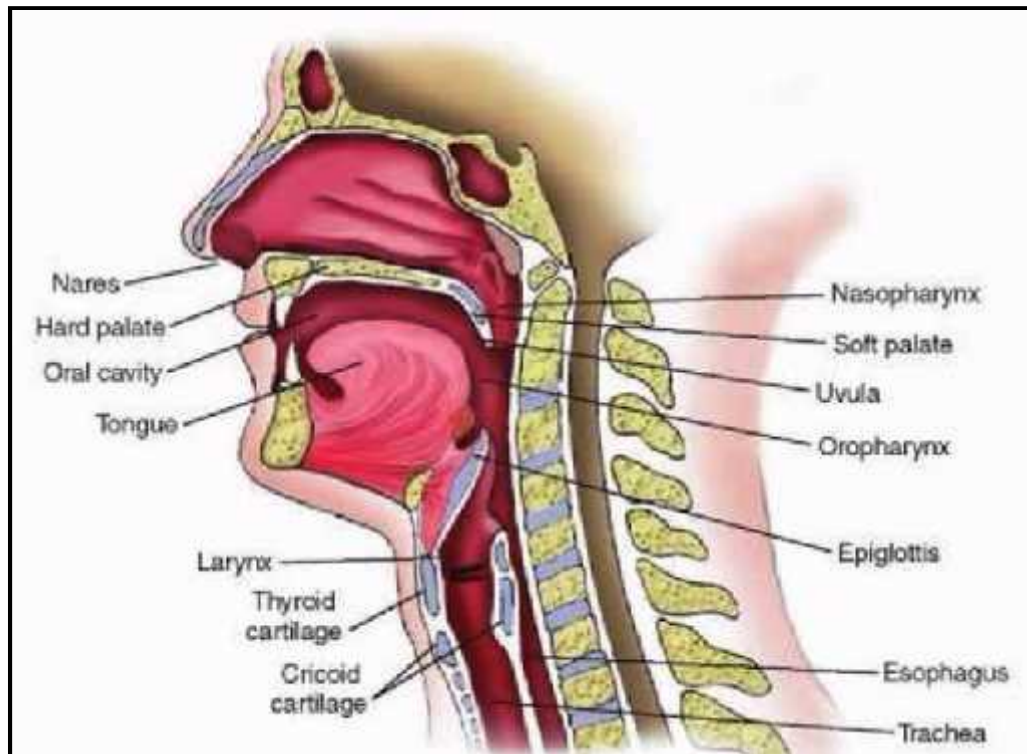


FIGURE 1: Anatomy of upper airway

LARYNX

It is the organ for production of voice situated at the crossroads between the food and air passages.

Situation and Extent

Larynx lies in the anterior midline of the neck extending from the root of the tongue to the lower border of the cricoid cartilage. In adult males, it lies in front of 3rd, 4th, 5th and 6th cervical vertebra. But in children and adult females, the level is slightly higher. Until puberty, no differences in the laryngeal size exist between males and females. At puberty, the male larynx develops more rapidly than that of female. The female larynx is smaller and more cephalad. The inlet to the larynx is bounded anteriorly

By upper edge of epiglottis, posteriorly by fold of mucous membrane stretched between the two arytenoids cartilages and laterally by aryepiglottic folds.

Larynx is made up of skeletal framework of cartilages, connected by joints, ligaments and membranes. The cartilages are moved by various muscles.

The skeleton of the Larynx

Consists of 3 paired and 3 unpaired cartilages:

Unpaired

Thyroid

Cricoid

Epiglottis

Paired

Arytenoid

Corniculate

Cuneiform

Thyroid Cartilage

The thyroid cartilage is 'V' shaped in cross section. In females, the sides join at approximately 120° and in males its closer to 90° . The smaller thyroid angle explains greater laryngeal prominence in males, the long vocal cords, and the lower pitched voice. The thyroid notch lies in the midline at the top of the fusion site of two laminae. On the inner side if this fusion line, are attached the vestibular ligaments and below them, the vocal ligament.

False and true vocal cords

Beneath the laryngeal mucosa, a sheet containing many elastic fibres, the fibro elastic membrane of the larynx and its upper area, the quadrangular membrane, extend in the aryepiglottic fold between the arytenoids and the epiglottis. The lower free border of membrane is called vestibular ligament and forms vestibular folds or false cords.

Cavity of Larynx

The cavity extends from inlet of larynx to the lower border of cricoid cartilage. The inlet is bounded anteriorly by the epiglottis, posteriorly by interarytenoid fold of mucous membrane, and on each side by aryepiglottic fold. Within the cavity of larynx, there are two folds of mucous membrane on each side, the upper fold is the vestibular fold and the lower fold the vocal fold. The space between the vestibular folds is rima vestibule, and between the vocal cords is called rima glottides. The vocal fold is attached anteriorly to midline of the thyroid cartilage and posteriorly to vocal process of arytenoids cartilage. The rima glottides is the narrowest part of larynx, in males it is about 23 mm and in females 17 mm in diameter.

The area extending from the laryngeal inlet to the vestibular folds is known as vestibular or supraglottic larynx. The laryngeal space from the free border of cords to inferior border of cricoid is called infraglottic or subglottic space. The region between vestibular folds and vocal cords is termed as ventricle. The ventricle may expand anterolateral to a pouch like area with lubricating mucous glands called laryngeal saccule. The pyriform sinus lies lateral to the aryepiglottic fold within the inner surface of the thyroid cartilage.

Intrinsic muscles of larynx

The functions of intrinsic muscles are:

- (1) Open the cords during inspiration, (2) Close the cords, the laryngeal inlet during deglutition, and (3) Alter the tension of cords during phonation.

	Muscles	Functions
1	Posterior cricoarytenoid	Abductor of vocal cords
2	Lateral cricoarytenoid	Adducts arytenoids, closing glottis
3	Transverse arytenoids	Adducts arytenoids
4	Oblique arytenoids	Closes glottis
5	Vocalis	Relaxes the cord
6	Thyro arytenoids	Relaxes the cord
7	Cricothyroid	Tensor of cords

All of the above muscles are paired except transverse arytenoids.

Blood Supply and venous drainage

1. Up to the vocal cords: superior laryngeal artery, a branch of superior thyroid artery. The superior laryngeal veins drains into superior thyroid vein.
2. Below the vocal cords: inferior laryngeal artery, a branch of inferior thyroid artery. The inferior laryngeal vein drains into inferior thyroid vein.

Innervation of larynx and surrounding structure

Larynx is innervated by superior laryngeal nerves and recurrent laryngeal nerves. Both are branches of vagus.

VAGUS

The tenth cranial nerve is mixed nerve. It lies vertically between the internal jugular vein and internal carotid artery above, and the common carotid artery below. Superior laryngeal nerve separates off the vagus, to pass behind the internal carotid artery following the superior margin of middle pharyngeal constrictor muscle.

Immediately before reaching the level of hyoid bone, the nerve divides into two branches:

- a) Sensory – internal laryngeal nerve
- b) Smaller motor – external laryngeal nerve

Internal laryngeal branch of superior laryngeal nerve

It passes under the greater cornu of hyoid bone to penetrate the thyrohyoid membrane near the greater cornu (inferior lateral edge). The upper branches of internal laryngeal nerve fan out into periglottic tissue to supply the vallecula, posterior surface of epiglottis and pyriform sinuses. Lower branches travel downward in the aryepiglottic fold supplying sensation to the level of true vocal folds. Few terminal fibres pass through inferior constrictor to unite with ascending fibres from recurrent laryngeal nerve.

External laryngeal nerve

Branch of superior laryngeal nerve, stays superficial to larynx until it submerges under the cricothyroid articulation to supply the cricothyroid muscle. It supplies the pharyngeal plexus, connects with superior cardiac nerve (branch of vagus) and also superior cervical sympathetic ganglion.

Recurrent laryngeal nerve

This has different points of origin from the vagus on two sides. The right recurrent laryngeal nerve originates from the right vagus, as the right vagus crosses the right subclavian artery curving under the artery and back up the neck. The left recurrent laryngeal nerve originates from left vagus which crosses over aortic arch, near the insertion of ligamentum arteriosum. It curves under the aorta to travel up the neck between trachea and esophagus.

