

EFFECT OF INTRAVENOUS LORNOXICAM ON THE  
HAEMODYNAMIC RESPONSE FOLLOWING  
LARYNGOSCOPY AND INTUBATION



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**M.D.{ANAESTHESIOLOGY}**

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**ENDORSEMENT BY THE HOD AND DEAN OF THE INSTITUTE**

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STUDIED BY DR.NIMISH DANIAL IN THE DEPARTMENT OF  
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THIS IS A CONSOLIDATED REPORT ON THE STUDY “ EFFECT OF INTRAVENOUS LORNOXICAM ON HAEMODYNAMIC RESPONSE FOLLOWING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION” BASED ON CASES STUDIED AND FOLLOWED UP BY ME AT THE DEPARTMENT OF ANAESTHESIOLOGY, THANJAVUR MEDICAL COLLEGE.

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## LIST OF ABBREVIATIONS USED

SBP	Systolic blood pressure
DBP	Diastolic blood pressure
HR	Heart rate
MAP	Mean arterial pressure
TMJ	Temperomandibular joint
ID	Internal diameter
PEEP	Positive end expiratory pressure
CPAP	Continuous positive airway pressure
NMBD	Neuromuscular blocking drug
TT	Tracheal tube
FFL	Flexible fibreoptic laryngoscope
SAD	Supraglottic airway device
NTG	Nitroglycerine
ATP	Adenosine triphosphate
SAYGO	Spray as you go
ASA	American society of Anaesthesiologists
NSAID	Non steroidal anti inflammatory drug



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**1**

**EFFECT OF INTRAVENOUS LORNOXICAM ON THE HAEMODYNAMIC RESPONSE FOLLOWING SCOPY AND INTUBATION**

**BY NIMISH DANIAL**

**ATION SUBMITTED TO**

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A STUDY OF THE EFFECT OF INTRAVENOUS LORNOXICAM ON THE  
HAEMODYNAMIC  
RESPONSE FOLLOWING LARYNGOSCOPY AND  
INTUBATION.

The present study was designed as a single-blind randomized controlled trial to investigate the effect of lornoxicam on the changes in blood pressure and heart rate (HR) observed during laryngoscopy and tracheal intubation in 50 ASA I & II patients. They were divided into two groups of 25 each, one being the study group receiving 16 mg iv lornoxicam and the other the control group receiving iv placebo. Heart rate and blood pressure were recorded at various intervals during laryngoscopy and endotracheal intubation. It was observed that there was a statistically significant attenuation in heart rate and blood pressure response to laryngoscopy and intubation for the lornoxicam group. Hence we can conclude that iv lornoxicam 16 mg 30 minutes before surgery is a simple and practical method for the attenuation of the stress response to laryngoscopy and endotracheal intubation.

## INTRODUCTION

Laryngoscopy and intubation are associated with a transient cardiovascular stress response characterized by hypertension, tachycardia, arrhythmias and increased circulating catecholamines. This was known, as early as 1951. This is of little consequence in most of the patients, but increases mortality and morbidity in patients with coronary arterial disease, systemic hypertension, pre eclampsia, increased intra ocular pressure and cerebrovascular pathologies such as aneurysms, tumors or elevated intracranial pressure.

Various techniques have been proposed to attenuate or prevent the stress responses following laryngoscopy and tracheal intubation, such as omitting Anticholinergic premedication, increasing the depth of anaesthesia, pretreatment with vasodilators such as NTG, opioids, beta antagonists and calcium channel blockers . The recent studies aiming at attenuating or controlling the haemodynamic stress response to laryngoscopy and intubation focused on the effect of lornoxicam with different doses.

## **AIM OF STUDY**

- To determine the hemodynamic effects of IV Lornoxicam during laryngoscopy and endotracheal intubation.
- To determine whether IV lornoxicam is effective in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation.

## **REVIEW OF LITERATURE**

Brace and Reid first described hemodynamic response to laryngoscopy and intubation as early as 1940. King et al described the stress response to laryngoscopy and tracheal intubation in the year 1951. They proposed that the cardiac dysrhythmias, hypertension and tachycardia related to laryngoscopy and endotracheal intubation were the result of either increased sympathetic activity or decreased vagal tone. They noted that laryngoscopy alone caused an increased blood pressure. Intubation augmented this effect and was capable of inducing arrhythmias. Wycoff compared laryngoscopy and endotracheal intubation under general anaesthesia with the same under cricothyroid block. The block produced smaller changes in blood pressure and heart rate. Dingle observed a rise in systolic BP of more than 100mm of Hg following endotracheal intubation. Timori and Widdicombe observed that mechanical stimulation of four areas of the upper respiratory tract, the epipharynx, the laryngopharynx, tracheobronchial tree and the nose induced reflex cardiovascular response.



Puri GD and Batra YK in 1988 conducted a study on effect of sublingual nifedipine in reducing the haemodynamic response due to laryngoscopy and tracheal intubation. They conducted the study on 40 patients who were divided into two groups to receive either 10mg nifedipine sublingually or 10 mg placebo capsules ten minutes before induction. They found that sublingual nifedipine is effective in reducing the stress response due to laryngoscopy and tracheal intubation. The placebo group had a significant increase in BP and HR. However HR increased significantly in both group following laryngoscopy and tracheal intubation.

Nishikawa T, Namiki A in 1989 studied the effect of iv verapamil in reducing the stress response following intubation and laryngoscopy. They gave .1mg/kg verapamil to the study group just after induction. They made a continuous monitoring of the MAP and HR. They concluded from their study that iv verapamil is effective in reducing the pressor response following laryngoscopy and intubation. This reduction in pressor response was more

evident in the hypertensive group. The HR was comparable in both groups

O'Sullivan G et. al in 1980 conducted a study to demonstrate the effect of droperidol 150mcg/kg in reducing the haemodynamic response to laryngoscopy and intubation. In their study they gave iv droperidol 150mcg/kg before anaesthesia. They found that MAP was significantly lower in the droperidol group compared to the control group

Mikawa et .al in 1990 conducted a study to evaluate the effect of iv diltiazem .2 to .3mg/kg in reducing the stress response following laryngoscopy and tracheal intubation. They conducted the study in a group of patients of 20. They gave iv diltiazem to the test group sixty seconds before laryngoscopy. The control group received saline instead. The study showed that MAP and rate pressure product was significantly increased in saline group and iv diltiazem is a simple and effective drug in attenuating the cardiovascular response associated with intubation.

Mikawa et.al in 1991 studied the efficacy of ATP .05-.1mg/kg in reducing the stress response associated with tracheal intubation and

laryngoscopy. They choose 20 patients for the study. A test group consisting of 10 patients received .05-.1mg/kg of ATP as iv bolus simultaneously with laryngoscopy. The control group were given iv saline. The study showed that the MAP and rate pressure product were increased significantly in the control group of patients who received iv saline. There was a significant reduction in the MAP and rate pressure product of the test group. The study showed that the use of iv ATP is a simple and practical method to blunt the effect of stress response following laryngoscopy and tracheal intubation.

Mikawa et.al in 1991 conducted another study to demonstrate the efficacy and safety of iv NTG in reducing the stress response due to laryngoscopy and endotracheal intubation. The study was conducted on a group of 30 patients who belongs to ASA I category. They were divided into 3 groups of ten patients. First group received normal saline iv ,the second group were given iv NTG 1.5mcg/kg and the third group was injected with iv NTG 2.5mcg/kg. NTG was given as a rapid iv bolus simultaneously with the starting of laryngoscopy. The study found that there was a significant rise in MAP and rate pressure product in the saline group associated with laryngoscopy and intubation whereas both MAP and rate pressure product are significantly lower in the NTG group. The

study concluded that a rapid iv dose of NTG is effective in reducing the haemodynamic response due to laryngoscopy and endotracheal intubation.

Marashi SM et.al in 2009 conducted a comparative study to demonstrate the effect of clonidine .2mg, gabapentin 900mg and placebo on hyperdynamic response associated with laryngoscopy and tracheal intubation. The study was done on 75 ASA I and ASA II patients who were divided into 3 groups to receive either .2mg clonidine,900mg gabapentin or placebo 2hr before surgery. The study concluded that both gabapentin and clonidine are effective in blunting the haemodynamic response following laryngoscopy and endotracheal intubation. In the study placebo group showed a rise in SBP,DBP,MAP and HR following laryngoscopy and subsequent intubation.

Achola KJ et.al in 1988 studied the catecholamine and circulatory response to laryngoscopy and endotracheal intubation and the role of beta antagonists in blunting these effects. They conducted the study in 20 patients who were given either practolol 10mg or saline just before induction. .SBP,HR and plasma adrenaline concentrations were monitored before and after laryngoscopy and intubation. The Study concluded that SBP, HR and plasma adrenaline all showed a rising trend following

laryngoscopy and intubation. The study also showed that practolol is not effective in attenuating the stress response following tracheal intubation.

Luizos AA et.al in 2007 conducted a study on the effect of esmolol in controlling the haemodynamic response associated with laryngoscopy and intubation in cigarette smokers. The study was done on 165 patients who are known smokers. They were divided into 2 groups to receive either esmolol 2mg/kg 2 minutes before laryngoscopy or placebo. The study showed a significant rise in SBP and HR IN the control group were as the esmolol group demonstrated a stable haemodynamic status following laryngoscopy and tracheal intubation. The study concluded that esmolol 2mg/kg is effective in controlling the cardiovascular response following tracheal intubation in smokers.

Kautto UM in 1982 studied the efficacy of fentanyl in different doses to blunt the cardiovascular response associated with tracheal intubation.45 patients were divided into 3 groups to receive fentanyl 2mcg/kg ,fentanyl 6mcg/kg or placebo before induction. The study noticed that there was a significant rise in SBP and HR in the placebo group whereas the group who received fentanyl 2mcg/kg showed a reduction in the stress response following laryngoscopy and intubation .The third

group who received fentanyl at the dose of 6mcg/kg showed complete abolition of stress response associated with tracheal intubation.

Shirbman AJ et.al in 1987 conducted a study to demonstrate the cardiovascular response due to laryngoscopy with or without tracheal intubation. 24 patients were selected for the study who were divided into 2 groups. Laryngoscopy was done in both groups for 10 seconds while one group of patients were intubated after laryngoscopy. SBP, HR and plasma catecholamines were recorded before and after the procedure. The study concluded that laryngoscopy is associated with an increase in SBP and plasma catecholamine level while tracheal intubation is associated with an increase in SBP, HR and plasma catecholamine level.

Riad and Moussa in 2008 conducted a study on the effects of preoperative iv lornoxicam on elderly patients. In this study 50 patients aged between 65 and 75 were selected. They were divided into two groups to receive iv lornoxicam 8mg or placebo. They were given either lornoxicam or placebo 30 min before surgery. SBP, DBP, MAP and HR were recorded before tracheal intubation and one, three, five and ten minutes after intubation. They concluded from their study that preoperative administration of iv lornoxicam is

useful in reducing the stress response following laryngoscopy and tracheal intubation in elderly patients.

M.Dabiss et.al in 2010 conducted a study to demonstrate the effect of 16mg iv lornoxicam on cardiovascular stress response and level of serum catecholamine following laryngoscopy and intubation.50 patients were chosen for the study..They were randomly divided into two groups to receive intravenous injection (i.v) of either Lornoxicam 16 mg diluted in 4ml saline or 4ml normal saline half an hour before induction of anaesthesia Their results showed a significant increase in the haemodynamic parameters and serum catecholamine in the control group. They concluded that 16mg iv lornoxicam is effective in blunting the cardiovascular stress response following laryngoscopy and intubation.

## ANATOMY OF THE AIRWAY

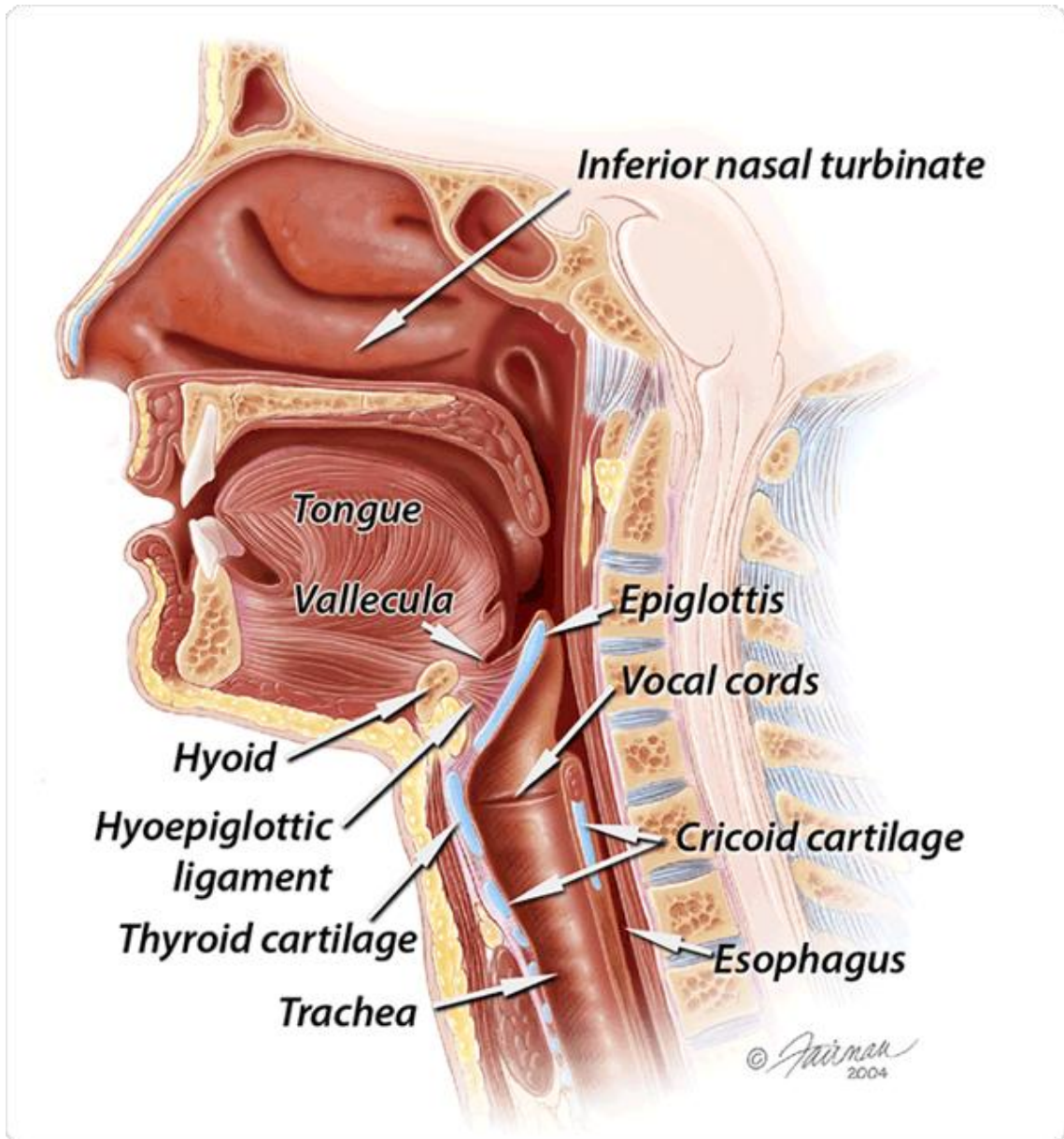


Fig.1 Anatomy of airway

The nose warms, filters, and humidifies incoming air and is the organ of smell. It consists of the external nose and the internal nasal cavity. The nasal cavities are divided by the nasal septum, which is frequently



deviated with the consequence that the nasal cavities are narrowed or obstructed. The roof of the nasal cavity is the cribriform plate, a thin bone that is easily fractured, thereby resulting in communication between the nasal and intracranial cavities. The bony lateral wall of the nasal cavity is the origin of the three bony turbinates that project into the nasal cavity. They are easily damaged by force during the passage of nasotracheal tubes. Openings in the lateral wall communicate with the paranasal sinuses. Prolonged nasotracheal intubation impairs drainage through these openings, causing sinusitis. The lining of the nasal cavity is very vascular, and application of nasal vasoconstrictors to shrink the mucosa and dilate the airway reduces the risk of haemorrhage during the insertion of airway devices or tracheal tubes.

The roof of the mouth is bounded by the alveolar arch and teeth and consists of the hard palate anteriorly and the soft palate posteriorly. The tongue makes up most of the floor of the mouth, which is bounded by the mandible and teeth. Nonencapsulated lymphoid tissue on the posterior surface of the tongue (lingual tonsil) is part of the ring of Waldeyer. This tissue is important in that hypertrophy can cause serious difficulty in airway management. The ability to achieve good mouth opening is important for many airway procedures. Initial mouth opening is achieved

by rotation within the temporomandibular joint (TMJ) and subsequent opening by sliding (also known as protrusion, translocation, or subluxation) of the condyles of the mandible within the TMJ. The jaw-thrust maneuver uses the sliding component of the TMJ to move the mandible and attached structures anteriorly. The scissors maneuver achieves maximum mouth opening by the application of internal pressure on the teeth to achieve both TMJ movements. It can facilitate the insertion of oropharyngeal airways, supraglottic airway devices (SADs), and laryngoscopes. All movements of the TMJ should be firm but gentle to minimize the risk of joint damage.

The pharynx is a fibromuscular tube that extends from the base of the skull to the lower border of the cricoid cartilage. It joins the nasal and oral cavities above with the larynx and esophagus below. Both the pharynx and esophagus can be perforated by blind attempts at tracheal intubation. The nasopharynx is the part of the pharynx that lies posterior to the nose. Nasotracheal tubes can impinge on the posterior wall of the nasopharynx, and application of increasing force when resistance is met can cause submucosal passage of the tube.

The larynx is situated at the upper end of the respiratory tract, where it extends from the epiglottis to the lower end of the cricoid cartilage. It evolved as a valve to protect the lower respiratory tract from

alimentary contents and later developed into an organ of speech. The larynx bulges posteriorly into the laryngopharynx, with the piriform fossa lying on each side. The larynx consists of a framework of articulating cartilage connected by fascia, muscles, and ligaments. It is suspended from the hyoid bone by the thyrohyoid membrane. The principal cartilages are the thyroid, cricoid, and posterior (arytenoid, corniculate, and cuneiform) cartilage and the epiglottis. The cricoid cartilage is a complete ring that articulates with the thyroid and arytenoid cartilage. The arytenoid cartilage sits on the posterolateral border of the cricoid, from where it can be dislocated during airway management. The laryngeal inlet is bounded by the epiglottis, aryepiglottic folds, posterior cartilage, and interarytenoid notch. The vocal cords run between the vocal processes of the arytenoid cartilage and the posterior surface of the thyroid cartilage. The lower end of the leaf-shaped epiglottis is attached to the middle of the posterior surface of the thyroid cartilage. The anterior surface is connected to the hyoid bone by the hyoepiglottic ligament and to the tongue by the median glossoepiglottic fold. The valleculae (often called vallecula) are depressions between the median and lateral glossoepiglottic folds that connect the lateral edges of the epiglottis to the base of the tongue. The Macintosh technique of laryngoscopy involves insertion of the tip of the

laryngoscope into the vallecula, where it tensions the hyoepiglottic ligament to achieve indirect elevation of the epiglottis.

During swallowing the larynx is protected by several mechanisms. The larynx is tucked up behind the tongue, and the epiglottis diverts food away from the laryngeal inlet. The laryngeal muscles can be grouped according to their actions on the vocal cords: abductors, adductors, and regulators of tension. Motor innervation to these muscles and the sensory innervation of the larynx are supplied by two branches of the vagus nerve: the superior and recurrent laryngeal nerves. The superior laryngeal nerve can be anesthetized at the point where it passes through the thyrohyoid membrane. The recurrent laryngeal nerve can be damaged during surgery on the thyroid gland or by pressure from a cuff that lies just below the vocal cords.

The cricothyroid membrane joins the thyroid with the adjacent cricoid cartilage. It is close to the skin, relatively avascular, and the widest gap between the cartilage of the larynx and trachea, so it provides the best access for percutaneous airway rescue techniques. It is normally easy to palpate, but identification may not be possible in obese patients. In patients with fixed neck flexion, the cricothyroid membrane may lie behind the sternum.

The trachea extends from the lower edge of the cricoid cartilage to the carina. It consists of U-shaped cartilage joined by fibroelastic tissue and is closed posteriorly by the longitudinal trachealis muscle. The tracheal rings and trachealis muscle are responsible for the characteristic endoscopic appearance of the trachea.

## DIRECT LARYNGOSCOPY

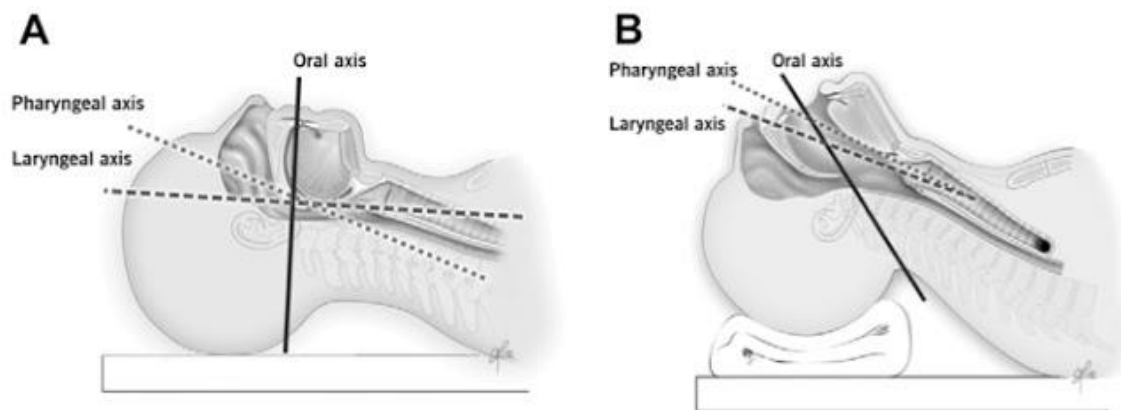


Fig 2.Alignment of axes

Direct laryngoscopy is used to facilitate tracheal intubation under vision. Successful direct laryngoscopy depends on achieving a line of sight from the maxillary teeth to the larynx. The tongue and epiglottis are the anatomic structures that intrude into the line of sight. Management of the tongue and epiglottis is therefore central to successful direct laryngoscopy. Before the laryngoscope is inserted, the patient is normally placed in the

“sniff” position . The direct laryngoscope is then used to displace the tongue and epiglottis out of the line of sight. The tongue is displaced horizontally (normally to the left) from the line of sight, the hyoid bone and attached tissues are moved anteriorly, and the epiglottis is elevated directly or indirectly to reveal the larynx. The force applied to the laryngoscope handle should lift the hyoid bone and attached tissues parallel to the line of sight. Adequate lifting force, which may cause considerable tissue distortion, is a key factor in successful direct laryngoscopy. It is important to achieve the best possible view of the larynx without causing tissue trauma. It is not always possible to achieve line of sight with direct laryngoscopy.

The theoretical basis of the head and neck position used for direct laryngoscopy was attributed to the need to align the axes of the oral cavity, pharynx, and larynx on the basis of a radiology study. Magnetic resonance imaging in awake patients has been used to challenge this hypothesis, but the conclusions have been controversial. Understanding of management of the tongue and the epiglottis is more likely than the axis alignment hypothesis to improve direct laryngoscopy technique.

The “sniff” position is usually the best starting position for direct laryngoscopy. In the sniff position, the cervical spine below C5 is

relatively straight, there is increasing flexion from C4 to C2, and the head is fully extended (occipito-atlanto-axial complex). Neck flexion between C2 and C4 is achieved by elevation of the head. Statistical advantage of the sniff position over simple head extension was found in one study, except in the presence of obesity or limited head extension. However, the sniff position facilitated a view of the larynx in 4% of patients in whom this was not possible with simple head extension. The sniff position also improves pharyngeal airway patency in patients with obstructive sleep apnoea. Head extension facilitates insertion of the laryngoscope, reduces contact between the laryngoscope and the maxillary teeth, improves the view of the larynx, and facilitates full mouth opening. Head extension should be used unless there is a contraindication.

## NERVE SUPPLY OF THE AIRWAY

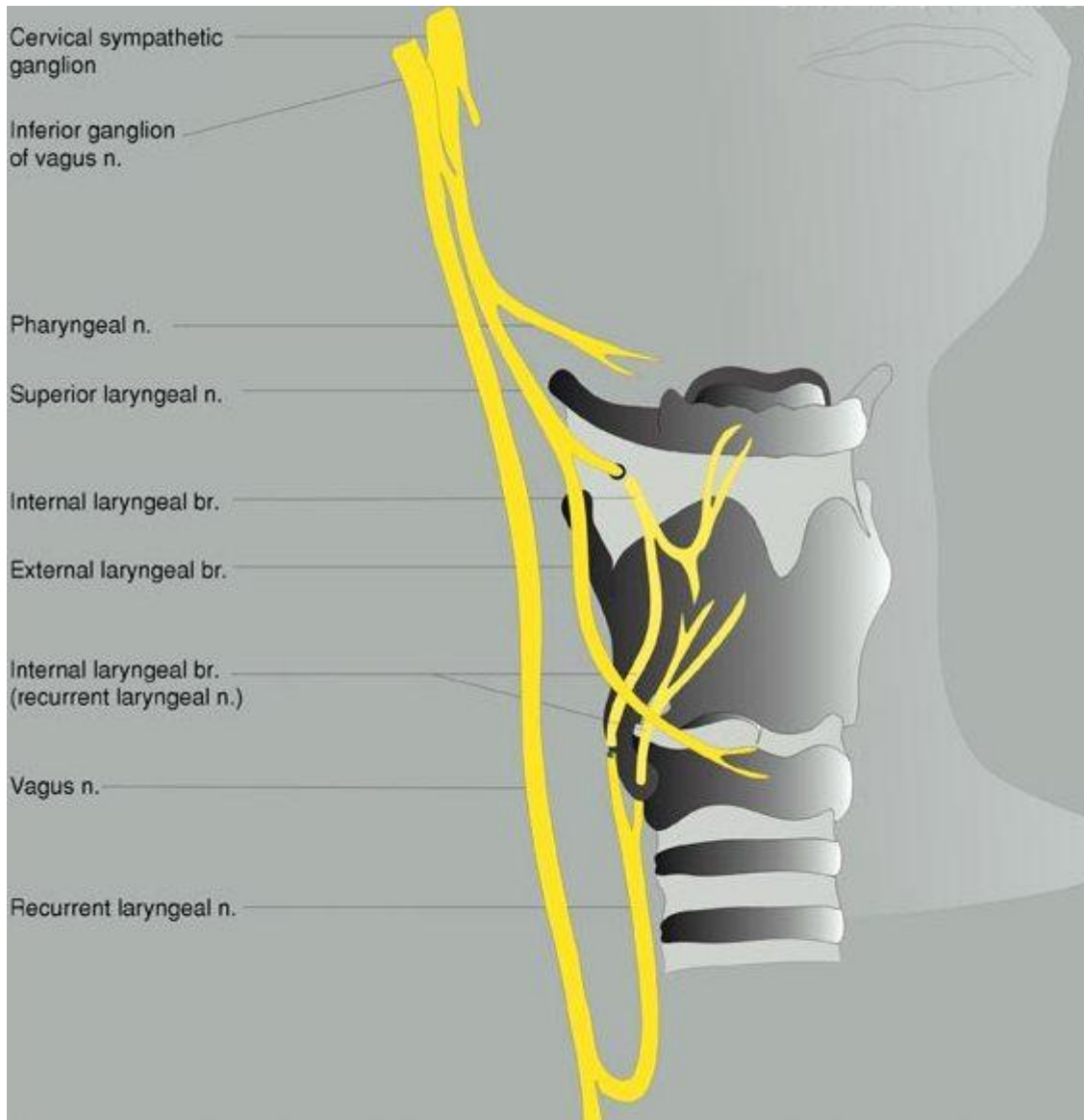
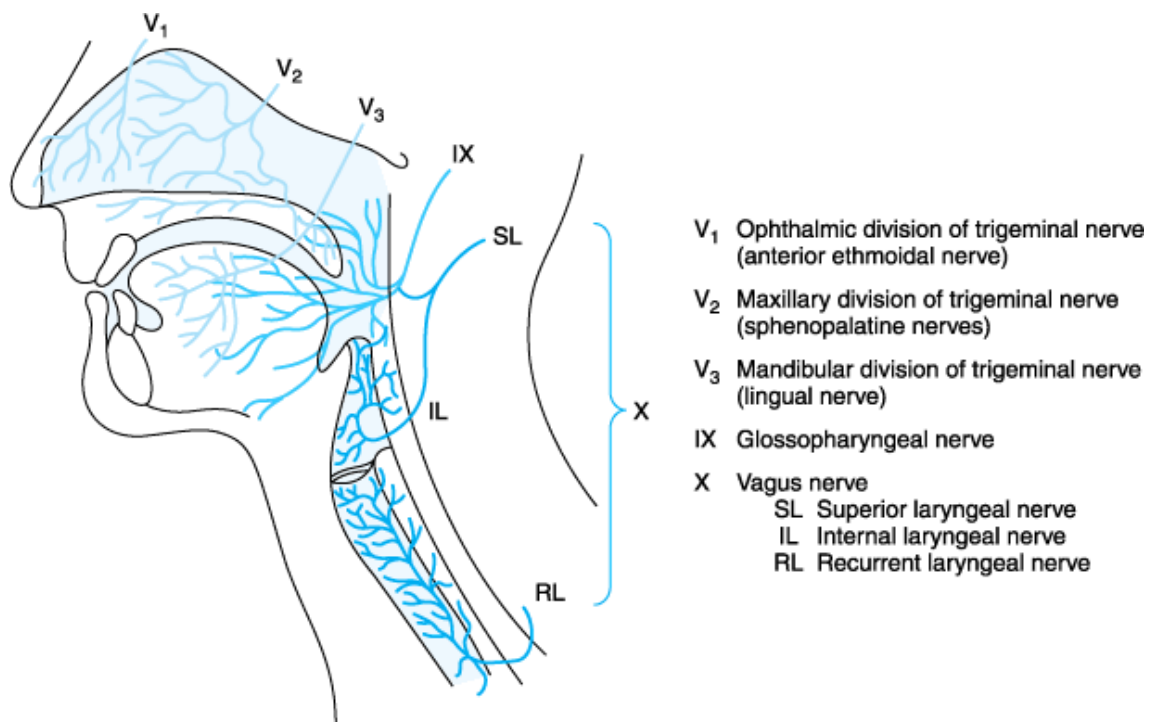


Fig 3.Nerve supply of larynx

The sensory supply to the upper airway is derived from the cranial nerves. The mucous membranes of the nose are innervated by the ophthalmic division ( $V_1$ ) of the trigeminal nerve anteriorly (anterior



ethmoidal nerve) and by the maxillary division ( $V_2$ ) posteriorly (sphenopalatine nerves). The palatine nerves provide sensory fibers from the trigeminal nerve ( $V$ ) to the superior and inferior surfaces of the hard and soft palate.