In larynx, recurrent laryngeal nerve innervates all ipsilateral intrinsic muscles of larynx except cricothyroid. The transverse arytenoids derive their motor innervation from both recurrent laryngeal nerves and from internal branch of superior laryngeal nerve as well. Sensory afferents from inferior surface of vocal cords and trachea are also carried by recurrent laryngeal nerves.

Autonomic innervation of pharynx

The laryngopharyngeal branches from the superior cervical ganglion supply the carotid body and pass to the sides of pharynx where they join with the branches from glossopharyngeal and vagus nerves to form pharyngeal plexus. Nerve supply to pharynx is derived from pharyngeal plexus which is formed from the branches of glossopharyngeal, vagus and sympathetic (from superior cervical ganglia) nerves.

Main sensory nerves are glossopharyngeal and vagus, much of the mucous membrane of nasal part of pharynx being supplied by branches of maxillary nerve. Mucous membrane of soft palate is supplied by lesser palatine and glossopharyngeal nerve.

PHARMACOLOGY OF KETAMINE ^(31,32,33)

History:

Ketamine was synthesized in 1962 by Stevens and was first used in humans in 1965 by Corssen and Domino. Ketamine was released for clinical use in 1970.

Chemistry

Ketamine is a phencyclidine consisting of two stereoisomers, S (+) and R (-). The S (+) is more potent and is associated with fewer side effects.

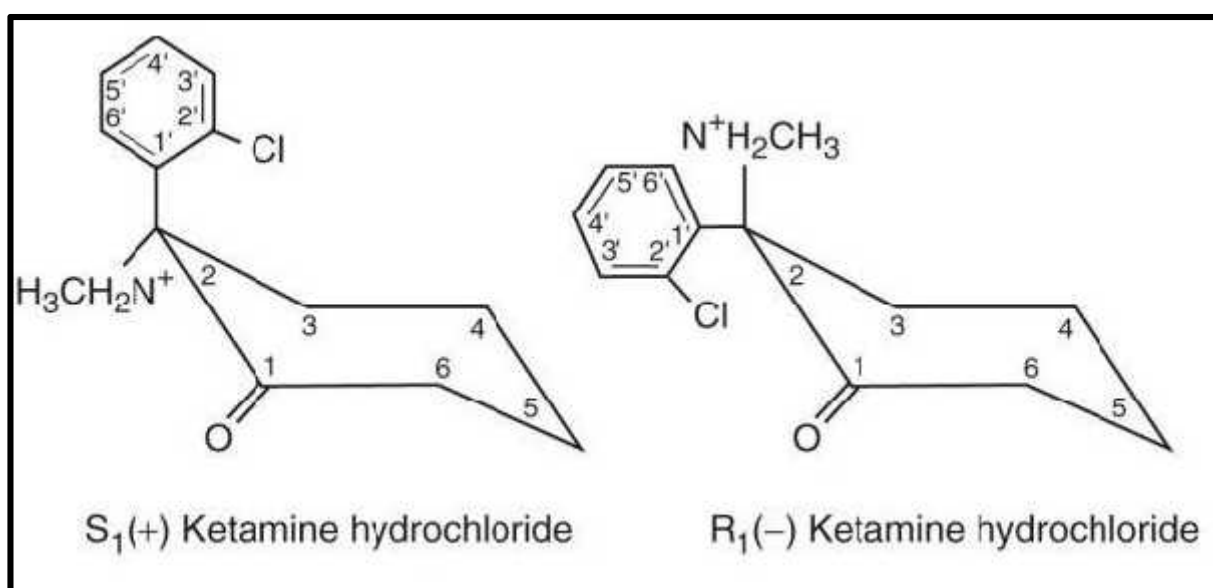


Figure 2: Showing the stereoisomers of Ketamine

Physicochemical Characteristics

- Molecular weight : 238 kD(kilo Daltons),
- Partially water soluble,
- Aqueous solutions of ketamine hydrochloride in clinical use have a pH range from 3.5 to 5.5.
- Forms a white crystalline salt with a pKa = 7.5.
- Lipid soluble : 5 to 10 times that of thiopental

Metabolism

Ketamine is metabolized by hepatic microsomal enzymes. The major pathway involves N-demethylation to form norketamine (metabolite I), which is then hydroxylated to hydroxynorketamine. These products are conjugated to water-soluble glucuronide derivatives and are excreted in the urine. Norketamine (metabolite I) has significantly less (20% to 30%) activity than the parent compound.

Pharmacokinetics

Ketamine plasma disappearance can be described by a two-compartment model.

- Distribution half-life : 11 to 16 minutes
- The high lipid solubility of ketamine is reflected in its large volume of distribution, nearly 3 litres/kg.
- Clearance is high, 890 to 1227 mL/minute, which accounts for the short elimination half-life of 2 to 3 hours. The mean total body clearance (1.4 litre/minute) is approximately equal to liver blood flow.
- The pharmacokinetics of the two isomers is different. S (+) ketamine has a larger elimination clearance and larger volume of distribution than R (-) ketamine.
- Ketamine clearance is not normally distributed, and this is not related to age.
- The bioavailability via oral administration is 20% to 30%, and via the intranasal route is approximately 40% to 50%.

Pharmacodynamics

IV: Onset of time for anaesthetic effect: 30- 60 seconds

Duration of anaesthetic effect: IV: 5 – 10 minutes

Peak effect: 1 minute

IM: Onset of anaesthetic effect: 3 -4 minute

IM: Duration: 12 – 25 minutes

Half-life elimination:

Alpha: 10-15 minutes

Beta: 2.5 hours

Excretion: primarily urine

Effect on CNS

- Causes a "dissociative anaesthetic state"
 - This is a functional and electrophysiological dissociation between the thalamoneocortical & limbic systems
 - Characterised by catalepsy in which eyes remain open with slow nystagmic gaze, while corneal and light reflexes remain intact
- Induces psychotomimetic activity and emergence reactions which can be disturbing.
- A higher incidence of reactions is associated with,
 - age > 16 years
 - sex : female > male
 - larger doses > 2mg/kg IV
 - rapid IV administration

- subjects who normally dream during sleep
- history of personality problems
- Increases cerebral metabolic oxygen consumption rate, cerebral blood flow and intracranial pressure.
- The excitatory effects of ketamine can be detected by the development of theta-activity and "petit-mal like" seizure activity.
- Inhibits nociceptive central hyper sensitization.
- Attenuates acute tolerance after opiate administration.
- Depresses transmission of impulses in the medial medullary reticular formation, which is important for transmission of the affective-emotional components of nociception from the spinal cord to higher brain centres.
- NMDA receptor interaction may mediate the general anaesthetic effects and some analgesic actions of ketamine.
- The spinal cord analgesic effect of ketamine is postulated to be due to inhibition of dorsal horn wide dynamic range neuronal activity. When administered in sub-anaesthetic concentrations, ketamine produces good analgesia at plasma levels one-eighth those required for anaesthesia this may be related to its ability to suppress laminae specific spinal cord activity (opioid k-receptors, laminae II & II)
- Involved in anti-apoptotic mechanisms in addition to reducing necrotic cell death mediated by inhibition of NMDA receptor-mediated ion currents.

Effects on Cardiovascular system

Increases mean arterial blood pressure, heart rate, pulmonary arterial and central venous pressures which are related to sympathetic stimulation, with increased circulating levels of adrenaline & noradrenaline, resulting in peripheral vasoconstriction and direct cardiac stimulation.

- Attenuates baroreceptor function via an effect on NMDA receptors in the nucleus tractus solitaries.
- Abolishes adrenaline-induced arrhythmias by prolonging the relative refractory period
- Increases pulmonary vascular resistance, thus increasing pulmonary artery pressure and right ventricular stroke work.

Effects on respiratory system

- Respiratory depression is minimal with anaesthetic doses but may be depressed with large doses.
- Results in bronchodilatation and is a useful agent for asthmatics.
- In patients with reactive airway disease, ketamine decreases airway resistance and bronchospasm.
- Produces marked salivation, especially in children; therefore an anti-sialagogue should be administered prior to its use.

Uses
Table 1: Showing various dosages of ketamine employed

Induction of Anaesthesia	0.5-2.0 mg/kg IV
	4.0-6.0 mg/kg IM
Maintenance of Anaesthesia + N ₂ O/O ₂ or opiates	0.5-1 mg/kg/hour IV with N ₂ O 50% in O ₂
	30-90 µg/kg/min IV without N ₂ O
Sedation and analgesia	0.2-0.8 mg/kg IV
	2.0-4.0 mg/kg IM
Pre emptive /preventive analgesia	0.15-0.25 mg/kg IV

- Used in hypervolemia, intrinsic myocardial disease, congenital heart disease, cardiac tamponade, restrictive pericarditis (with the exception of ischemic heart disease)
- In respiratory disorders especially bronchospastic airway disease.
- In healthy patients with trauma/hypervolemia

Anaesthesia

- Produces analgesia without loss of consciousness at infusion rates ~ 50 µg/kg/min.
- May also be used in conjunction with N₂O & muscle relaxants to provide sleep and analgesia at doses of 15-30 µg/kg/min.
- Muscle relaxants are often necessary as ketamine increases muscle tone.

Obstetrics

- Reportedly used successfully as an induction agent in caesarean section but doses > 1.5 mg/kg IV may lead to foetal depression .
- Useful as a supplement to epidural anaesthesia and spinal anaesthesia in low "analgesic" doses (0.2-0.3 mg/kg)

Day care Surgery

Useful in children for short procedures as it may be given IV, IM, orally or rectally.

- IM doses for children are $\sim 5-10$ mg/kg with an onset of surgical anaesthesia in 3-5 minutes and duration of 10-30 minutes. The use in children is more versatile as the incidence of emergence reactions is much lower.
- Lower dose may be used for diagnostic procedures such as cardiac catheterization, radiation therapy, dressing changes, or dental work.

Adjunct to Local and Regional Anaesthesia

- During performance of painful blocks, ketamine produces analgesia, sedation and amnesia without cardiovascular depression.
- Also used for sedation during regional anaesthesia in combination with benzodiazepines.

Antinociception

- Ketamine produces antinociceptive actions via inhibition of NMDA receptors and activation of descending inhibitory monoaminergic pain pathways.
- NMDA receptor-mediated spinal reflexes are intimately involved as the pharmacological basis for wind up, which contributes to neuropathic pain.

- Norketamine has antinociceptive actions and enhances opioids' antinociceptive action to thermal nociception, peripheral neuropathy and tonic inflammatory pain and block tolerance.
- Low-dose ketamine (0.5mg/kg) attenuated the increases in serum C-reactive protein, IL-6 and IL-10 associated with inflammation after cardiac surgery with cardiopulmonary bypass.

Burns Patients

- Used extensively for dressing changes, debridement and skin grafting (1.5-2.5 mg/kg IM)
- Higher dosages (4-6 mg/kg IV) are adequate for eschar excision.

Miscellaneous

- Successfully used in patients with malignant hyperthermia susceptibility, myopathies, porphyria, etc. In acute hypovolemia, the use of ketamine results in a more stable and better functioning cardiovascular system than with other induction agents.

Disadvantages

- increased muscle tone
- spontaneous movements during induction & anaesthesia
- cardiovascular system stimulation
- slow recovery
- emergence reactions
- postoperative nausea & vomiting
- elevated intracranial & intraocular pressure
- potent sialagogue, especially in children

Contraindications

- poorly controlled hypertension
- unstable angina or recent myocardial infarction & right or left heart failure
- valvular heart disease - but may be useful in congenital heart disease
- intracranial, thoracic or abdominal aneurysms
- cerebrovascular disease & raised intracranial pressure conditions
- recent penetrating eye injury

METHODOLOGY

The present study was conducted at KLE'S Dr.Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi from January 2014 to December 2014.

Study design

One year double blinded randomized controlled trial

Source of data

Patients undergoing general anaesthesia with endotracheal intubation

Sample size

A total sample size of 106 cases, 53 in Group A and the other 53 in Group B

Sample size calculation

The sample size was calculated by considering incidence of POST as 30 % (p_1) with ketamine gargle and with that of normal saline as 60 % (p_0).

With type I error rate = 0.05 and

Type II error rate = 0.02

with a power of 80% and using the formula-

$$n = \frac{2(Z_{\alpha} + Z_{\beta})^2 pq}{(p_0 - p_1)^2}$$

$$n = \frac{2(1.96 + 0.84)^2 (60)(50)}{(60 - 30)^2}$$

$$n = 52.66$$

n = number of samples

$$Z = 1.96$$

$$Z = 0.84$$

$$P_0 = 60\%$$

$$P_1 = 30\%$$

Thus the sample size was calculated as 106, 53 in each group.

Selection Criteria:

Inclusion Criteria:

- 1. ASA physical status I and II.
- 2. Age between 18 to 60 years.
- 3. Airway assessment by Mallampati grade I and II.
- 4. Patients undergoing elective surgeries under general anaesthesia.

Exclusion Criteria:

- Patients not willing to give consent
- Patients requiring more than one attempt for endotracheal intubation.
- Patients with upper respiratory tract infection
- Patients with preoperative sore throat

Methodology:

- After obtaining the approval of the Ethical committee and written informed consent, a total of 106 patients undergoing elective surgeries of a maximum duration of 3 hours under general anaesthesia were included in the study. Patients randomly divided into two groups by using computer generated table.
- Group A received preservative free ketamine 1 ml (50mg) in 29ml Normal saline(NS)
- Group B received 30 ml of NS

Patients were asked to gargle for 30 seconds 5 minutes prior to induction. Standard non-invasive monitoring was done throughout the anaesthesia. Following preoxygenation, patient were premedicated with Inj.glycopyrrolate 0.005mg/kg iv, Inj.midazolam 0.05mg/kg iv and Inj.fentanyl 2mcg/kg iv.

Induction of anaesthesia was done with 5mg/kg of Inj.thiopentone sodium iv sufficient to obtund the eye-lash reflex, followed by Inj.vecuronium 0.1 mg/kg iv with an appropriate sized endotracheal tube. Tracheal intubation was performed by an experienced anaesthesiologist having experience of >3 years. The endotracheal tubes was lubricated with 2% lignocaine jelly at room temperature. Immediately after intubation, cuff of the endotracheal tubes was filled with a volume of room air required to prevent a palpable air leak.

Anaesthesia was maintained with isoflurane, fentanyl, vecuronium and supplemented with oxygen 33% in nitrous oxide. Intracuff pressure was maintained throughout the procedure between 18-22 cm H₂O using handheld pressure gauge.

Residual neuromuscular relaxation with vecuronium was antagonized with Inj. Neostigmine iv (0.05mg/kg body weight) and Inj. Glycopyrrolate iv (0.01mg/kg body weight) on completion of surgery. Oropharyngeal suction before extubation was done under direct vision to avoid trauma to the tissues, confirming that secretion clearance was complete.

The patients were interviewed regarding post operative complaints. If they did not complain about sore throat then a leading direct question was asked regarding the same at 0, 4, 8, 12 and 24 hours after the procedure.

POST was graded on a four point scale (0-3):

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).

Other side-effects, if any, were also noted.

STATISTICAL ANALYSIS

To compare patient characteristics, duration of anaesthesia and surgery student's t-test was used. To compare gender distribution between the two groups Chi square test was used. To analyse the association of sore throat in two groups Chi square test was used. $P < 0.05$ was considered statistically significant.