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Fig 4. Nerve supply of airway

The lingual nerve (a branch of the mandibular division [ $V_3$ ] of the trigeminal nerve) and the glossopharyngeal nerve (the ninth cranial nerve) provide general sensation to the anterior two-thirds and posterior third of the tongue, respectively. Branches of the facial nerve (VII) and glossopharyngeal nerve provide the sensation of taste to those areas,

respectively. The **glossopharyngeal nerve** also innervates the roof of the pharynx, the tonsils, and the under surface of the soft palate. The **vagus nerve** (the tenth cranial nerve) provides sensation to the airway below the epiglottis. The superior laryngeal branch of the vagus divides into an external (motor) nerve and an internal (sensory) laryngeal nerve that provide sensory supply to the larynx between the epiglottis and the vocal cords. Another branch of the vagus, the **recurrent laryngeal nerve**, innervates the larynx below the vocal cords and the trachea.

### **Macintosh Laryngoscope and Technique of Orotracheal Intubation**

The Macintosh curved laryngoscope is radically different from the pre-existing straight laryngoscopes. In particular, the long axis of the blade is curved, the cross section is a right-angled “Z” section, the web and flange are bulky, the tip is atraumatic, and the light bulb is shielded by the web. However, Macintosh's key innovation was his novel technique of indirect elevation of the epiglottis, achieved by tensioning the hyoepiglottic ligament after the tip of the laryngoscope was positioned in the vallecula. This technique is the key to success of the Macintosh laryngoscope—and its fundamental flaw. When it works well, the epiglottis is elevated completely and lies behind and along the posterior surface of the laryngoscope blade. However, it is not possible to position the Macintosh

laryngoscope correctly in some patients. Minor difficulty results in partial elevation of the epiglottis, erroneously described as a “floppy epiglottis,” and major difficulty leads to complete failure to elevate the epiglottis with the consequence that the vocal cords cannot be seen.

Tracheal intubation is normally achieved with a rapid sequence of maneuvers in which all components of a complex technique merge into one another. The best technique will develop if all components are optimized. The three component steps of direct laryngoscopy are insertion of the laryngoscope, adjustment of its position and lifting force, and use of other maneuvers to optimize the view of the glottis.

The “sniff” position is used. Full mouth opening facilitates insertion of the laryngoscope. It is inserted from the right side of mouth and to the right of the tongue while taking care to not trap the lips between the laryngoscope blade and the teeth. The laryngoscope is advanced and simultaneously moved into the midline to displace the tongue to the left. Progressive visualization of anatomic structures minimizes the risk of trauma. The epiglottis is the first key anatomic landmark. The tip of the laryngoscope is advanced into the vallecula, and the epiglottis is elevated indirectly by applying a force that tensions the hyoepiglottic ligament. Elevation of the epiglottis is optimized and a further lifting force is applied

to the laryngoscope to achieve the best view of the larynx . It is very important not to lever on the maxillary teeth because this may cause dental damage and reduce the view of the larynx. If visualization of the larynx cannot be achieved without pressure on the teeth, use of this laryngoscope should be abandoned and another technique of tracheal intubation used.

When a good view of the larynx is achieved, the vocal cords, aryepiglottic folds, posterior cartilage, and interarytenoid notch can be identified . The view should be optimized to facilitate passage of the tracheal tube. If the view of the larynx is poor, it is important to check that the basic technique has been performed optimally and other maneuvers used . External laryngeal manipulation (better described as “bimanual laryngoscopy,” which implies internal movement of the laryngoscope with external manipulation of the larynx), performed by the anaesthesiologist who guides an assistant , consistently improves the laryngeal view. It is a key manoeuvre.

TABLE 1

**Maneuvers Used to Optimize the View at Direct Laryngoscopy**

- ❖ Maximum head extension
- ❖ Tongue entirely to the left of the laryngoscope
- ❖ Optimal depth of insertion of the laryngoscope
- ❖ Strong lifting force applied in the correct direction to the laryngoscope
- ❖ External laryngeal manipulation—applied initially with the right hand of the anaesthesiologist

## Tracheal Tubes

Tracheal tubes are designed to provide a secure channel through the upper airway. The distal end lies in the mid to lower part of the trachea, whereas the proximal end lies outside the mouth or nose, where it is connected to an anaesthesia circuit or other device. Tracheal tubes used in adult patients have a cuff near the distal end that is inflated to provide a seal against the tracheal wall to protect the lungs from pulmonary aspiration and to ensure that the tidal volume delivered ventilates the lungs rather than escapes into the upper airway. Cuffs are normally inflated with air and have an inflation tube with a pilot balloon that indicates cuff inflation.

The size of the tracheal tube is normally described as the internal diameter (ID) in millimetres, but the relationship of the ID to the external diameter varies between different designs and manufacturers. Use of the largest possible tracheal tube was once considered good practice. Very small tracheal tubes may allow insufficient time for completion of exhalation and produce air trapping (“auto-PEEP”) with the risk of barotrauma and circulatory compromise. Others have found no evidence of obstruction to expiration with tube sizes as small as 6-mm ID, and the

increased workload created is usually of little clinical significance during anaesthesia. Use of small tracheal tubes reduces the incidence of sore throat and hoarseness. Small tracheal tubes are easier to insert than larger tubes and may cause less tissue pressure at the larynx. It is easier to pass small tracheal tubes over introducers or FFLs. Restriction of gas flow through a tracheal tube is markedly increased by the presence of an FFL or suction catheter within the lumen of the tracheal tube. Tracheal tube sizes of 8 mm (ID) for males and 7.5 mm (ID) for females are often used.

Specialized tracheal tubes produced for anaesthesia include preformed, adjustable shape, and reinforced. Specialized tubes are also used for ear, nose, and throat (ENT) surgery (laser and microlaryngeal surgery) and for thoracic anaesthesia and critical care. Tracheal tubes can become kinked and hence obstructed when they are angulated. Armored (reinforced) tubes have an embedded coil (usually stainless steel) that minimizes kinking of the tube when it is subjected to angulation. Armored tracheal tubes are the tubes of choice in many head and neck procedures and patient positions other than supine. However, an armored tube that has been compressed remains pinched, so it is particularly important to prevent biting on such a tube.

The material and bevel shape of the tip of the tracheal tube can affect the ease and probably the trauma of tube passage. The tip of the earliest Magill tracheal tubes had a soft, simple bevel. The Murphy eye, a hole in the wall of a firm tip opposite the bevel, was designed to provide a patent airway if the tracheal tube became occluded at the bevel. Air leakage through the Murphy eye may facilitate early diagnosis of tracheal tube displacement before complete accidental extubation has occurred.

Cuff inflation achieves a seal between the tracheal tube and the wall of the trachea. There should be no air leak at airway pressures required for positive-pressure ventilation, and the lungs should be protected from aspiration. The cuffs of early tracheal tubes produced a high pressure that could cause mucosal ischemia. High-volume, low-pressure cuffs were developed to conform to the D-shaped cross section of the trachea and provide a seal at a lower cuff pressure, thereby reducing the risk of tracheal damage.

Inflation of the cuff with a volume that just prevents an air leak (“just-seal volume”) is often recommended. However, this cuff pressure varies greatly. Prevention of excessive cuff pressure may reduce the incidence of tracheal damage, vocal cord dysfunction from recurrent laryngeal nerve palsy, and sore throat after surgery. Because palpation is



not a good guide to cuff pressure, use of a monitor to maintain cuff pressure in the range of 25 to 30 cm H<sub>2</sub>O is recommended.

Cuff pressure can change after initial inflation. Inhaled N<sub>2</sub>O diffuses into tracheal tube cuffs that have been inflated with air and increases the volume and pressure within the cuff enough to cause tracheal lesions and an increased incidence of sore throat. A leak in the cuff or valve or a reduction in trachealis muscle tone can lower cuff pressure and increase the risk for pulmonary aspiration. Early detection of both low and high pressure is important.

A properly inflated cuff protects against massive pulmonary aspiration, but silent aspiration (micro-aspiration) of pharyngeal contents occurs along channels between folds in the cuff and is a major contributor to ventilator-associated pneumonia in intensive care. New materials and cuff designs attempt to eliminate cuff channels and may help prevent micro-aspiration.

### **Tracheal Intubation**

Tracheal intubation (insertion of the tracheal tube) is an essential skill in anaesthetic practice. Indications for tracheal intubation are shown in table 2.

TABLE 2

### Indications for tracheal intubation

#### Surgical and Anaesthetic Indications

- ❖ Surgical requirement for neuromuscular blocking drugs, e.g., abdominal surgery
- ❖ Airway access shared with the surgeon, including ear, nose, and throat surgery
- ❖ Patient position in which access to the airway is restricted or precludes rapid tracheal intubation, e.g., lateral, prone
- ❖ Predicted difficult airway
- ❖ Risk of aspiration of gastric contents or blood, e.g., upper gastrointestinal obstruction or sepsis, facial trauma, bleeding into the respiratory tract from any cause
- ❖ Surgery that impairs gas exchange
- ❖ Prolonged surgery
- ❖ Other airway techniques ineffective

### **Critical Illness**

- ❖ Inability to protect the airway, e.g., coma from any cause
- ❖ Impaired respiratory function (hypoxemia or hypercapnia)  
unresponsive to noninvasive management
- ❖ Prevention of hypercapnia, e.g., raised intracranial pressure

### **COMPLICATIONS OF LARYNGOSCOPY & INTUBATION**

The complications of laryngoscopy and intubation include hypoxia, hypercarbia, dental and airway trauma, tube malpositioning, physiological responses to airway instrumentation, or tube malfunction. These complications can occur during laryngoscopy and intubation, while the tube is in place, or following extubation.

**TABLE 3: COMPLICATIONS OF INTUBATION**

<u>During laryngoscopy and intubation</u>
❖ Intubation of the esophagus
❖ Bronchial intubation
❖ Laryngeal cuff position
❖ Trauma of airway
❖ Damage to the teeth
❖ Laceration of lip, tongue, or mucosa
❖ Sore throat
❖ Dislocation of the mandible
❖ Haemodynamic response
❖ Retropharyngeal dissection
❖ Hypoxia and hypercarbia

❖ Hypertension, tachycardia
❖ ICT
❖ Intraocular hypertension
❖ Laryngospasm
❖ Malfunctioning of the tube
❖ Perforation of cuff
<b><u>While the tube is in place</u></b>
❖ Malpositioning of tube
❖ Unintentional extubation
❖ Bronchial intubation
❖ Laryngeal cuff position
❖ Trauma of the airway
❖ Inflammation and ulceration of mucosa
❖ Nasal Excoriation

❖ Malfunctioning of tube
❖ Fire/explosion
❖ Obstruction of tube
<b><u>Following extubation</u></b>
❖ Airway trauma
❖ Edema and stenosis (glottic, subglottic, or tracheal)
❖ Hoarseness of voice (vocal cord granuloma or paralysis)
❖ Laryngeal malfunction and aspiration
❖ Laryngospasm
❖ Negative-pressure pulmonary oedema

### **Airway Trauma**

Instrumentation with a metal laryngoscope blade and insertion of a stiff TT often traumatize delicate airway tissues. Although tooth damage is the most common cause of malpractice claims against anaesthesiologists, laryngoscopy and intubation can lead to a range of complications from sore throat to tracheal stenosis. Most of these are due to prolonged external

pressure on sensitive airway structures. When these pressures exceed the capillary–arteriolar blood pressure (approximately 30 mm Hg), tissue ischemia can lead to a sequence of inflammation, ulceration, granulation, and stenosis. Inflation of a TT cuff to the minimum pressure that creates a seal during routine positive-pressure ventilation (usually at least 20 mm Hg) reduces tracheal blood flow by 75% at the cuff site. Further cuff inflation or induced hypotension can totally eliminate mucosal blood flow.

Postintubation croup caused by glottic, laryngeal, or tracheal edema is particularly serious in children. The efficacy of corticosteroids (eg, dexamethasone—0.2 mg/kg, up to a maximum of 12 mg) in preventing postextubation airway edema remains controversial; however, they have been demonstrated to be efficacious in children with croup from other causes. Vocal cord paralysis from cuff compression or other trauma to the recurrent laryngeal nerve results in hoarseness and increases the risk of aspiration. Some of these complications may be decreased by using a TT shaped to conform to the anatomy of the airway (eg, Lindholm Anatomical Tracheal Tube). The incidence of postoperative hoarseness appears to increase with obesity, difficult intubations, and anaesthetics of long duration. Applying a water-soluble lubricant or an anaesthetic-containing gel to the tip or cuff of the TT does not decrease the incidence of postoperative sore throat or hoarseness. Smaller tubes (size 6.5 in women

and size 7.0 in men) are associated with fewer complaints of postoperative sore throat. Repeated attempts at laryngoscopy during a difficult intubation may lead to periglottic edema and the inability to ventilate with a face mask, thus turning a bad situation into a life-threatening one.

## PHYSIOLOGY AND PATHPHYSIOLOGY OF THE UPPER AIRWAY

### Upper Airway Obstruction

In an awake patient, airway patency is maintained by muscle tone in the head and neck, particularly the pharynx and tongue. As consciousness is lost and muscle tone is reduced, tissues fall backward under the influence of gravity in a supine patient and can obstruct the upper airway. The order of importance of these obstructing tissues is the soft palate (velopharynx), epiglottis, and tongue. Head extension (as a consequence of tensioning the strap muscles) and jaw thrust move the hyoid bone and attached structures anteriorly and relieve airway obstruction to a variable extent. Jaw thrust is also effective in reducing obstruction at the velopharynx in slim but not in obese patients. The lateral position can be used alternatively or in addition to the aforementioned techniques to allow the obstructing tissues to move downward so that obstruction is reduced.



There is now evidence of an additional dynamic component of upper airway obstruction when consciousness is reduced. In the conscious state the tone of the pharyngeal muscles is increased by neural discharge just before phrenic nerve discharge. Loss of pharyngeal tone and collapse of the narrow velopharynx play an important role in upper airway obstruction during spontaneous ventilation in an anesthetized patient. The airway in the nose and nasopharynx is held open by bone and cartilage and in the larynx and trachea by cartilage. Dynamic collapse of the intervening pharynx can occur when muscle tone is reduced. The structure of a collapsible segment between two rigid tubes corresponds to the basic elements of a Starling resistor in that flow can depend on the intraluminal pressure gradient or on transmural pressure in the collapsible area. Flow through the collapsible segment depends on how the intraluminal pressure upstream and downstream relate to the tissue pressure around the pharynx. Factors that narrow the pharynx, increase pressure around it, reduce pressure within it, or make its walls more compliant will increase upper airway obstruction. The therapeutic consequence of dynamic collapse is that nasal continuous positive airway pressure (CPAP) reduces dynamic upper airway obstruction. Nasopharyngeal airways might reduce this dynamic airway obstruction.

## Laryngospasm

Laryngospasm (reflex closure of the true vocal cords alone or with the false cords because of stimulation of the intrinsic laryngeal muscles) can result from the combination of reflex hyperactivity at an intermediate depth of anaesthesia and noxious distant surgical or local stimuli.

Laryngospasm is usually maintained well beyond the duration of the stimulus. It is responsible for a significant proportion of postoperative critical events. Morbidity and mortality may result from the immediate (hypoxemia and hypercapnia) and delayed (“negative-pressure pulmonary edema”) consequences of laryngospasm, and thus every effort should be made to rapidly relieve the airway obstruction caused by laryngospasm..

Negative-pressure pulmonary edema is a consequence of forceful inspiratory effort in the presence of a closed glottis or other cause of upper airway obstruction. The subatmospheric alveolar pressure generated promotes transudation of fluid from pulmonary capillaries into the interstitial space and alveoli. Small vessel damage may be responsible for frank hemorrhage into alveoli. Management consists of relief of the obstruction, oxygen therapy, and standard management of pulmonary edema. Most cases resolve rapidly, but reintubation and positive-pressure ventilation are sometimes required.

## Oxygenation and Preoxygenation

Hypoxemia can occur in the time between induction of anaesthesia and attainment of airway security and is particularly likely if airway management proves difficult. It makes sense to maximize oxygen stores before induction to prolong the period before the onset of hypoxemia in the event of serious difficulty with airway management. The principal oxygen stores are in the lungs. These stores can be increased by using a maneuver called “preoxygenation” (also known as denitrogenation), which is achieved by having the patient breath 100% oxygen from a close-fitting facemask before induction of anaesthesia. Several techniques of preoxygenation have been described, and the most effective technique should be used. Deep breathing with a high fresh gas flow for 1.5 minutes and tidal breathing for 3 minutes are equally effective. It is particularly important to avoid leaks in the circuit, which are indicated by a flaccid reservoir bag and absence of a normal capnograph waveform. Wherever possible, the end-tidal oxygen concentration should be used as a guide to the adequacy of preoxygenation, with a value of 90% being well accepted. Preoxygenation in the semi-sitting position prolongs the time to development of hypoxemia by increasing functional residual capacity in relation to the supine position, particularly in an obese patient. Use of

positive end-expiratory pressure (PEEP) during induction may further improve oxygenation.

## **PHARMACOLOGY OF AIRWAY MANAGEMENT**

The choice of pharmacologic technique is part of the essential planning of airway management and will be influenced by both airway and surgical requirements, particularly for surgical access and neuromuscular blockade. Satisfactory conditions for tracheal intubation are particularly demanding and may be facilitated by several pharmacologic techniques, each of which has advantages and disadvantages. Direct laryngoscopy is facilitated by a reduction in tone of the head and neck muscles. A high success rate and low risk for laryngeal trauma are facilitated when the vocal cords are open and nonreactive, at the cost of reduced protection against pulmonary aspiration.

## Inhaled Induction of Anaesthesia

Induction plus maintenance of anaesthesia by the inhalation of gaseous and volatile anaesthetics was the original pharmacologic technique for anaesthesia. It remains an important technique in situations such as lack of venous access and anticipated airway difficulty in a patient who refuses awake techniques. A major advantage of inhaled induction of anaesthesia is that spontaneous ventilation is maintained while changes in the depth of anaesthesia and associated respiratory and cardiovascular effects occur gradually. Good facemask technical skills are essential to prevent airway obstruction and leaks around the mask.

Deep anaesthesia is necessary for direct laryngoscopy and tracheal intubation with inhaled anaesthetics alone. It can be complicated by hypotension, hypoventilation, and airway obstruction. A depth of anaesthesia that allows controlled ventilation has been recommended when sevoflurane is used. Prior administration of topical anaesthesia (e.g., 4% lidocaine, 3 to 5 ml) can facilitate tracheal intubation under lighter inhaled anaesthesia.

Sevoflurane has advantages over other volatile anaesthetics for inhaled induction of anaesthesia. It has a low blood-gas partition coefficient and causes minimal airway irritation, which facilitates rapid smooth

attainment of a depth of anaesthesia sufficient for airway procedures.

A rapid technique (“single breath”) in which the patient breathes 8% sevoflurane from a prefilled anaesthesia circuit has been advocated rarely but causes apnea more frequently than the traditional technique does.

Furthermore, seizure activity with sevoflurane is more likely with rapid induction of anaesthesia.

Inhaled induction of anaesthesia is very useful in a wide variety of difficult airway conditions. Its use has been advocated in patients with stridor but can result in sudden airway obstruction, which prevents rapid reduction of the depth of anaesthesia. Relief of obstruction may be difficult or impossible, even when CPAP is used with mask ventilation, so emergency cricothyrotomy may be required. Propofol infusion, with topical anaesthesia before endotracheal intubation, has been used successfully for the management of patients with a difficult airway. Caution is required because apnoea can occur when propofol is infused in patients with normal airways.

### Intravenous Anaesthesia with Neuromuscular Blocking Drugs

The combination of an intravenous anaesthetic with an NMDB is the pharmacologic technique most frequently used for tracheal intubation in routine practice . It provides good conditions rapidly in most patients

inasmuch as neuromuscular blockade facilitates laryngoscopy, opens the vocal cords, and prevents coughing. The high quality of intubating conditions produced by NMBDs reduces the risk for postintubation laryngeal damage. However, the apnea caused by this pharmacologic approach has disadvantages. If tracheal intubation of an apneic patient proves impossible, oxygenation requires effective ventilation with a facemask or SAD, neither of which is completely reliable. Pharmacologic techniques that produce apnea should not be used when difficulty with tracheal intubation or mask ventilation is predicted. As indicated previously, the use of sugammadex may alter the approaches to difficult intubation.

In routine practice, nondepolarizing NMBDs are often preferable to succinylcholine to prevent its side effects . Succinylcholine is chosen when rapid onset and offset are important. Use of rocuronium as an alternative to succinylcholine has been suggested to avoid the side effects unique to succinylcholine. Although the duration of paralysis produced by rocuronium is very much longer, the use of sugammadex as a reversal agent makes recovery from an NMBD as quick as that from succinylcholine and more predictable. It is now clear that a combination of rocuronium and sugammadex can restore spontaneous ventilation more

rapidly than waiting for succinylcholine to wear off. Possibly the need for succinylcholine may disappear completely.

### Intravenous Anaesthesia with Narcotics

The use of short-acting narcotics instead of NMBDs to facilitate tracheal intubation has been advocated as a means of avoiding the side effects of succinylcholine. This technique is effective in many patients who have no risk factors for difficult intubation. However, it has serious disadvantages. Conditions for direct laryngoscopy and tracheal intubation are worse than when NMBDs are used, so there is a higher frequency of failed intubation and airway trauma. Arterial hypotension is more likely when large doses of intravenous anaesthetics and narcotics are given. A higher incidence of laryngeal trauma when intubation is performed without NMBDs has been reported. Use of a large dose of narcotics when ventilation with a facemask or SAD is intended has other significant disadvantages. It may produce apnea and delay the return of spontaneous ventilation. More importantly, it can make ventilation of the lungs with a mask or SAD difficult or impossible as a consequence of vocal cord closure, a problem sometimes attributed to “chest wall rigidity.” The combination of intravenous anaesthesia with topical anaesthesia of the



larynx produces good conditions and may be a better alternative to the use of NMBDs.

### Local Anaesthetic and “Awake” Techniques of Airway Management

Tracheal intubation of a conscious patient can allow uninterrupted respiration and airway protection while avoiding the risk to airway maintenance and protection inherent with general anaesthesia. It is indicated when there is a possibility of difficulty with airway management. Tracheal intubation of a conscious patient is often called “awake” intubation. Good topical airway anaesthesia, rapport, and gentleness are the keys to success. Sedation is often used but cannot compensate for inadequate topical anaesthesia and is dangerous in patients with a critical airway.

Topical anaesthesia of the airway can be used to facilitate the performance of many airway procedures in a conscious patient in whom reduced consciousness is likely to cause difficulty in airway management. Direct laryngoscopy has long been used for awake intubation but is often difficult and can be distressing for all involved. Use of a flexible fiberoptic laryngoscope (FFL) for tracheal intubation under topical anaesthesia was a milestone in safe airway management because intubation of a conscious patient could now be achieved with minimal discomfort. This technique has

become the standard for management of an anticipated difficult airway. Options are preserved if awake flexible fiberoptic intubation is not successful, surgery can be postponed and the patient awakened, an unhurried surgical airway can be performed, or tracheal intubation can be attempted in a breathing patient (awake or inhaled induction) with other visual techniques.

TABLE 4

<b>Airway Techniques That Can Be Performed Under Topical Anaesthesia in an Awake Patient</b>
❖ Supraglottic airway device insertion
❖ Direct laryngoscopy and intubation
❖ Blind nasal intubation
❖ Retrograde intubation
❖ Flexible fiberoptic laryngoscopy and intubation
❖ Rigid indirect optical devices and intubation
❖ Tracheotomy/Cricothyrotomy”

Topical anaesthesia reduces the calibre of a normal airway. Use of topical anaesthesia in a patient with a compromised airway can lead to loss of the airway and should be performed only by experts who have a team prepared for immediate creation of a surgical airway.

Lidocaine has a better safety profile than other agents used for airway anaesthesia. However, excessive doses can cause fatal toxicity. Administration should be titrated and the mental state of the patient monitored. Blood concentrations are influenced by the technique chosen, and aerosol delivery to the lower respiratory tract should be minimized.

Several techniques of airway anaesthesia are shown in table 5 in the next page . Each has advantages and disadvantages. Nebulizers have been used to deliver topical anaesthesia to the airway. The optimum particle size is larger than that required for the treatment of asthma. Simple aerosol techniques, such as injection into oxygen flowing in a narrow tube, appear to work satisfactorily. Most of the inhaled solution is exhaled, and up to 20 minutes may be required to achieve satisfactory topical anaesthesia. Inhalation of an aerosol of local anesthetic is usually well tolerated and can anesthetize the entire respiratory tract. The quality of topical anaesthesia achieved with nebulizers is not as good as that achieved

with other techniques, but it is a useful option when other techniques cannot be used or coughing is particularly undesirable.

TABLE 5

<b>Techniques of Airway Anaesthesia</b>
❖ Nebulizers—entire airway
❖ Topical sprays and gels—upper airway
❖ Transtracheal injection—larynx and trachea
❖ “Spray as you go”—larynx and trachea
❖ Nerve blocks—distribution of the nerve supply
❖ Combinations of the above

Local anesthetic sprays and gels achieve rapid topical anaesthesia of the nose, mouth, and pharynx. Pressurized aerosol sprays contain preservatives that may cause a sore throat postoperatively, and they are less effective than gels. Lidocaine 4% administered by a spray attachment for syringes is popular. The first spray is pungent and patients should be warned. Lidocaine gel (2%) is very effective and well tolerated, but subsequent optical images through the gel may be slightly impaired.

Most of the lidocaine applied with sprays or gels is swallowed and the absorbed drug metabolized in first-pass hepatic metabolism.

Topical anaesthesia of the larynx and trachea may be achieved by transtracheal injection or a “spray as you go” (SAYGO) technique. SAYGO is an intermittent application technique that causes coughing and requires time for recovery after each application. Use of an epidural catheter within the working channel of the fiberscope is an effective means of administering SAYGO. Transtracheal injection through the cricothyroid membrane is more invasive but quickly produces good topical anaesthesia. Coughing spreads the local anesthetic. A bolus of narcotic is frequently given before transtracheal injection to prevent excessive coughing. Narcotics themselves can cause coughing, which can be suppressed by the inhalation of salbutamol or beclomethasone or by intravenous lidocaine. The quality of transtracheal anaesthesia is preferred by patients and endoscopists over that produced by nebulizers or SAYGO.

Nerve blocks produce more profound and longer-lasting anaesthesia than topical anaesthesia does. A superior laryngeal nerve block created by injection through the thyrohyoid membrane is the least invasive of the airway nerve blocks and provides good anaesthesia of the area between the vocal cords and the epiglottis.

## **PHYSIOLOGIC RESPONSE TO TRACHEAL INTUBATION**

Direct laryngoscopy and passage of a tracheal tube are noxious stimuli that can provoke adverse responses in the cardiovascular, respiratory, and other physiologic systems.

Significant hypertension and tachycardia are associated with tracheal intubation under light anesthesia. The magnitude of the response is greater with increasing force and duration of laryngoscopy. The elevation in arterial pressure typically starts within 5 seconds of laryngoscopy, peaks in 1 to 2 minutes, and returns to control levels within 5 minutes. Such hemodynamic changes can result in myocardial ischemia but seem to cause little harm to most patients. However they are undesirable in patients with cardiac disease.

It is possible to separate the factors that contribute to the hemodynamic response. Hemodynamic changes start within seconds of direct laryngoscopy, and there is a further increase in heart rate and blood pressure with passage of the tracheal tube. Tracheal intubation through the ILMA causes a hemodynamic effect similar to that caused by direct laryngoscopy. When orotracheal intubation or NTI is performed with the FFL under general anesthesia without topical anesthesia of the airway,

hemodynamic changes are similar to those seen with the direct laryngoscope.

Many techniques have been tried in an effort to attenuate adverse hemodynamic responses to intubation, but none is ideal. Prevention by use of an increased depth of anesthesia is attractive in theory. However, changes in the concentration of anesthetic agents in blood and at effector sites occur slowly in relation to the onset and offset of airway stimuli and hemodynamic responses. Use of N<sub>2</sub>O with a volatile agent may be beneficial. Large doses of narcotics (other than morphine), such as fentanyl, 6 µg/kg, suppress the hemodynamic response but risk prolonged respiratory depression. Aerosol or other application of topical anesthetics may be beneficial with a low risk of adverse effects. Application of such topical anesthesia may cause minor adverse hemodynamic effects, much less than those caused by tracheal intubation. Combinations of topical anesthetics with other drugs such as opioids may be useful.

Drugs that act primarily on the cardiovascular system have been studied. Many can reduce either the blood pressure or the heart rate response, but not both, and can cause hypotension or bradycardia. Labetalol and esmolol have been recommended, particularly in combination with narcotics. Use of such drugs is rarely indicated, however.