RESULTS

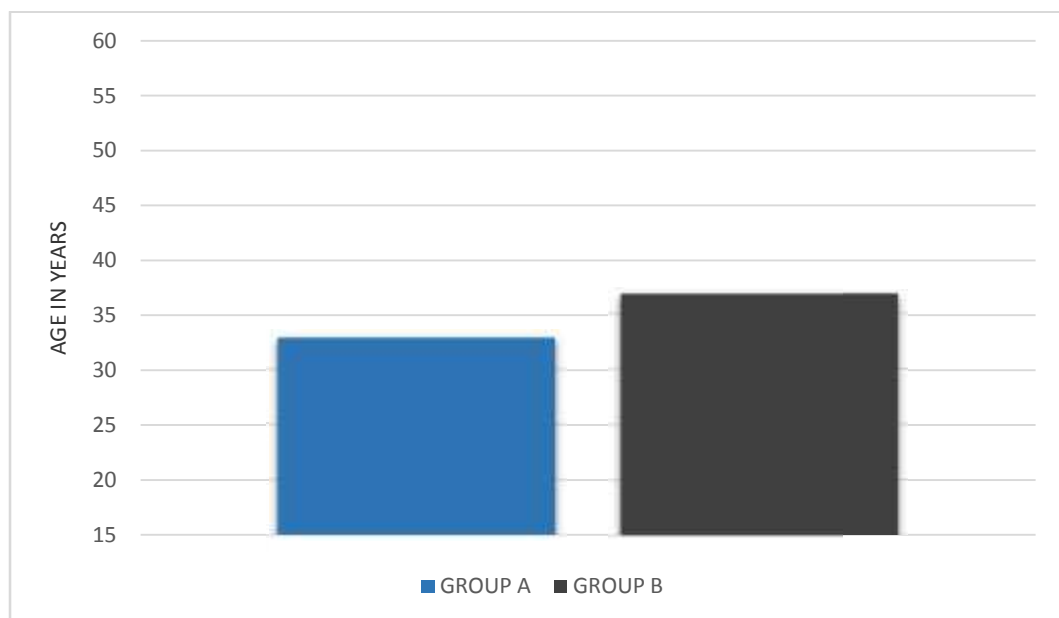
The present study was conducted to study the efficacy of ketamine gargle in prevention of postoperative sore throat following endotracheal intubation in patients receiving general anaesthesia.

110 patients were enrolled for the study, keeping in mind the inclusion and the exclusion criteria. 4 patients however could not gargle for 30 seconds and hence had to be excluded from the study.

106 ASA grade I-II patients between 18-60 years of age, of both the sexes were included in the study. 53 patients in Group A (Ketamine gargle) and 53 patients in Group B (Normal saline gargle)

DEMOGRAPHIC DATA

Graph 1:

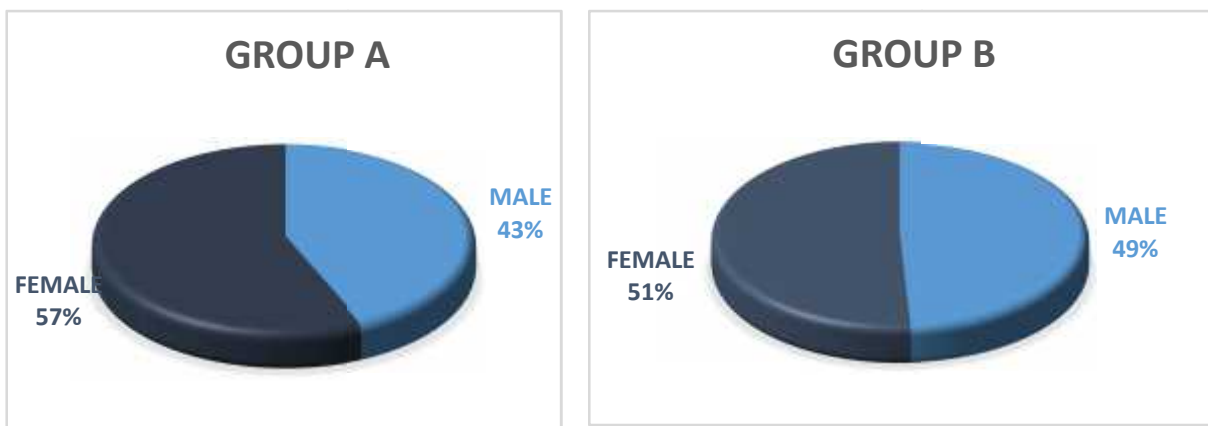


The average age of patients in Group A was 33 years & average age of patients in Group B was 37 years.

When compared statistically the difference was not found to be significant ($p=0.087$).

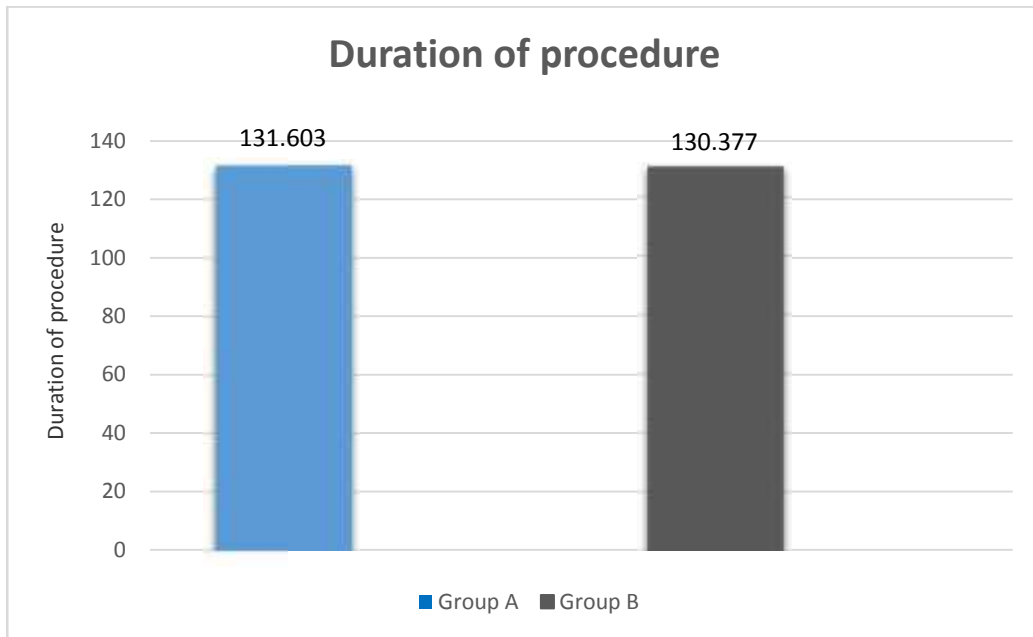
The 2 groups were comparable with respect to age.

Graph 2:



Of the total 53 patients in Group A, 30(57%) were female & 23(43%) were male. Of the total 53 patients in Group B, 27 (51%) were females and 26(49%) were males. When compared the difference between the two groups was not found to be statistically significant ($p=0.342$).

Graph 3:



Mean duration of procedure was 131.603 minutes in Group A, Mean duration of procedure was 130.377 minutes in Group B. When compared the difference between the two groups was not found to be statistically significant ($p=0.8$).

Table I – Demographic Data.

PARAMETER	Group A Ketamine (Mean ± S.D.)	Group B Normal saline (Mean ± S.D.)	P Value
Age(in years)	32.9±11.7	36.8±11.9	0.087
Duration of procedure (in minutes)	131.603±30.52	130.377±30.522	0.8
Sex(M/F)	23/30	26/27	0.342

Demographic data were comparable in both the groups.

TABLE II: shows incidence of sore throat at 0 hr

Groups	Grade 0	Grade 1	Grade 2	Grade 3	Total
Group A	2	34	15	2	53
Group B	0	6	30	17	53
Total					106
p value < 0.001					

TABLE III: shows incidence of sore throat at 4 hr

Groups	Grade 0	Grade1	Grade 2	Grade 3	Total
Group A	18	30	5	0	53
Group B	3	21	29	0	53
Total					106
p value< 0.001					

TABLE IV: shows incidence of sore throat at 8 hr

Groups	Grade 0	Grade1	Grade 2	Grade 3	Total
Group A	39	14	0	0	53
Group B	8	36	9	0	53
Total					106
p value< 0.001					