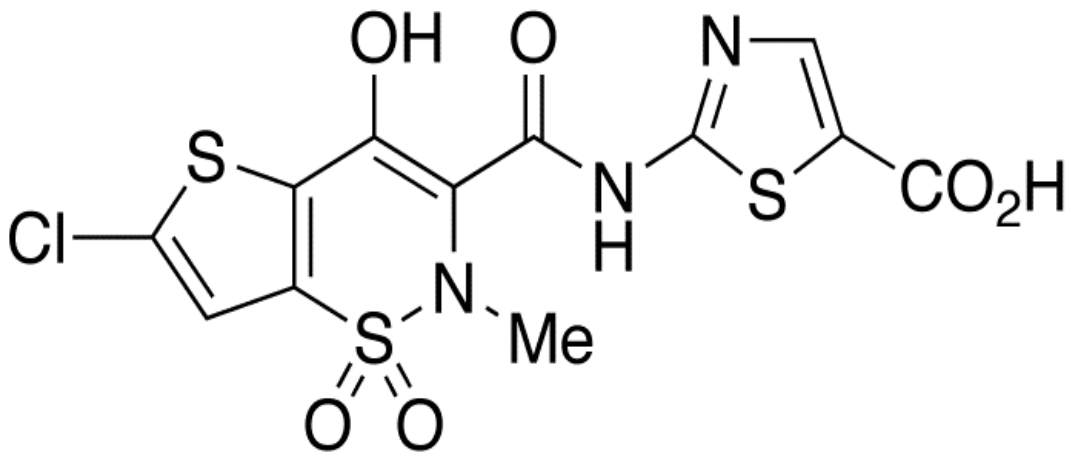
Another approach to reducing the cardiovascular response to tracheal intubation is to modify the technique of tracheal intubation. Awake flexible fiberoptic intubation with effective topical anesthesia almost eliminates the hemodynamic response to tracheal intubation.

Direct arterial pressure monitoring throughout induction of anesthesia is desirable in a high-risk patient so that the anesthesiologist can respond to accurate, continuous hemodynamic information. Moderate depression of arterial pressure and heart rate before laryngoscopy might limit the rise in arterial pressure at the expense of initial cardiorespiratory depression. Prolonged attempts at laryngoscopy should be avoided. Careful cardiovascular monitoring and willingness to interrupt direct laryngoscopy while anesthesia is deepened are keys to maintenance of reasonable homeostasis.



## PHARMACOLOGY OF LORNOXICAM

Lornoxicam (chlortenoxicam) is a non-steroidal anti-inflammatory drug (NSAID) which belongs to the oxicam class with analgesic, anti-inflammatory and antipyretic properties. It is available in oral and parenteral formulations



**Molecular structure of lornoxicam**

### INDICATIONS

1. Inflammatory diseases of the joints.
2. Osteoarthritis
3. Pain following surgery
4. Sciatica injection
5. For the relief of postoperative pain or acute painful conditions requiring parenteral analgesic

## **MODE OF ACTION**

Lornoxicam is a non-steroidal anti-inflammatory drug with analgesic properties and belongs to the class oxicams. Lornoxicam inhibits synthesis of prostaglandins via inhibition of cyclooxygenase enzyme. *In vitro* the inhibition of cyclooxygenase does not result in an increase in leukotrienes formation. The mechanism of the analgesic action of lornoxicam has not been fully determined.

Lornoxicam inhibits both isoforms that is, COX-1 inhibition: COX-2 inhibition=38. It readily penetrates into the synovial fluid.

Synovial fluid : plasma AUC ratio is 0.5 after administration of 4 mg twice daily.

## **PHARMACOKINETICS**

### **ABSORPTION**

Lornoxicam is absorbed rapidly and almost completely from the gastrointestinal tract. Maximum plasma concentrations are achieved after approximately 1 to 2 hours of oral therapy. Lornoxicam Injection is intended, for intravenous or intramuscular administration. After intramuscular injection maximum plasma concentrations are achieved after approximately 20-25 minutes

## **DISTRIBUTION**

The absolute bioavailability of Lornoxicam is 90-100%. No first - pass effect was observed.

## **METABOLISM**

- Better safety profile regarding renal and hepatic function tests,
- Better gastrointestinal tract tolerability compared to selective COX-2 inhibitors

Lornoxicam is found in the plasma in unchanged form and as its hydroxylated metabolite. The hydroxylated metabolite exhibits no pharmacological activity. CYP2C9 has been shown to be the primary enzyme responsible for the biotransformation of the lornoxicam to its major metabolite, 5-hydroxylornoxicam. Recently, it was reported that lornoxicam 5'-hydroxylation by the variant CYP2C9\*3 and CYP2C9\*13 was markedly reduced compared with wild type, both in vitro and in vivo.

## **ELIMINATION**

Approximately 2/3 is eliminated via the liver and 1/3 via the kidneys as inactive substance.

## **DRUG INTERACTIONS**

- Anticoagulants/ Sulphonylureas
- Diuretics/ACE inhibitors / Digoxin
- Lithium
- Methotrexate/Cylosporin
- Cimetidine

## **DOSAGE AND ADMINISTRATION**

Lornoxicam injections are supplied for intramuscular or intravenous administration. Lornoxicam 8 mg powder for injection has to be dissolved in 2 ml water for injection immediately prior to use. Lornoxicam must be administered as an intramuscular (5 seconds) or intravenous (>15 seconds) injection. Lornoxicam may exclusively be injected by a trained medical/paramedical personal. After preparation of the solution, change the needle. For intramuscular injection use a sufficiently long needle for a deep intramuscular deposition of the drug. The total daily dose should not exceed 24 mg.

Lornoxicam is a potent NSAID from the chemical class of oxicams, and is marketed in a number of European countries for the treatment of various painful conditions associated with inflammation. In

contrast to the other oxicams, lornoxicam has a very short half-life (approximately 4 hours as compared with >24 hours for the others) and is therefore especially suitable for short-term treatment. The short half-life of the drug probably explains the improved gastrointestinal safety profile observed with lornoxicam. A quick-release formulation of lornoxicam has also been developed.

## **USE IN SPECIAL POPULATIONS**

### **PEDIATRIC PATIENTS**

No pharmacokinetic data available in pediatric patients.

### **HEPATIC INSUFFICIENCY**

There is no significant change in the kinetic profile of lornoxicam in patients with mild hepatic dysfunction. However, accumulation of major inactive metabolite occurred in patients with hepatic dysfunction. For patients with hepatic impairment the maximal recommended daily dose is reduced to 12 mg. Careful clinical monitoring and laboratory assessment at regular intervals is recommended.

## **RENAL INSUFFICIENCY**

There is no significant change in the kinetic profile of lornoxicam in patients with mild kidney dysfunction (Creatinine Clearance , 60 ml/min), however no data on multiple doses appear to be available. Dosage limitation of the drug may compensate for reduced renal elimination in those with severe renal dysfunction. However, clinical significance of this is unknown.

## **PREGNANCY AND LACTATION**

No clinical data on exposed pregnancy & lactation are available for lornoxicam. The potential for human risk in pregnancy is unknown. As with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia and delayed parturition occurred in rats. No clinical data on use during labor is available. Administration of lornoxicam is not recommended during labor and delivery

## **GERIATRIC USE**

No special dosage modification is required for elderly patients, unless renal or hepatic function is impaired, in which case the daily dosage should be restricted.

## **CONTRAINDICATIONS & PRECAUTIONS**

Lornoxicam is contraindicated in following

1. Allergy to lornoxicam.
2. (bronchospasm, rhinitis, angioedema or urticaria) to other non-steroidal anti-inflammatory medicines, including, acetylsalicylic acid
3. History of gastrointestinal bleeding, cerebrovascular bleeding
4. Patients with bleeding disorders
5. Patients with history of recurrent peptic ulceration
6. Patients with severe hepatic or renal insufficiency
7. Patient with thrombocytopenia
8. Patients with severe cardiac failure
9. Pregnancy & Lactation.

## **ADVERSE EFFECTS OF LORNOXICAM**

Lornoxicam has a tolerability profile characteristics of NSAIDs, with gastrointestinal adverse effects (pain, dyspepsia, nausea, vomiting) being the most common.

GENERAL: Headache, dizziness, changes in appetite, edema, allergic reactions

GASTROINTESTINAL : Abdominal pain, diarrhea, dyspepsia, vomiting  
gastro esophageal reflux

HAEMETOLOGICAL: Very rarely prolonged bleeding time,  
thrombocytopenia or increased transaminases.

SKIN: Allergic skin reactions

### **STORAGE**

Store at temperature below 25<sup>0</sup>C



## **RELEVANCE OF THE STUDY**

Laryngoscopy and subsequent tracheal intubation result in the activation of the sympathetic nervous system due to stimulation of somatic and visceral nociceptive afferents of the airway. This leads to cardiovascular stimulation which result in an increased blood pressure and heart rate. Various techniques have been tried to prevent or attenuate hemodynamic responses due to laryngoscopy and endotracheal intubation. Among them opioids, alpha-2-agonists, iv NTG, beta-blockers etc have been shown to be effective agents in blunting stimulatory effects on cardiovascular system. Unfortunately most of these agents are having well known side effects. Hence minimizing the peri-operative adverse events is of utmost importance. There for other agents have been tried, to replace or to reduce the use of these agents.

This study is to demonstrate the effect of pre operative administration of lornoxicam on hemodynamic changes during laryngoscopy and tracheal intubation.

- ❖ Simple and practical method of stress response attenuation.
- ❖ Well tolerated with few adverse effects.
- ❖ Already being used in the treatment of acute postoperative pain and to reduce the postoperative use of opioids.
- ❖ Studies on haemodynamic effects needed before it is routinely used as an agent for attenuation of stress response.

## **PATIENTS AND METHODS**

### **STUDY DESIGN**

- ❖ Single - blind randomized placebo-controlled trial

### **INCLUSION CRITERIA**

1. Patients who required tracheal intubation for elective surgical procedures
2. ASA Class I and Class II
3. Age between 18 & 50 years
4. Weight of patients 40 - 70 kg

### **EXCLUSION CRITERIA**

1. Anticipated difficult intubation.
2. At risk of regurgitation or pulmonary aspiration
3. With renal or hepatic impairment
4. Taking drugs known to affect BP & HR
5. Allergy to NSAIDS
6. ASA Physical status III or greater
7. Acid peptic disease, Bronchial Asthma, coagulation disorders
8. Pregnancy & Lactation

## **PLAN OF STUDY**

After routine pre-anaesthetic check up and applying exclusion criteria 50 patients about to undergo general anaesthesia with endotracheal intubations were randomly allocated into two groups by drawal of lots.

### **GROUP 1 -LORNOXICAM GROUP**

This group received intravenous lornoxicam 16 mg 30 minutes before laryngoscopy and intubation after test dose.

### **GROUP 2-CONTROL GROUP**

This group received placebo (normal saline) intravenously 30mts before laryngoscopy and intubation.

## **PREMEDICATION**

Patients were not premedicated in this study.

## **ANAESTHETIC TECHNIQUE**

After obtaining approval from ethical committee 50 patients aged between 18 to 50 years, ASA class I and Class II requiring tracheal intubation for elective surgical procedure were enrolled in this randomized single blind placebo controlled study. All patients included in the study were fasted overnight from 10 pm. In the holding area an IV cannula is inserted and Lactated ringers infusion was started with standard

monitoring. Based on randomization , the patients received either lornoxicam 16mg iv or placebo (iv saline) half an hour before surgery after obtaining informed consent from the patient and the relatives.

Randomization was done in the preoperative holding area by the anaesthesiologist who is to administer the trial drug/placebo.

Medications iv lornoxicam or normal saline will be administered by a different anesthetist who is not involved in the study. Induction technique will be standardized. On arrival in operating room and after preoxygenation using Bain's co-axial circuit, anaesthesia will be induced with propofol 2 mg/kg. Succinyl Choline 2mg/kg will be given to facilitate tracheal intubation. Systolic and diastolic BP, Mean arterial pressure, heart rate and ECG changes will be recorded before and after administration of the intra-venous anaesthetic and at 1,3,5 and 10 minutes after laryngoscopy and tracheal intubation. During observation period:

#### **PARAMETERS COMPARED**

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial pressure (MAP)
- Heart Rate(HR)

After the documentation of results of all the fifty patients, the anesthesiologist who has administered the injections, revealed the identity of the drug. Based on this, results were analyzed as lornoxicam group and placebo group.

### **STATISTICAL TECHNIQUES**

Data was entered in Microsoft Excel and statistical analysis done in SPSS. Student's test was used to analyze demographic profile, heart rate changes, pressure changes. Student's 't' test is used for comparing means of two populations.

P value > 0.05 is not significant  
< 0.05 is significant  
< 0.01 is highly significant

Intubation time is defined as period from termination of manual ventilation using a face mask to restarting of ventilation through endotracheal tube. Patients requiring >20 sec to achieve successful tracheal intubation are excluded from the study.

Anaesthesia was maintained using O<sub>2</sub> & N<sub>2</sub>O Mixture and supplemented with intravenous agents as necessary and a non-depolarizing muscle relaxant is used to maintain muscle relaxation. After surgery after meeting all criteria of reversal, patients are reversed with Inj. Neostigmine

0.05 mg/kg and Inj. Glycopyrrolate 8mcg/kg. Patients were observed for 24 hours for any nausea, vomiting allergic reactions and urine output.

## **OBSERVATIONS AND RESULTS**

Fifty patients each with similar characteristics were divided into two groups of 25 each, one being the lornoxicam group and the other placebo group.

Two groups were perfectly matched in terms of no. of patients, age, sex, weight, height, ASA physical status and Duration of laryngoscopy.

## **DEMOGRAPHIC DATA**

### **MATCHING**

	Group 2 (Saline)	Group 1 (Lornoxicam)
No. of patients	25	25
Age	31.12+/.5.1	32.16+/-4.3
Sex M/F	10/15	12/13
Weight	57.72+/-4.1	58.9+/-5.4
Height	166.44 ±6.4	167.2±4.5
ASA I/II	11/14	12/13
Duration of Laryngoscopy	14.48 (1.7)	15.48 (1.1)

## SYSTOLIC BLOOD PRESSURE CHANGES

Systolic blood pressure changes before and after laryngoscopy and intubation is analyzed and shown in Table 6.

TABLE 6

Systolic BP (Mean)	Lornoxicam group	Placebo group	P Value
Before Laryngoscopy	112.48	113.92	0.6723
1mt	121.6	135.92	0.0001
3mt	116	127.92	0.0213
5mt	114.16	115.12	0.74
10mt	113.12	114.64	0.5715

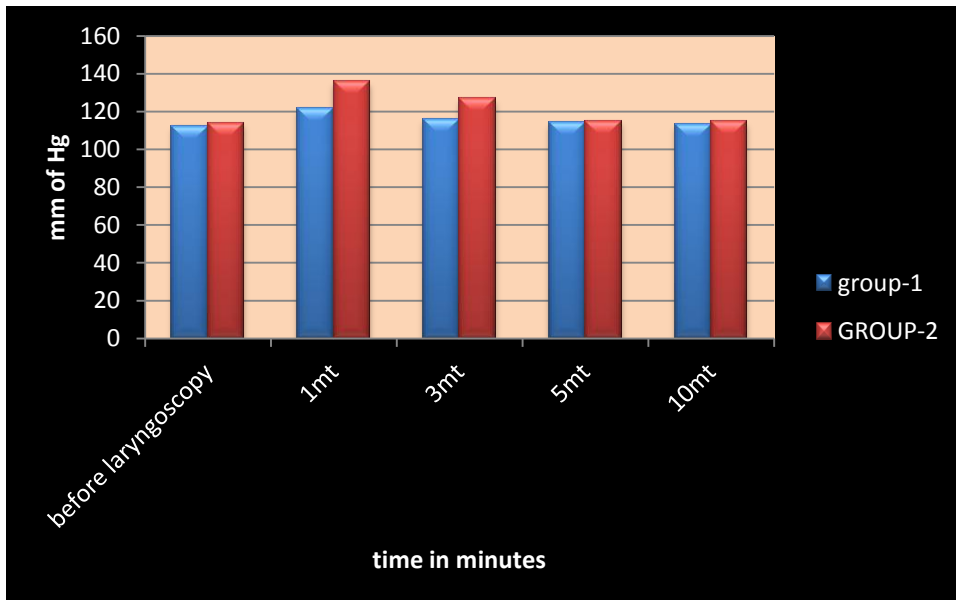
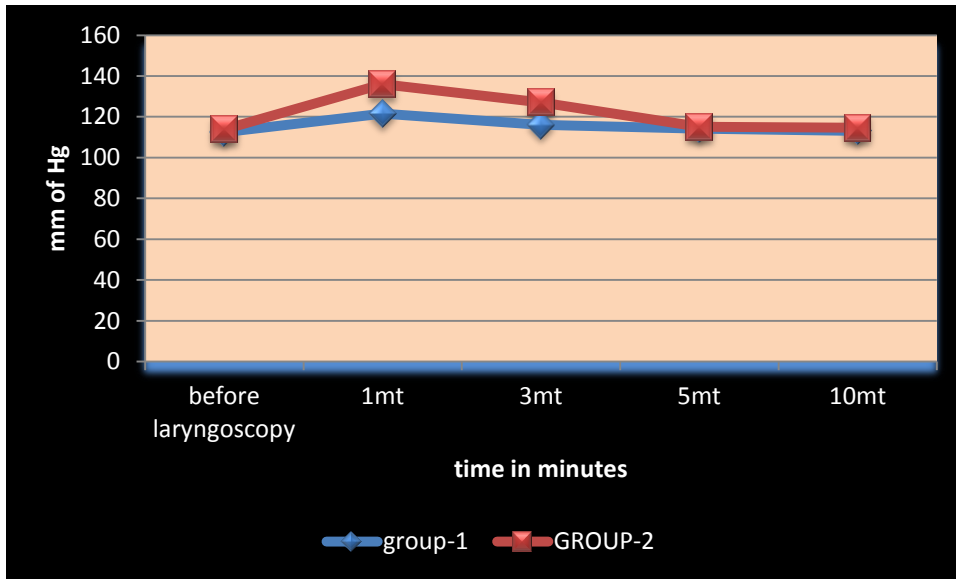
Percentage of rise in systolic BP in both groups at 1 minute

Systolic BP	Lornoxicam group	Placebo group
1mt	8%	19.3%

From graph 1 it is evident that systolic BP before laryngoscopy after induction was comparable in both groups but there was definite reduction in stress response in lornoxicam group and difference was significant at 1 minute and 3 minute intervals.



Graph-1... **SYSTOLIC BP CHANGES**



## DIASTOLIC BP CHANGES

Diastolic Blood pressure changes analyzed and shown in Table 7

TABLE 7

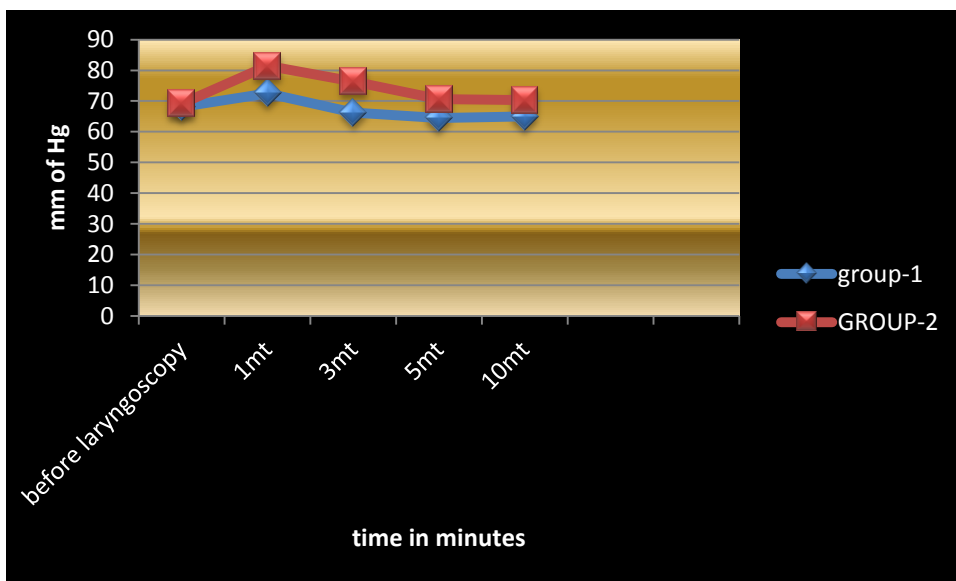
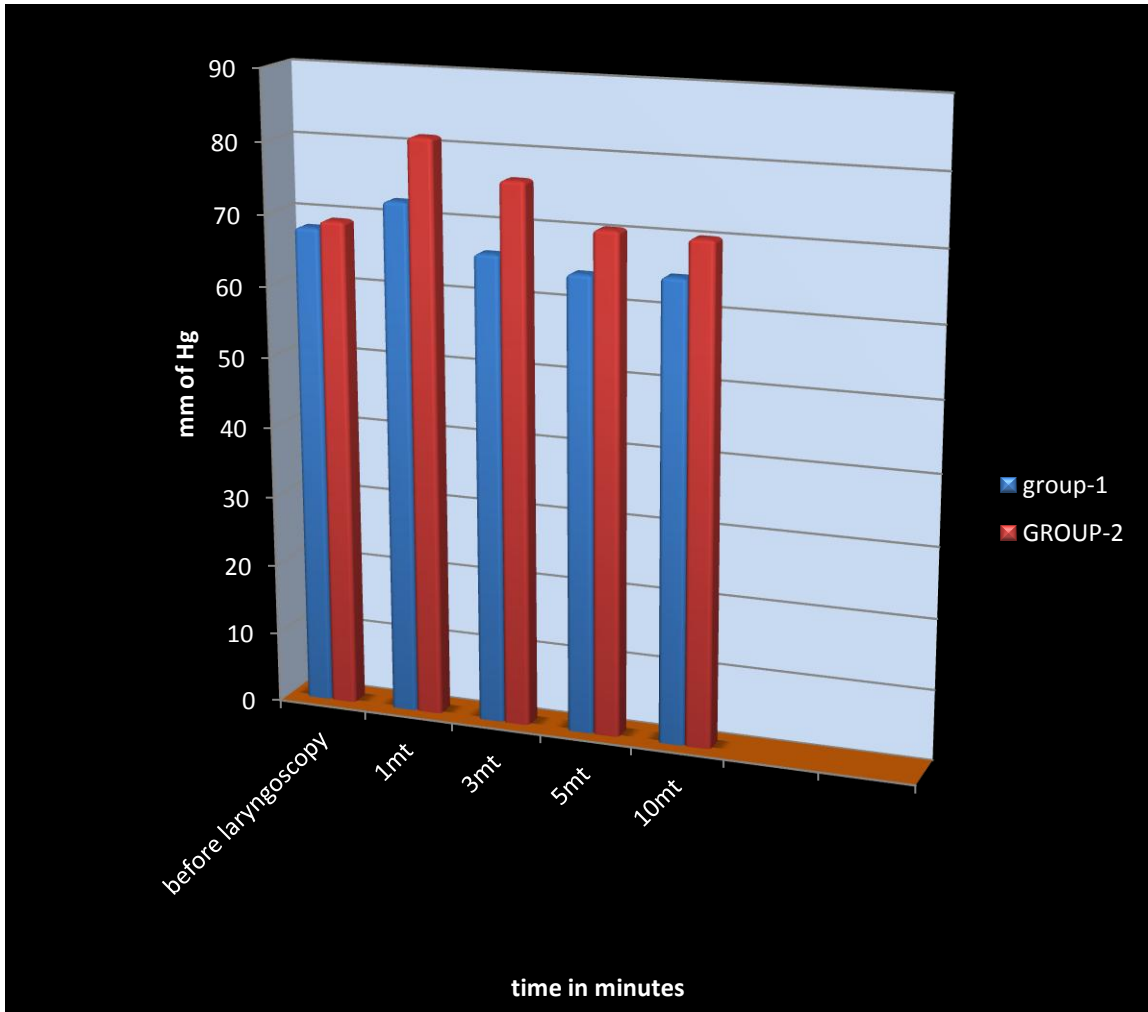
Diastolic BP	Lornoxicam group	Placebo group	P Value
Pre- Laryngoscopy	68.08	69.2	0.48
1mt	72.52	81.44	0.0001
3mt	66.24	76.4	0.0001
5mt	64.44	70.64	0.0007
10mt	64.96	70.32	0.001

Percentage of rise in Diastolic BP in both groups at 1 minute

Diastolic BP	Lornoxicam group	Placebo group
3mt	6.5%	17.7%

There was a significantly reduction in diastolic BP in lornoxicam group when compared with placebo in response to laryngoscopy and intubation.

Graph -2 **DIASTOLIC BP CHANGES**



## MEAN ARTERIAL PRESSURE

Table 8 Compares the changes in mean arterial pressure for both the groups. Mean arterial pressure is calculated using the formula.

$$\text{MAP} = \text{DBP} + 1/3 (\text{SBP}-\text{DBP})$$

Where, DBP = diastolic blood pressure, SBP=systolic blood pressure.

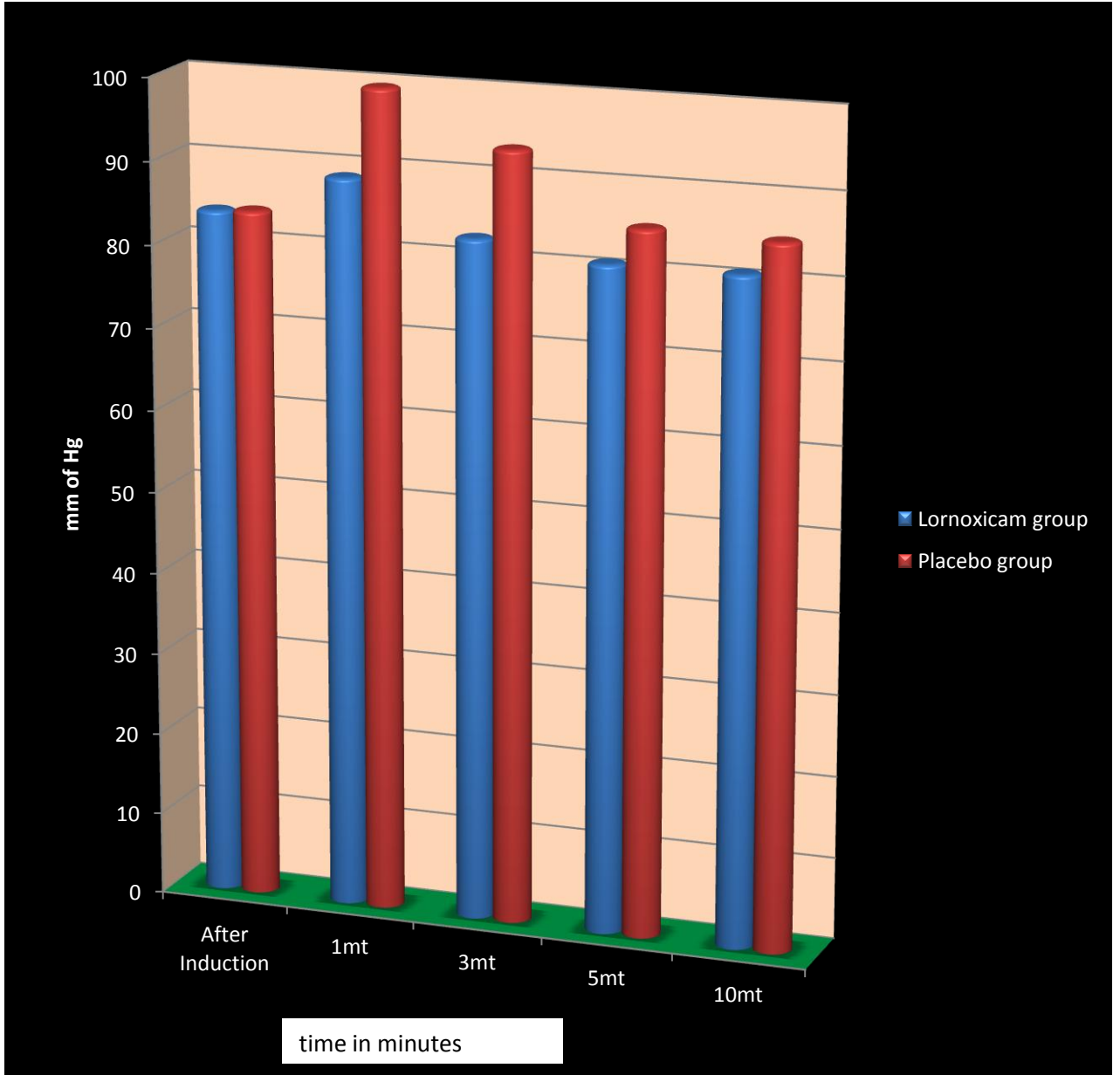
TABLE 8

MAP (Mean)	Lornoxicam group	Placebo group	P Value
After Induction	82.88	84.1	0.46
1mt	88.88	99.75	0.13
3mt	82.82	93.57	0.0001
5mt	81.01	85.47	0.0007
10mt	81.01	85.09	0.01

Percentage of rise in MAP in both groups at 1 minute

MAP	Lornoxicam group	Placebo group
1mt	7.14%	18.6%

Graph -3  
MAP CHANGES



Mean arterial pressure was definitely lower in lornoxicam group and difference was significant at 3 minute, 5 minute and 10 minute intervals.

## HEART RATE CHANGES

Heart Rate changes during various stages of anaesthesia induction is analyzed and shown in Table 9.