TABLE V: shows incidence of sore throat at 12 hr

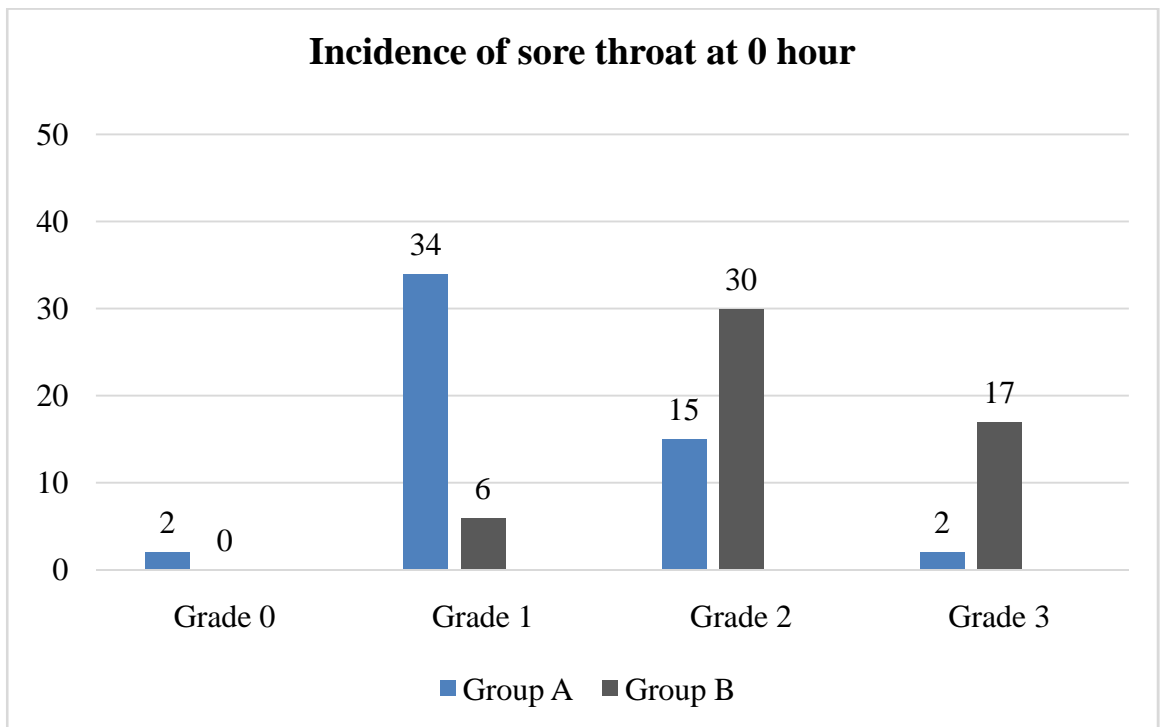
Groups	Grade 0	Grade1	Grade 2	Grade 3	Total
Group A	51	2	0	0	53
Group B	28	25	0	0	53
Total					106
p value< 0.001					

TABLE VI: shows incidence of sore throat at 24 hr

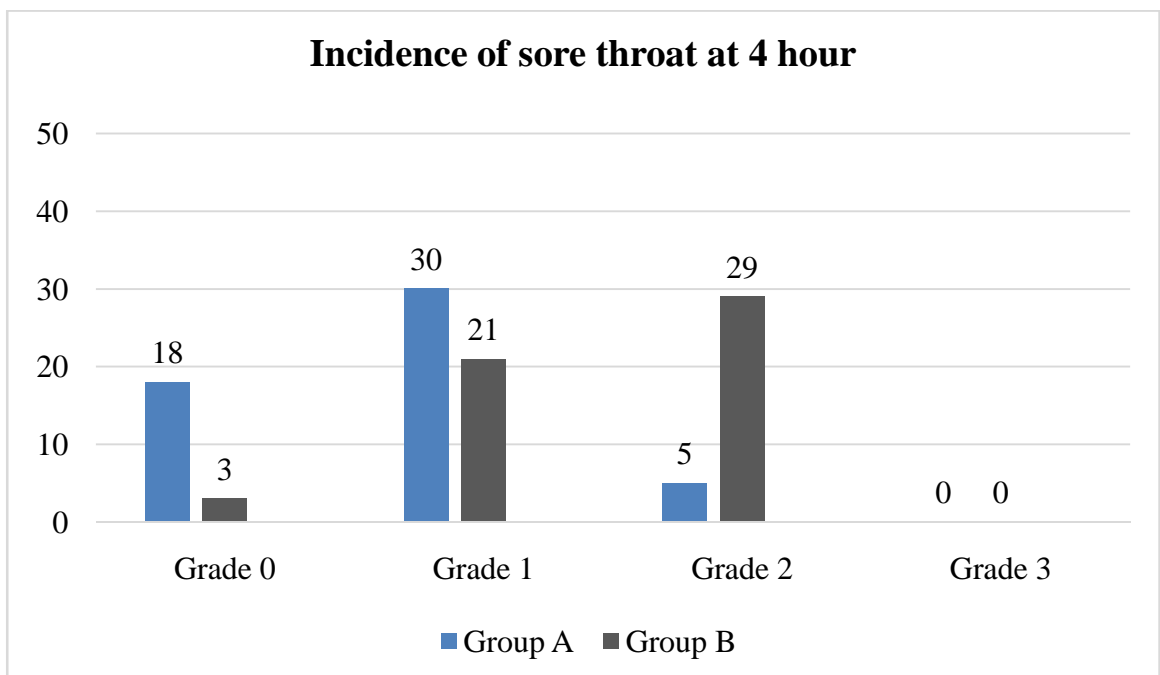
Groups	Grade 0	Grade1	Grade 2	Grade 3	Total
Group A	53	0	0	0	53
Group B	45	8	0	0	53
Total					106
p value= 0.010					

Incidence of sore throat was lower in Group A than in Group B at intervals 0 hr, 2 hrs, 4 hrs, 8 hrs, 12 hrs, 24 hrs. Statistically significant at all instances with p value of <0.05.

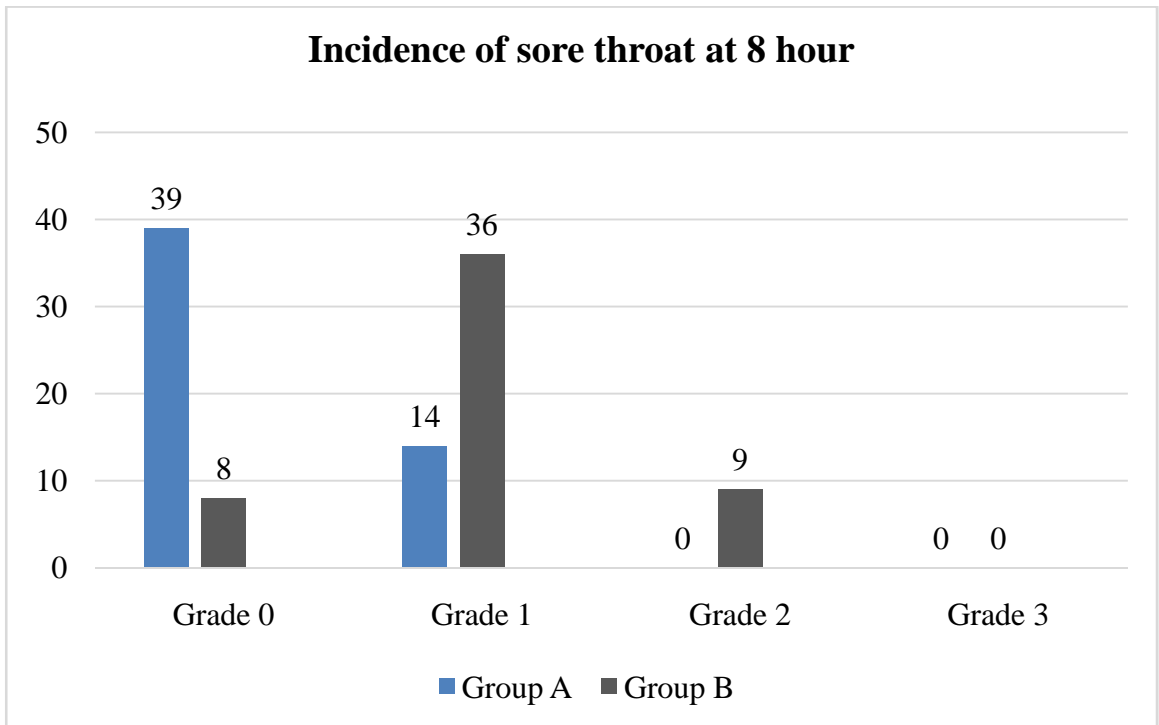
Graph 4:



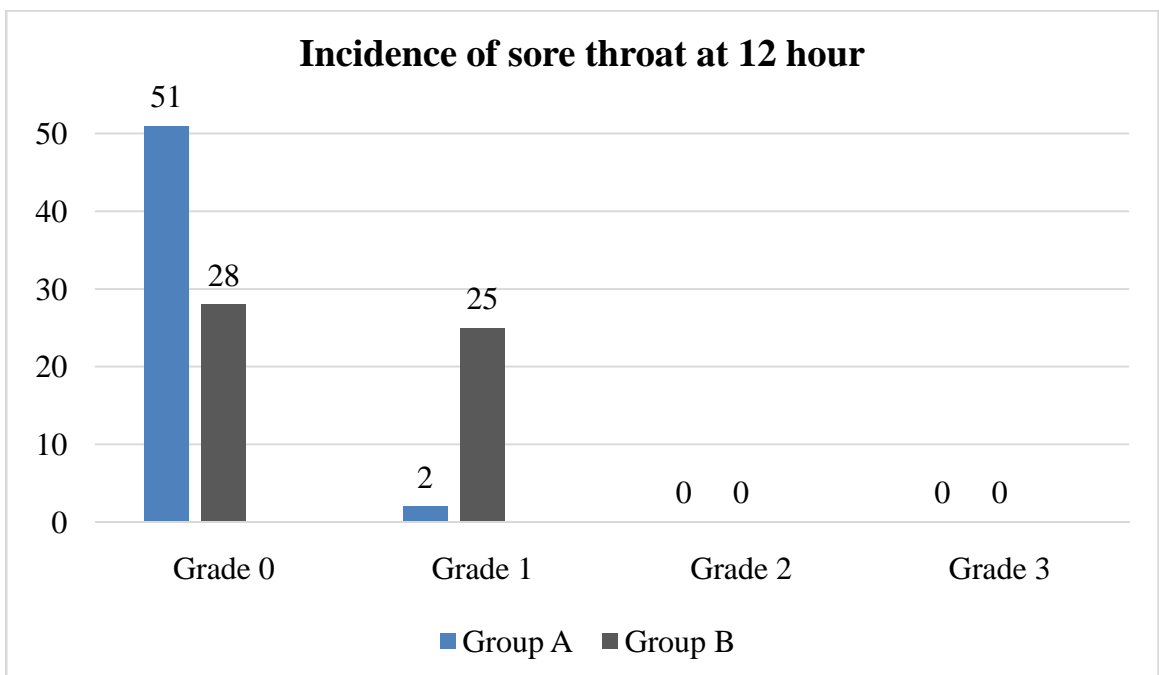
Graph 5:



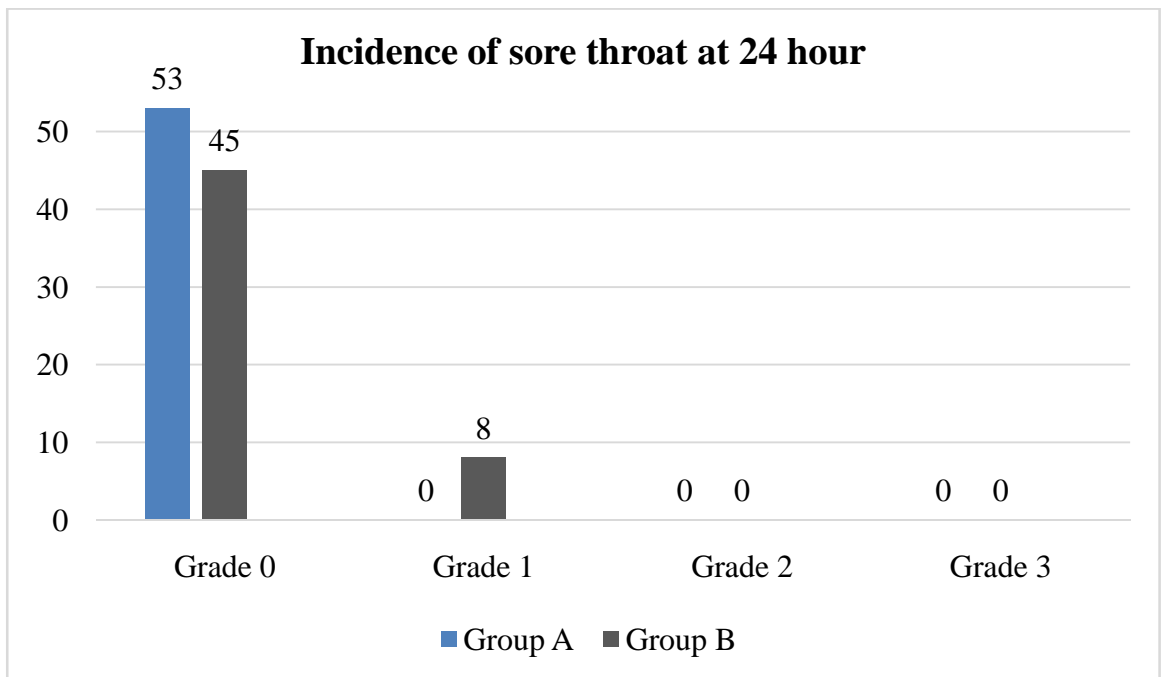
Graph 6:



Graph 7:



Graph 8:



DISCUSSION

In modern anaesthetic practice, many of the general anaesthetic procedures are carried out with endotracheal intubation. Postoperative sore throat (POST) is a well-recognized side effect, albeit minor after endotracheal intubation¹⁸. But the discomfort produced by sore throat makes it one of the most undesirable side effect in the postoperative period.¹⁴

POST(Post-operative sore throat) represents a broad constellation of signs and symptoms of laryngitis, tracheitis, hoarseness, cough or dysphagia with incidence varying from (21-65%)¹⁵ after endotracheal intubation. Post operative sore throat was rated by patients as 8th adverse effect in the post operative period.⁹

Several contributing factors for sore throat after surgery have been reported including patient sex¹⁸, age¹⁸, use of succinylcholine¹⁸, large tracheal tube¹, cuff design & intra cuff pressure¹⁴.

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 post anaesthetic outcomes. Multi modal approach can be used for attenuation of POST. These consist of non-pharmacological and pharmacological interventions. Smaller sized endotracheal tubes¹, lubricating the endotracheal tube with water soluble jelly³, careful airway instrumentation, intubation after full relaxation, gentle oropharyngeal suctioning, minimizing intra-cuff pressure¹⁸ and extubation when the tracheal tube cuff is fully deflated are some of the non-pharmacological measures to reduce the incidence of POST.

Pharmacological interventions include beclomethasone inhalation⁵, IV steroids⁴, IV preservative free lignocaine³⁴, gargling with azulene sulfonate³⁴ etc. But all such manoeuvres have their own limitations and have not been able to successfully deal with this distressing side-effect.

An increasing amount of experimental data shows that N-methyl-D-aspartate (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 anti-nociception and anti-inflammatory cascade^{14,36,37} by reducing NF activity, TNF- (tumour necrosis factor) production³⁸, expression of inducible nitric oxide synthase³⁹ serum C-reactive protein, IL-6 and IL-10³². 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 sensitization⁴⁰. It has been further reported that peripherally administered NMDA receptor antagonist such as Ketamine have anti-nociceptive and anti-inflammatory effects⁶. Hence in our study we compared pre-emptive ketamine gargle with normal saline gargle as a means to prevent post-operative sore throat.

Incidence of POST has been found to be higher in females as compared to males (17.7% vs 9 %)⁹. In our study the number of male patients was 23 in ketamine group & 26 in saline group. The number of female patients was 30 in ketamine group and 27 in saline group. When compared the difference was not found to be statistically significant (p=0.342).

The incidence of sore throat increases with the duration of procedure. Hence in our study the duration of procedure was defined. Duration was standardized in both the groups. Any patient whose surgery lasted for more than 3 hrs was excluded from our study. The duration of the procedure in ketamine group was 131.603 ± 30.52 minutes while in normal saline group it was 130.377 ± 30.52 minutes. When compared the difference was not found to be statistically significant ($p=0.8$).

Increased incidence of sore throat has been reported in patients when succinylcholine is used to facilitate endotracheal intubation (14% in the group that received succinylcholine as compared to 17% in the group that did not)¹⁸. Hence in our study we did not use succinylcholine for endotracheal intubation. All intubations were facilitated using Vecuronium.

The use of cuffed tubes, Stout D M. et al (1987)¹ showed a higher incidence of sore throat by larger size tube compared with smaller size, hence in our study we use 7.5 mm tube for female patients and 8.5mm tube for male patients in both the groups.

Incidence of post operative sore throat has been found to be higher when tubes with high pressure low volume cuffs are used in comparison with tubes with high volume low pressure cuffs. Hence in our study we used portex tubes that have a high volume low pressure cuff in all patients¹⁸.