TABLE 9

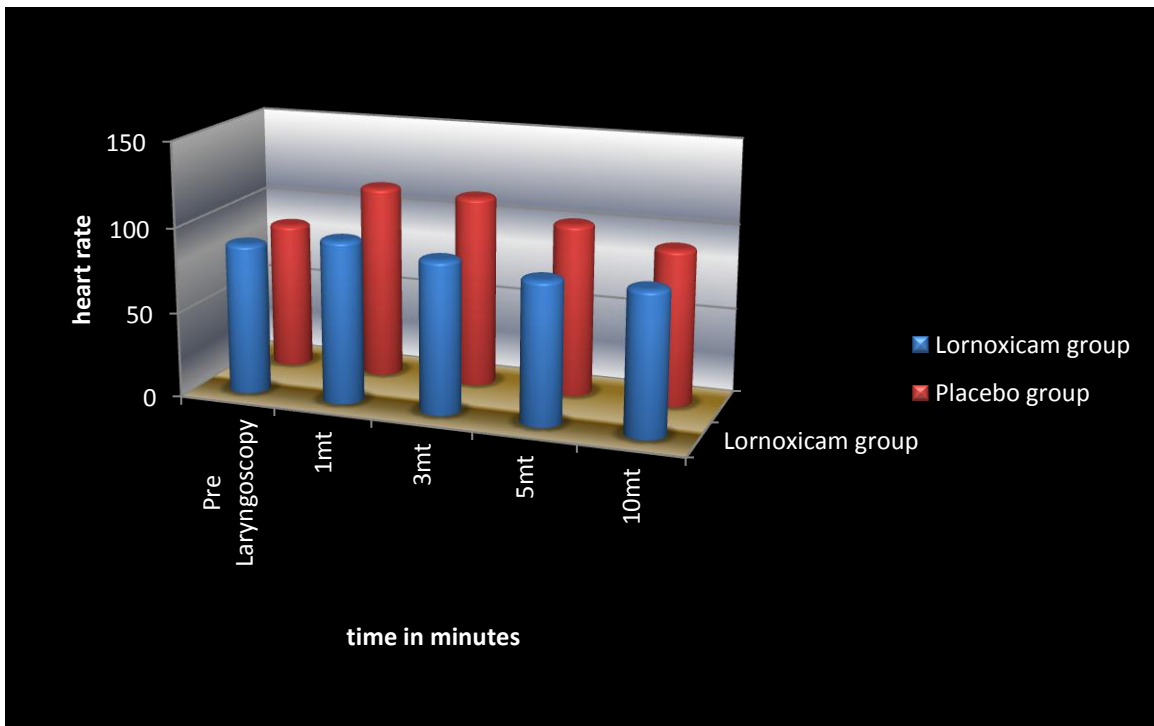
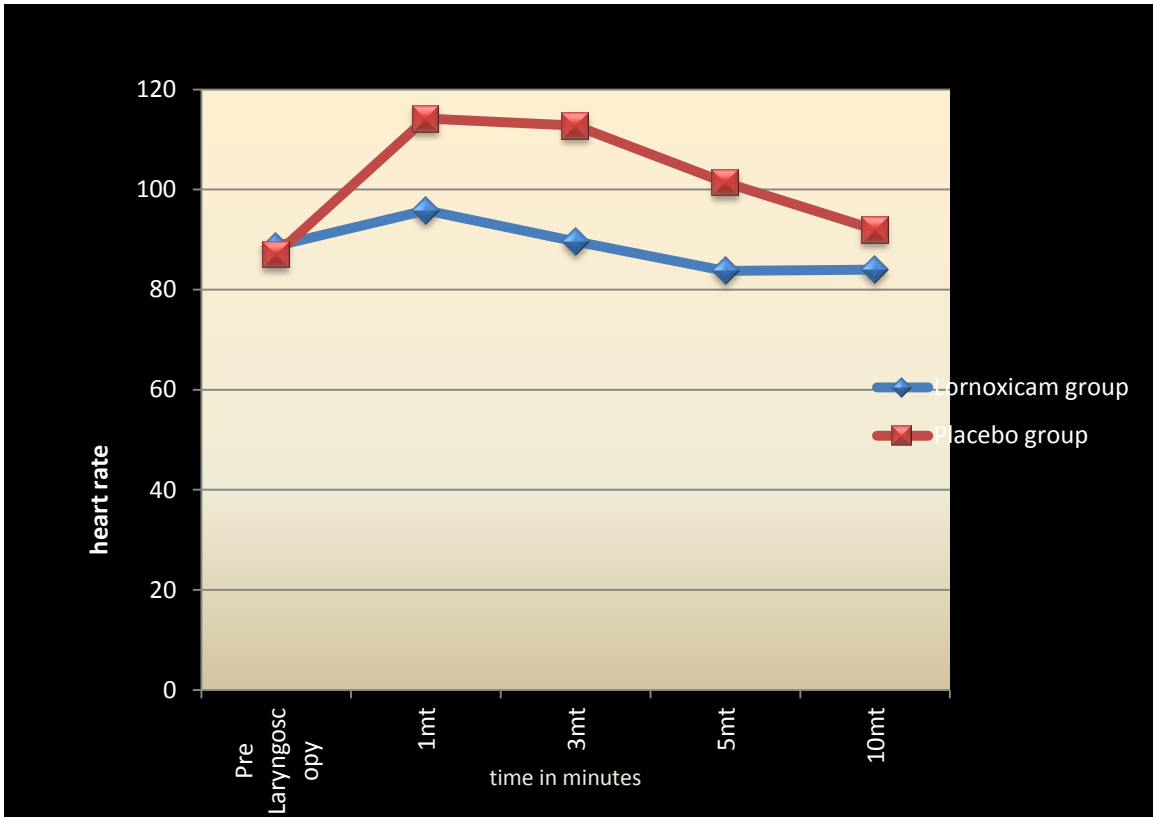
MAP (Mean)	Lornoxicam group	Placebo group	P Value
Pre Laryngoscopy	88.72	87.04	0.54
1mt	95.84	114.16	0.001
3mt	89.6	112.76	0.001
5mt	83.76	101.4	0.001
10mt	84	91.96	0.003

Percentage of rise in HR in both groups at 1 minute

MAP	Lornoxicam	Placebo
1mt	8%	31.1%

Heart rate followed the same path as diastolic BP. Rise in heart rate was significantly lower in lornoxicam group and difference was significant at 1 minute, 3 minute, 5 minute and 10 minute intervals.

Graph-4... HEART RATE CHANGES



## STATISTICAL EVALUATION AND SUMMARY

TABLE 10

Significant attenuation in rise of	1mt	3mt	5mt	10mt
Systolic BP	0.0001+	0.02+	0.74X	0.57X
Diastolic BP	0.0001+	0.0001+	0.0007+	0.001+
MAP	0.13X	0.0001+	0.007+	0.01+
Heart Rate	0.0001+	0.001+	0.001+	0.003+

Prelaryngoscopic Blood pressure and heart rate was comparable in both lornoxicam and control group but after laryngoscopy, there was definite reduction in systolic BP, diastolic BP, Mean arterial pressure and heart rate in lornoxicam group and the difference was significant at 1mt and 3mt in case of systolic BP 1mt 3mt 5mt 10mt in case of diastolic BP 3mt 5mt and 10mt in case of mean arterial pressure 1mt 3mt 5mt and 10mt in case of heart rate.



## **SIDE EFFECTS**

1. Two out of 50 patients developed allergic reaction on test dose and were excluded from the study.
2. Urine output was normal in both groups postoperatively for 24 hours.
3. No one developed nausea and vomiting.

## DISCUSSION

Lornoxicam is a nonsteroidal anti-inflammatory drug of Oxicam class with analgesic and anti-inflammatory property. It acts by inhibiting synthesis of prostaglandins via inhibition of cyclo-oxygenase but does not inhibit 5-lipo-oxygenase. Lornoxicam may be administered orally, intramuscularly or intravenously. After intramuscular injection maximum plasma concentration is achieved approximately after 20-25 minutes. The absolute bioavailability after IM injection is 97%. It is present in plasma in unchanged form and as hydroxylated metabolites. It undergoes extensive hepatic metabolism to inactive metabolite 5-hydroxy lornoxicam. 51% of the drug is excreted through faeces and 42% via kidneys with a mean elimination half life of 3-4 hours. Lornoxicam is a drug with very good tolerance and very low incidence of adverse effects. The most common among them is gastrointestinal disturbances. Head ache, dizziness, allergic reactions are less common adverse reactions.

## MECHANISM OF STRESS RESPONSE ATTENUATION BY LORNOXICAM

1. Decreases serum catecholamine levels, thus obtunding cardiovascular sympathetic response during laryngoscopy and tracheal intubation.
2. Increases endogenous opioids dynorphine and beta endorphine
3. Prostaglandin inhibition and thus cut-off visceral and somatic nociceptive afferents contributing to stress response during laryngoscopy.

The analgesic potency of 8 mg iv lornoxicam is equal to that of 20mg morphine or 50mg pethidine. The analgesic effect of 16mg lornoxicam is superior to 100mg tramadol and was comparable to 100mcg. fentanyl when used as an intraoperative analgesic in mild to moderate day care ENT surgeries .

The haemodynamic stress response to laryngoscopy and intubation is supposed to be initiated by sympathetic response which starts within 5 seconds of laryngoscope pressing the base of tongue. It reaches the baseline value between 5 to 10 minutes after intubation. In the present study we have made an attempt to determine the efficacy of intra venous

lornoxiam 16mg 30 minutes before laryngoscopy and intubation, in attenuating the haemodynamic stress response.

In our study the lornoxiam group and control group were comparable in various parameters like age, weight, height, sex, ASA grading and duration of laryngoscopy.

The baseline values of both groups showed no significant difference. Lornoxiam group has a significantly lower mean heart rate of 95.84 compared to control group at 1 minute after intubation which showed a heart rate of 114.16. Likewise lornoxiam group also has significantly lower heart rate at 3 minute 5 minute and 10 minutes after intubation.

In comparison with control group the lornoxiam group did not show rise of systolic blood pressure at 1 minute and 3 minute intervals. Control showed a peak in blood pressure at 1 minute after intubation with a systolic BP of 135.92 at 1 minute. The values of systolic blood pressure were near the baseline values at 10 minutes in both the groups.

Likewise diastolic blood pressure and mean arterial pressure of both groups were having an increase from basic values but the diastolic BP and

MAP recorded from the lornoxicam group showed a significantly lower value.

From the observation it is evident that the peak values reached by lornoxicam group are significantly lower compared to control group. So we concluded that pretreatment with 16mg intravenous lornoxicam is effective in attenuating the cardiovascular stress response to laryngoscopy and tracheal intubation . Stress mediators such as endogenous plasma catecholamines or cortisone were not measured in our study. This can be considered as limitations of the study since measurements of endogenous catecholamines would have given useful information. As the peri-operative use of lornoxicam is becoming more frequent, more studies which focus on its effects on old age, ASA III & IV patients and its effect on stress mediators are needed.

### **COMPARISON WITH INTERNATIONAL STANDARDS**

Riad and Moussa in 2008 conducted a study on the effects of preoperative iv lornoxicam on elderly patients. In this study 50 patients aged between 65 and 75 were selected .They were divided into two groups to receive iv lornoxicam 8mg or placebo. They were given either lornoxicam or placebo 30 min before surgery. SBP,DBP, MAP and HR were recorded before tracheal intubation and one ,three, five and ten

minutes after intubation. The results showed a significant increase in all the parameters they were monitoring in the control group. They concluded from their study that preoperative administration of iv lornoxicam 8mg is useful in reducing the cardiovascular stress response following laryngoscopy and tracheal intubation in elderly patients.

In agreement with the above study our results also showed a significant increase in SBP,DBP,HR and MAP in the control group compared to lornoxicam group eventhough we used a higher dose of lornoxicam..Again, in comparison with the above study by Riad and Moussa we used lornoxicam alone while lornoxicam and fentanyl was used by them. This can be considered as an advantage of our study because we can attribute the reduction in cardiovascular parameters in lornoxicam group to lornoxicam alone.

M.Dabiss et.al in 2010 conducted a study to demonstrate the effect of 16mg iv lornoxicam on cardiovascular stress response and level of serum catecholamine following laryngoscopy and intubation.50 patients were chosen for the study.They were randomly divided into two groups to receive intravenous injection (iv) of either Lornoxicam 16 mg diluted in 4ml saline or 4ml normal saline half an hour before induction of anaesthesia .No premedications were given to the patients. An iv line was established and ringerlactate solution was started for all patients 30 minutes

before induction. After 3 min of preoxygenation anaesthesia was induced with propofol 2.5mg/kg and cis-atracurium 0.15 mg/kg to facilitate tracheal intubation which was performed using direct laryngoscopy when neuromuscular block was achieved by train of four guard monitor. Baseline values for SBP, DBP, HR, MAP, and SpO<sub>2</sub> were recorded and blood was drawn for measuring the serum catecholamine level before induction. All these parameters were recorded immediately after intubation and every minute followed, for ten minutes except serum catecholamine.

Their results showed a significant increase in the haemodynamic parameters and serum catecholamine level in the control group. They concluded that 16mg iv lornoxicam is effective in blunting the cardiovascular stress response following laryngoscopy and intubation.

The results of our study was also in agreement with the above study. In our study there was a significant reduction in all the haemodynamic parameters following intubation in the lornoxicam group. In comparison with the above study we could not measure the serum catecholamine levels, as the facility was not available in our centre. This can be considered as a drawback of our study.

## SUMMARY

A haemodynamic stress response is associated with laryngoscopy and tracheal intubation almost all the time. This would not cause much harm to most of the patients, but can increase morbidity in patients with coronary arterial disease, systemic hypertension, pre eclampsia, increased intra ocular pressure and cerebrovascular pathologies such as tumors, aneurysms or increased intracranial pressure.

Several techniques have been proposed to prevent or attenuate the haemodynamic responses following laryngoscopy and intubation, such as deepening of anaesthesia, omitting anticholinergic premedication, pretreatment with vasodilators such as nitroglycerin, beta-blockers, calcium channel blockers and opioids. The recent studies aiming at controlling or attenuating the haemodynamic response to intubation and laryngoscopy focused on the effect of lornoxicam at different dosing regimens.

Lornoxicam is a relatively new drug, which was introduced as analgesic and antiinflammatory. The drug is well tolerated with limited side effects as compared with other NSAIDS. Lornoxicam has been used in



randomized controlled trials to treat acute postoperative pain and to reduce the postoperative opioid requirements.

The present study was designed as a single-blind randomized controlled trial to investigate the effect of lornoxicam on the changes in blood pressure and heart rate (HR) observed during laryngoscopy and tracheal intubation in 50 ASA I & II patients. They were divided into two groups of 25 each, one being the study group receiving 16 mg iv lornoxicam and the other the control group receiving iv placebo. Heart rate and blood pressure were recorded at various intervals during laryngoscopy and endotracheal intubation. It was observed that there was a statistically significant attenuation in heart rate and blood pressure response to laryngoscopy and intubation for the lornoxicam group. Hence we can conclude that iv lornoxicam 16 mg 30 minutes before surgery is a simple and practical method for the attenuation of the stress response to laryngoscopy and endotracheal intubation.

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## **CONCLUSION**

From this study we conclude that intravenous lornoxicam 16mg given half an hour before surgical procedure significantly reduces haemodynamic responses to laryngoscopy and intubation.