Previous studies have reported that POST is associated with increase in cuff pressure. Excessive inflation of endotracheal tube cuff produces high pressure on the tracheal wall thereby affecting perfusion of the tracheal mucosa resulting in its ischaemic necrosis. When pressure in the endotracheal tube cuff exceeds 22 mm hg, blood flow in the tracheal mucosa begins decreasing and reduces markedly when the

pressure reaches 30 mm hg hence in our study we maintained the intra-cuff pressure between 18-22 mm hg in both the groups.

Trauma during insertion of the endotracheal tube is associated with higher incidence of post operative sorethroat¹⁸, hence in our study all the intubations were done by an anaesthesiologist with a minimum experience of 3 years to avoid unnecessary trauma.

Blind suctioning causes trauma to the pharyngolaryngeal structures that increases the chances of post-operative sore throat. Suctioning was strictly done under vision in our study.

High anaesthetic air flow rates cause drying of the mucosa that inturn leads to increased incidence of post-operative sore throat, our study used O₂:N₂O in a ratio of 1:1 with fresh gas flow of 4 liters⁴¹.

The incidence of postoperative sore throat varied with the type of questioning employed. Various investigators in have used various techniques to elicit sore throat in postoperative period. Harding C J. et al ¹¹conducted a study in 1987 that showed higher incidence of sore throat by direct questioning. Hence in our study we have used a scale in which patient is asked about his complains in the postoperative period. If the patient does not complain of sore throat then a direct question pertaining to sore throat, cough, hoarseness was asked.

Coughing or bucking on the endotracheal tube has been found to be associated with greater incidence of POST. However none of our patients experienced coughing or bucking on the tube. All patients had a smooth recovery and were extubated following complete deflation of the cuff.

Placement of throat pack around the endotracheal tube increases the incidence of POST²³. However, in our study, throat pack was not inserted in any of the patients.

Our study found that Gargling with 50mg of Ketamine diluted with 29ml of NS 5 minutes before induction successfully reduced the incidence & severity of post-operative sore throat. Immediately after extubation 17/53 patients in normal saline group complained of severe POST as compared to only 2/53 patients in ketamine group.

At four hours post extubation 29/53 patients in normal saline group complained of moderate sore throat while only 5/23 in ketamine group experienced sorethroat. When compared statistically the difference in incidence of POST at 0 and 4 hours post extubation was found to be statistically significant ($p < 0.001$).

At 12 hours post extubation only 2/53 patients in ketamine group complained of mild sore throat while none had moderate or severe symptoms. However in saline group, although no patients had moderate or severe symptoms, 25/53 patients still experienced mild sore throat. 8/53 patients had mild sore throat even at 24 hours following extubation in saline group while none of the patients in ketamine group complained of any sore throat. When compared statistically the difference in incidence of POST at 12 and 24 hours post extubation was found to be statistically significant ($p < 0.001$).

This shows that ketamine gargle just prior to induction of general anaesthesia significantly reduces the incidence and severity of POST. However it was not found to be effective in prevention of POST as 34/53 patients in ketamine group complained of mild sore throat at 0 hours i.e., immediate post extubation.

The findings of our study correlate with a study done by **Canbay et al**¹⁴ in 2008. In this study the author studied the effects of a ketamine gargle on POST. Forty-six patients undergoing septorhinoplasty were included in the study and divided into two groups, one received ketamine gargle 40mg and other normal saline for thirty seconds prior to induction of general anesthesia. They found that both the incidence and severity of POST was reduced in the ketamine group. None of the ketamine patients reported severe POST symptoms at any interval while fifteen of the saline gargle patients reported severe symptoms. Two patients of ketamine group reported moderate symptoms in the immediate postoperative period while thirteen patients in the saline group reported moderate symptoms thus showing that ketamine gargle significantly reduces the incidence and severity of POST.

The findings of our study also correlated with the following studies. In 2009, **Rudra et al**¹⁵, conducted a prospective, randomized, placebo-controlled, and single – blinded study assigning 40 ASA grade I patients undergoing abdominal and pelvic surgery under general anaesthesia to 2 groups, one group received drinking water 30 ml and another received preservative free ketamine 1ml (50mg) in 29ml of drinking water to gargle for 40 seconds. The researchers reported that the number of patients in Control group had significantly more incidence of POST at 4, 8 and 24hours (85%, 75%, and 60%) than in patients having ketamine gargle (40%, 35%and 25%) concluding that gargling with ketamine effectively attenuated POST, with no adverse reactions.

In 2010, **Shresta et al**⁴², designed a prospective comparative study assigning 40 ASA grade III, elective patients undergoing abdominal and orthopedics surgery under general anaesthesia into 2 groups, one that received drinking water 30 ml and

another that received ketamine 50 mg (1ml) in 30 ml drinking water for gargling for 30 seconds, 5 minutes before the induction of anaesthesia. At 4, 8, 24 hours after the surgery the patients were interviewed in a standard fashion by a blind investigator. The researchers concluded that the overall incidence of POST in the control group at 4, 8 and 24 hours was 75%, 60% and 50% respectively which was less than in patients having ketamine gargle (35%, 30%, 15%). There was significantly lower incidence of POST with ketamine gargle at 8 and 24 hours. No significant differences in mild sore throat at 4, 8 and 24 hours were noted among the groups. No severe sore throat was noted in either group eventually concluding that gargling with ketamine decreases the incidence and severity of POST after endotracheal intubation for general surgical procedures.

Chan et al⁶ in 2011 conducted double-blind randomized control study, assigning 44 adult ASA I or II patients undergoing elective gynaecological procedures to 2 groups, 22 patients gargling with 20 ml of normal saline & other 22 patients with ketamine 40 mg in 20 ml normal saline. The same anaesthetist performed all intubations and extubations. During surgery, blood samples were collected at intervals for ketamine and norketamine analysis. At the end of the study period, serum samples were assayed by liquid chromatography and mass spectrometry. After extubation, POST was assessed at 0 (on arrival at the post-anaesthetic care unit), 2, and 24 hour using a four-point grading scale (none, 0; mild, 1; moderate, 2; and severe, 3). POST was significantly reduced in the ketamine gargle group compared with control at 0 and 2 hour after surgery but not at 24 hour. There was significantly less moderate-to-severe POST in the Ketamine group at 0 hour. The highest average ketamine and norketamine concentrations were 16.16 and 11.43 nanogram/ 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. They concluded that pre-induction ketamine gargle can attenuate POST in the early postoperative period. Drug levels detected were much lower than reported measurements for analgesia after oral and parenteral administration. Hence by using ketamine in the form of a gargle we can avoid the ill effects of parenteral administration of the drug, and reap the beneficial local effects of the same. The study confirms that pharyngotracheal sequelae after endotracheal intubation are due to local inflammation and pain, ketamine in the form of gargle acts on NMDA receptors. It reduces inflammation and has anti nociceptive effects. Hence helps in reducing the incidence of postoperative sore throat.

Our study however had some limitations.

- 1) Dry gases were used in the study which may have increased the incidence of sore throat, especially in the immediate post operative period. Humidification of gases should be considered. However, since dry gases were used in both the groups, bias was eliminated.
- 2) 4 patients were unable to gargle for a period of 30 seconds and hence had to be excluded from the study

In the future studies may be done which use lower dose of ketamine 25mg in 2 ml in the form of a spray instead of a gargle to improve patient compliance.

Alternatively the duration of gargling may be reduced, making the patients gargle 50 mg of ketamine in 29 ml of normal saline for 15 seconds which again may improve patient compliance.

CONCLUSION

Ketamine gargle significantly reduces the incidence and severity of postoperative operative sore throat. Hence contributing to smoother recovery and greater patient satisfaction.

SUMMARY

We conducted a study to determine the effect of ketamine gargle on the incidence & severity of postoperative sore throat amongst 106 patients belonging to ASA grade I & II scheduled to undergo elective surgeries under general anaesthesia with endotracheal tube. Pre operatively the patients received either Ketamine gargle (Group A) or Normal saline gargle (Group B).

The study was conducted after obtaining Institutional ethical committee clearance & written informed consent from all the patients. Thorough pre- anaesthetic evaluation was done, investigations were noted. Using a computer generated randomisation table the patients were allocated into 2 groups, Ketamine gargle (Group A) or Normal saline gargle (Group B). Patients received either 50mg of ketamine in 29ml of normal saline, in the form of a gargle or 30 ml of normal saline based on the group they were allocated to. Other parts of anaesthetic management were standardised.