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Lornoxicam attenuates the haemodynamic responses to laryngoscopy and  
tracheal intubation in the elderly

EFFECT OF INTRAVENOUS LORNOXICAM ON THE HAEMODYNAMIC  
RESPONSE FOLLOWING LARYNGOSCOPY AND INTUBATION

CONTROL GROUP/TEST GROUP

NAME:

AGE/SEX:

IPNO:

WT:

HT:

DATE OF SURGERY:

DIAGNOSIS:

PROCEDURE:

ASA GRADE:

MPG:

INVESTIGATIONS

HB:

BT:

CT:

RFT:

LFT:

RBS:

CXR:

ECG:

DURATION OF LARYNGOSCOPY:

RELEVANT MEDICAL SURGICAL HISTORY:

## PARAMETERS MONITORED

TIME	HEART RATE	SYSTOLIC BP	DIASTOLIC BP	MAP
PRE LARYNGOSCOPY				
1mt				
3mt				
5mt				
10mt				

COMPLICATIONS:

URINE OUTPUT:

## DIASTOLIC BLOOD PRESSURE LORNOXICAM GROUP in mm of Hg

SLNO:	IP NO	PRE LARYNGOSCOPY	1 mt	3mt	5mt	10mt
1.	1403494	68	75	66	65	66
2.	1403526	64	68	60	58	60
3.	1403314	64	70	62	60	60
4.	1403146	72	78	70	68	68
5.	1402840	68	74	66	64	64
6.	1398343	74	80	72	70	72
7.	1410943	76	82	70	72	70
8.	1410827	74	80	72	70	70
9.	1410865	68	72	66	64	66
10.	1408038	64	64	62	60	60
11.	1408674	70	76	68	66	64
12.	1402830	70	74	68	66	66
13.	1402840	64	70	62	60	60
14.	1410478	78	80	76	74	74
15.	1402946	76	82	84	72	72
16.	1410753	74	80	72	70	72
17.	1410762	70	72	68	66	64
18.	1399542	68	68	66	64	66
19.	1410883	60	62	58	58	60
20.	1410911	62	68	60	60	62
21.	1410734	64	70	62	60	60
22.	1398842	70	76	68	66	64
23.	1408657	62	68	60	60	62
24.	1409871	62	64	60	60	62
25.	1408649	60	60	58	58	60
		68.08	72.52	66.24	64.44	64.96

## SYSTOLIC BLOOD PRESSURE LORNOXICAM GROUP In mm of Hg

SLNO:	IP NUMBER	PRE LARYNGOSCOPY	1 mt	3mt	5mt	10mt
1.	1403494	116	120	118	126	120
2.	1403526	110	128	120	120	110
3.	1403314	80	100	96	90	90
4.	1403146	100	130	116	116	120
5.	1402840	110	148	106	100	100
6.	1398343	122	130	132	110	110
7.	1410943	98	110	100	108	110
8.	1410827	104	110	100	108	100
9.	1410865	128	140	132	126	126
10.	1408038	98	100	104	100	100
11.	1408674	100	116	112	112	112
12.	1402830	130	138	128	126	126
13.	1402840	124	128	126	120	128
14.	1410478	114	120	110	116	110
15.	1402946	134	130	128	128	126
16.	1410753	120	140	132	124	124
17.	1410762	100	110	112	110	104
18.	1399542	108	106	108	110	110
19.	1410883	112	114	112	110	110
20.	1410911	110	124	116	110	112
21.	1410734	96	100	112	100	100
22.	1398842	112	120	110	112	110
23.	1408657	130	136	130	132	132
24.	1409871	128	132	126	122	122
25.	1408649	108	130	124	124	116
		112.48	121.6	116	114.16	113.12

SYSTOLIC BP PLACEBO GROUP in mm of Hg

SL NO:	IP NO:	PRE LARYNGOSCOPY	1mt	3mt	5mt	10mt
1.	1395638	130	150	146	132	124
2.	1393608	124	140	128	120	120
3.	1396362	110	134	126	100	108
4.	1400079	100	128	120	116	116
5.	1400413	120	130	116	108	108
6.	1400674	130	144	132	120	120
7.	1403106	98	126	112	100	100
8.	1402830	96	130	126	110	110
9.	1406364	126	150	130	126	120
10.	1403106	112	132	116	110	110
11.	1393052	124	134	120	120	130
12.	1393289	112	132	126	110	114
13.	1393147	120	138	130	116	116
14.	1403718	100	124	116	102	112
15.	1403687	108	116	108	100	100
16.	1407753	126	140	132	122	120
17.	1401753	116	132	120	120	120
18.	1406862	100	130	122	112	110
19.	1406771	124	142	130	120	116
20.	1416236	104	128	108	110	100
21.	1410928	106	134	120	104	108
22.	1410091	124	146	126	120	120
23.	1408212	112	148	140	134	126
24.	1407355	120	150	128	126	120
25.	1410973	106	140	120	120	118
		113.92	135.92	127.92	115.12	114.64

## DEMOGRAPHIC DATA LORNOXICAM GROUP

SLNO:	IPNO:	AGE	SEX	Wt in kg	Ht in cm	ASA GRADE	DURATION OF LARYNGOSCOPY IN SECONDS
1.	1403494	36	M	61	175	ASA II	16
2.	1403526	30	F	50	149	ASA II	15
3.	1403314	37	M	64	170	ASA II	18
4.	1403146	29	M	63	176	ASA II	14
5.	1402840	24	F	54	158	ASA I	17
6.	1398343	43	M	70	174	ASA II	14
7.	1410943	23	M	68	171	ASA I	18
8.	1410827	45	F	52	158	ASA II	16
9.	1410865	40	M	68	173	ASA I	13
10.	1408038	25	F	51	166	ASA II	13
11.	1408674	35	F	47	164	ASA II	14
12.	1402830	30	M	64	179	ASA I	12
13.	1402840	22	F	48	160	ASA II	19
14.	1410478	44	M	69	176	ASA I	15
15.	1402946	38	F	46	165	ASA I	18
16.	1410753	26	M	61	178	ASA II	17
17.	1410762	39	F	50	163	ASA I	15
18.	1399542	27	M	69	177	ASA II	16
19.	1410883	38	F	58	157	ASA I	14
20.	1410911	21	M	63	178	ASA II	16
21.	1410734	41	F	53	162	ASA II	13
22.	1398842	23	M	61	172	ASA I	17
23.	1408657	43	F	52	161	ASA I	16
24.	1409871	19	F	64	158	ASA II	18
25.	1408649	25	F	65	160	ASA I	13
		32.16+/- 4.3	12/13	58.9+/- 5.4	167.2+/-4.5	12/13	15.48 (1.1)

## DEMOGRAPHIC DATA PLACEBO GROUP

SLNO:	IPNO:	AGE	SEX	Wt in kg	Ht in cm	ASA GRADE	DURATION OF LARYNGOSCOPY IN SECONDS
1.	1395638	41	F	64	163	ASA II	12
2.	1393608	34	F	51	160	ASA I	17
3.	1396362	36	M	48	172	ASA II	13
4.	1400079	22	F	68	156	ASA I	15
5.	1400413	21	M	69	168	ASA II	14
6.	1400674	33	M	70	154	ASA II	16
7.	1403106	27	F	52	162	ASA II	18
8.	1402830	38	M	61	173	ASA II	13
9.	1406364	35	F	57	163	ASAI	13
10.	1403106	44	M	70	177	ASA II	19
11.	1393052	39	F	55	163	ASA I	15
12.	1393289	21	F	50	162	ASA II	12
13.	1393147	23	F	48	162	ASA II	10
14.	1403718	27	M	62	180	ASA I	11
15.	1403687	31	F	52	148	ASA II	17
16.	1407753	19	M	64	173	ASA II	13
17.	1401753	35	M	58	178	ASA I	15
18.	1406862	40	F	51	157	ASA II	18
19.	1406771	31	F	49	150	ASA I	13
20.	1416236	26	F	52	155	ASA II	15
21.	1410928	26	M	65	180	ASA II	14
22.	1410091	43	F	54	152	ASA II	12
23.	1408212	38	M	68	177	ASA II	17
24.	1407355	29	F	53	158	ASA I	16
25.	1410973	19	F	52	160	ASA II	14
		31.12+/- 5.1	10/15	57.72+/- 4.1	166.44+/- 6.4	11/14	14.5(1.7)



## DIASTOLIC BP PLACEBO GROUP im mm of Hg

SL NO:	IP NO;	PRE LARYNGOSCOPY	1mt	3mt	5mt	10mt
1.	1395638	72	80	74	68	70
2.	1393608	70	88	80	72	74
3.	1396362	76	82	72	66	88
4.	1400079	64	76	78	70	66
5.	1400413	76	82	74	66	68
6.	1400674	68	72	60	60	62
7.	1403106	60	78	70	64	66
8.	1402830	72	80	72	70	62
9.	1406364	76	94	88	80	82
10.	1403106	68	74	74	68	66
11.	1393052	70	78	74	68	68
12.	1393289	68	78	64	60	60
13.	1393147	62	66	72	66	64
14.	1403718	60	80	74	72	64
15.	1403687	64	74	76	72	68
16.	1407753	62	82	76	70	72
17.	1401753	70	88	76	70	70
18.	1406862	72	80	76	70	70
19.	1406771	74	80	74	68	70
20.	1416236	70	92	96	86	82
21.	1410928	84	94	88	80	80
22.	1410091	66	72	68	60	60
23.	1408212	72	98	90	84	82
24.	1407355	72	94	88	80	80
25.	1410973	62	74	76	76	64
		69.2	81.44	76.4	70.64	70.32

## HEART RATE PLACEBO GROUP

SLNO:	IP NO:	PRE LARYNGOSCOPY	1mt	3mt	5mt	10mt
1.	1395638	82	108	100	92	84
2.	1393608	88	110	106	100	90
3.	1396362	90	110	110	98	98
4.	1400079	94	120	120	114	98
5.	1400413	88	116	118	94	90
6.	1400674	78	104	106	94	88
7.	1403106	96	118	1110	92	90
8.	1402830	72	98	100	96	90
9.	1406364	72	98	100	96	90
10.	1403106	96	120	126	110	108
11.	1393052	80	114	113	96	92
12.	1393289	84	116	115	96	92
13.	1393147	80	114	115	98	92
14.	1403718	82	110	110	103	90
15.	1403687	80	114	113	100	88
16.	1407753	84	112	114	104	88
17.	1401753	86	113	112	100	88
18.	1406862	82	118	120	110	80
19.	1406771	94	108	98	96	96
20.	1416236	92	116	118	104	104
21.	1410928	96	108	106	94	88
22.	1410091	68	110	109	104	90
23.	1408212	82	113	112	104	84
24.	1407355	102	132	128	110	96
25.	1410973	100	126	120	106	90
		87.04	114.16	112.76	101.4	91.96

## HEART RATE LORNOXICAM GROUP

SL NO:	IP NO:	PRE LARYNGOSCOPY	1mt	3mt	5mt	10mt
1.	1403494	80	82	80	72	72
2.	1403526	80	100	92	80	80
3.	1403314	112	120	120	96	96
4.	1403146	92	104	90	88	80
5.	1402840	96	96	92	90	90
6.	1398343	88	90	90	86	86
7.	1410943	100	114	118	88	90
8.	1410827	92	104	90	90	90
9.	1410865	88	100	104	100	96
10.	1408038	76	78	74	72	72
11.	1408674	100	110	92	90	90
12.	1402830	84	98	80	80	80
13.	1402840	86	100	84	80	82
14.	1410478	90	92	90	84	86
15.	1402946	78	72	74	74	74
16.	1410753	86	98	84	80	82
17.	1410762	116	128	104	92	100
18.	1399542	92	90	88	88	88
19.	1410883	80	82	80	76	76
20.	1410911	88	90	90	86	86
21.	1410734	80	96	92	80	80
22.	1398842	92	100	96	88	88
23.	1408657	72	78	70	68	68
24.	1409871	82	86	80	80	82
25.	1408649	88	88	86	86	86
		88.72	95.84	89.6	83.76	84

MEAN ARTERIAL PRESSURE CONTROL GROUP in mm of Hg

SL NO:	IP NO:	PRE LARYNGOSCOPY	1mt	3mt	5mt	10mt
1.	1395638	91.33333	103.3333	98	89.33333	88
2.	1393608	88	105.3333	96	88	89.33333
3.	1396362	87.33333	99.33333	90	77.33333	94.66667
4.	1400079	76	93.33333	92	85.33333	82.66667
5.	1400413	90.66667	98	88	80	81.33333
6.	1400674	88.66667	96	84	80	81.33333
7.	1403106	72.66667	94	84	76	77.33333
8.	1402830	80	96.66667	90	83.33333	78
9.	1406364	92.66667	112.6667	102	95.33333	94.66667
10.	1403106	82.66667	93.33333	88	82	80.66667
11.	1393052	88	96.66667	89.33333	85.33333	88.66667
12.	1393289	82.66667	96	118	76.66667	78
13.	1393147	81.33333	90	91.33333	82.66667	81.33333
14.	1403718	73.33333	94.66667	88	82	80
15.	1403687	78.66667	88	86.66667	81.33333	78.66667
16.	1407753	83.33333	101.3333	94.66667	87.33333	88
17.	1401753	85.33333	102.6667	90.66667	86.66667	86.66667
18.	1406862	81.33333	96.66667	91.33333	84	83.33333
19.	1406771	90.66667	100.6667	92.66667	85.33333	85.33333
20.	1416236	81.33333	104	100	94	88
21.	1410928	91.33333	107.3333	98.66667	88	89.33333
22.	1410091	85.33333	96.66667	87.33333	80	80
23.	1408212	85.33333	114.6667	106.6667	100.6667	96.66667
24.	1407355	88	112.6667	101.3333	95.33333	93.33333
25.	1410973	776.66667	96	90.66667	90.66667	82
		84.1	99.75	93.57	85.47	85.09

## MEAN ARTERIAL PRESSURE LORNOXICAM GROUP In mm of Hg

SLNO:	IP NUMBER	PRELARYNGOSCOPY	1MT	3MT	5MT	10MT
1.	1403494	84	90	83.33333	85.33333	84
2.	1403526	79.33333	88	80	78.66667	76.66667
3.	1403314	69.33333	80	73.33333	70	70
4.	1403146	88	95.33333333	85.33333	84	85.33333
5.	1402840	82	92	79.33333	76	76
6.	1398343	90	96.66666667	92	83.33333	84.66667
7.	1410943	83.33333	91.33333333	80	84	83.33333
8.	1410827	84	90	81.33333	80.66667	80
9.	1410865	88	94.66666667	88	84.66667	86
10.	1408038	75.33333	76	76	73.33333	73.33333
11.	1408674	80	89.33333333	82.66667	81.33333	80
12.	1402830	90	95.33333333	88	86	86
13.	1402840	84	89.33333333	83.33333	80	82.66667
14.	1410478	90	93.33333333	87.33333	88	86
15.	1402946	95.33333	98	98.66667	90.66667	90
16.	1410753	89.33333	100	92	88	89.33333
17.	1410762	80	84.66666667	82.66667	80.66667	77.33333
18.	1399542	81.33333	80.66666667	80	79.33333	80.66667
19.	1410883	77.33333	79.33333333	76	75.33333	76.66667
20.	1410911	78	86.66666667	78.66667	76.66667	78.66667
21.	1410734	74.66667	80	75.33333	73.33333	73.33333
22.	1398842	84	90.66666667	82	81.33333	79.33333
23.	1408657	84.66667	90.66666667	83.33333	84	85.33333
24.	1409871	84	86.66666667	82	80.66667	82
25.	1408649	76	83.33333333	80	80	78.66667
		82.88	88.88	82.82	81.01	81.01