Patients were questioned in the post-operative period by an anaesthesiologist who was blinded with regard to the gargle the patient had received.

We observed that the age, gender distribution & duration of procedure were comparable between the two groups. Incidence of postoperative sore throat was significantly lower in the group that received ketamine, with a p value of <0.001 at 0, 4, 8, 12, 24 hours post extubation. This shows that pre-operative ketamine gargle significantly reduces the incidence as well as severity of POST(Postoperative sore throat) in patients undergoing endotracheal intubation during general anaesthesia.

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ANNEXURE – I – ETHICAL CLEARANCE LETTER



K.L.E.SOCIETY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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Date: 03/12/2013

To,


PG student in M.D. Anaesthesiology,
J.N.Medical College,
BELGAUM.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled
“ Efficacy of ketamine gargle in prevention of postoperative sore throat in patients
undergoing general anesthesia with endotracheal intubation, A 1 year double blinded
placebo controlled randomized trial ” is ethical and justifiable. The proposed research project
has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.


(Dr. Hema Dhumale)
Member Secretary

JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.


(Dr. Ganga Pilli)
Chairman,

JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.

ANNEXURE – II - CONSENT FORM

Mr/Mrs/Miss. _____ we are requesting you to enrol yourself in study titled **“EFFICACY OF KETAMINE GARGLE IN PREVENTION OF POSTOPERATIVE SORE THROAT IN PATIENTS UNDERGOING GENERAL ANESTHESIA WITH ENDOTRACHEAL INTUBATION, A 1 YEAR DOUBLE BLINDED PLACEBO CONTROLLED RANDOMIZED TRIAL**, conducted by Dr. _____ Post Graduate in M.D. Anaesthesiology under the guidance of Dr. _____ M.D,DNB Professor, Department of Anaesthesiology, J.N. Medical College, Belagavi under KLE university, Belagavi.

Respected Sir/Madam, We request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.Medical College. If you decide to participate you are free to withdraw at any time.

Purpose of the study:

The purpose of research is to know whether ketamine gargle is useful for prevention of sore throat in adult patients undergoing general anaesthesia.

Procedure Involved:

If you agree to enroll yourself in my study, I will ask your present past and family history. Then you will be clinically examined in detail and routine investigations like Hb, TC, DC, Platelet Count, RBS, Blood Urea, Serum Creatinine, Blood Grouping, Chest X-ray, ECG, will be done accordingly. You will be allotted into one of the two groups randomly using a computer generated software. One group will receive ketamine gargle and the other group will receive a placebo- which has no effect POST. This will be a double blinded procedure, where neither you nor I will know as to which group you have been allotted to.

Risks:

There is almost no risk involved with use of ketamine gargle.

Benefits:

It is an effective and safe in prevention / reduction of POST in patients undergoing general anaesthesia

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E. hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury related to the study, treatment will be made available through KLES' Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr. _____, at Department of Anaesthesiology, KLES Hospital& MRC or by Ph. No: _____.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of Anaesthesiology, KLES Hospital and MRC, Belagavi, phone number: _____.
Or Dr. _____ M.D.,DNB Professor, Dept. Of Anaesthesiology, KLES Hospital and MRC, Belagavi Ph.:_____.

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Professor, Department of Pathology and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number- 9448863866, or extension 4052 at J.N. Medical College, Belagavi.

I, Mr/Ms/Mrs. _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject : _____

Date :

Witness Name : _____

Signature:_____

Date :

Investigators Name: _____

Signature:_____

Date :

Place : _____

ANNEXURE - III – PROFORMA

“EFFICACY OF KETAMINE GARGLE IN PREVENTION OF POSTOPERATIVE SORE THROAT IN PATIENTS UNDERGOING GENERAL ANESTHESIA WITH ENDOTRACHEAL INTUBATION, A 1 YEAR DOUBLE BLINDED PLACEBO CONTROLLED RANDOMIZED TRIAL”.

Name & Address of the patient:

Age of the Patient: _____ IP. No. _____

Weight of Patient: _____ Sex. _____

Anaesthesiologist: _____ Surgeon: _____

PREANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

- History of Diabetes Mellitus/Hypertension/Asthma/Tuberculosis
- Drug Therapy:
- Previous Anaesthetic procedure/Previous surgeries:
- History of renal disease, hepatic disease and neurological diseases.

Family History

General Physical Examination:

Weight: Temperature: Pallor: Height

Cyanosis: Pedal Oedema: Clubbing:

Pulse : B.P: RR:

Airway Assessment:

Mouth Opening: Teeth:

Jaw Movements: MP Grading:

SYSTEMIC EXAMINATION:

Cardiovascular System:

Respiratory System:

Per Abdomen:

Central Nervous system:

Spine assessment:

INVESTIGATIONS:

Hb%: Urine Routine:

Any Other:

ASA STATUS: Grade 1 / 2

Diagnosis:

Proposed Surgery:

Inclusion Criteria:

- 1. ASA physical status I and II.
- 2. Age between 18 to 60 years.
- 3. Airway assessment by Mallampati grade I and II.
- 4. Patients undergoing elective surgeries under general anaesthesia.

Exclusion Criteria:

- Patients not willing to give consent
- Patients requiring more than one attempt for endotracheal intubation.
- Patients with upper respiratory tract infection
- Patients with preoperative sore throat

Methodology:

- After obtaining the approval of the Ethical committee and written informed consent, a total of 106 patients undergoing elective surgeries of a maximum duration of 3 hours under general anaesthesia were included in the study. Patients randomly divided into two groups by using computer generated table.
- Group A received preservative free ketamine 1 ml (50mg) in 29ml Normal saline(NS)
- Group B received 30 ml of NS

Patients were asked to gargle for 30 seconds 5 minutes prior to induction. Standard non-invasive monitoring will be done throughout the anaesthesia. Following preoxygenation, patient were premedicated with Inj.glycopyrrolate 0.005mg/kg iv, Inj.midazolam 0.05mg/kg iv and Inj.fentanyl 2mcg/kg iv.

Induction of anaesthesia will be done with 5mg/kg of Inj.thiopentone sodium iv sufficient to obtund the eye-lash reflex, followed by Inj.vecuronium 0.1 mg/kg iv with

an appropriate sized endotracheal tube. Tracheal intubation will be performed by an experienced anaesthesiologist having experience of >3 years. The endotracheal tubes will be lubricated with 2% lignocaine jelly at room temperature. Immediately after intubation, cuff of the endotracheal tubes will be filled with a volume of room air required to prevent a palpable air leak.

Anaesthesia will be maintained with isoflurane, fentanyl , vecuronium and supplemented with oxygen 33% in nitrous oxide. Intracuff pressure will be maintained throughout the procedure between 18-22 cm H₂O using handheld pressure gauge.

Residual neuromuscular relaxation with vecuronium will be antagonized with Inj. Neostigmine iv (0.05mg/kg body weight) and Inj. Glycopyrrolate iv (0.01mg/kg body weight) on completion of surgery. Oropharyngeal suction before extubation will be done under direct vision to avoid trauma to the tissues, confirming that secretion clearance will be complete.

The patients will be interviewed regarding post operative complaints. If they do not complain about sore throat then a leading direct question will be asked regarding the same at 0, 4, 8, 12 and 24 hours after the procedure.

POST will be graded on a four point scale (0-3):

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).

Other side-effects, if any, were also noted.

To compare patient characteristics, including age and duration of anaesthesia and surgery student's t-test will be used. To compare gender distribution between the

two groups Chi square test will be used. To analyse the association of sore throat in two groups Chi square test will be used. $P < 0.05$ will be considered statistically significant.

Observations:

Readings will be recorded in the following manner:

DRUG Administered: _____.

Group: _____.

Variable	Preoperative	0 hr	4 hr	8hr	12hr	24hr
Sorethroat						
Hoarseness						

Side Effects –

Signature of staff in charge:

ANNEXURE – IV - PHOTOGRAPHS



**Photograph 1: Endotracheal tubes (8.5mm, 7.5mm ID)
High volume low pressure cuff**



Photograph 2: 50 mg Ketamine diluted with 29 ml normal saline