ATTENUATION OF THE HEMODYNAMIC RESPONSE TO TRACHEAL INTUBATION

A COMPARATIVE STUDY BETWEEN INTRAVENOUS LIGNOCAINE HYDROCHLORIDE AND INTRAVENOUS MAGNESIUM SULPHATE

By

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the administration of both study drug and observing the said cardiovascular responses.

A standardized anesthetic technique was used for both groups of patients. An indwelling venous cannula was inserted under local anesthesia and a running intravenous drip was set.Vital signs monitoring were monitored and chartered before induction which served as a baseline to the hemodynamic changes expected to be seen at different stages of the induction period.

Induction of anesthesia was performed by using sodium thipentone 2.5% solution titrated to the loss of the eye lash reflex, the study drugs of each allocated population sample was administered accordingly and a single attempt at cannulation of the endotracheal tube by a single operator through out the study was performed 3 minutes after the neuromuscular blocking agent was given.

Anesthesia was maintained with oxgen:nitrous oxide in a 1:2 flow ratio and expired isoflurane mean alveolar concentration (MAC) was kept at 1% while pharmacological paralysis was maintained via imtermittent bolus doses of intravenous atracurium.Patients were then reversed with intravenous neostigmine 2.5 mg and intravenous atropine at 1 mg.

Data collection consisted of pulse rate, systolic, diastolic and mean arterial blood pressure (via a non invasive blood pressure monitoring

device) at selected intervals of pre induction, post induction, post study drug adminstration and post intubation attempt.

Findings of this study when comparing the hemodynamic variables in question between the two groups revealed that although there were increases in the systolic, diastolic, mean arterial pressure, and heart rate parameters in each of the two groups these changes were statistically not significant within the respective group and also changes in the cardiovascular response varaible were not statistically significant comparing the two groups.

Thus the results of this study pointed to the fact that both intravenous lignocaine and intravenous magnesium were able to minimize the hemodynamic changes occuring during the act of intubation and more importantly, that intravenous magnesium was able to blunt the sympathoadrenomedullary responses to stimulation of the upper respiratory tract and tracheobronchial tree by the act of endotracheal cannulation.

ABSTRAK

Doktor bius telah mencuba berbagai-bagai regim farmakologi dalam usaha mereka untuk menghalang penghantaran impuls yang menyalurkan isyarat untuk respons hemodinamik tidak kira sama ada dari saluran afferen atau efferen atau pun kedua-duanya sekali walaupun tidak ada satu pun cara yang boleh di katakan sempurna kerana ke semua langkah-langkah yang telah di ilhamkan mempunyai kesan sampingannya yang tertentu.

Peningkatan tekanan darah aterial, peningkatan tekanan intra kranial, peningkatan kadar denyut nadi dan berlakunya komplikasi aritmia adalah antara kesan-kesan langsung komplikasi dari percubaan laringoskopi dan cubaan intubasi.

Sungguh pun perubahan yang di kesani berlaku di dalam sirkulasi manusia adalah bersifat sementara dan kesan langsung ini ke atas pesakit dari segi perubatan di klasifikasikan sebagai sihat adalah tidak memudaratkan tetapi kesan perubahan hemodinamik ini jika berlaku ke atas pesakit yang menghidapi sakit jantung koronari, penghidap penyakit darah tinggi, dan pesakit yang mengalami kompromi saluran darah otak adalah amat berbahaya.

Sejumlah 50 pesakit ASA I, di pilih secara rambang yang di jadualkan untuk pembedahan minor elektif ie. "excision biopsy, herniotomy, split skin grafting, removal of implant, subtotal thyroidectomy", dan memerlukan pembiusan secara total yang mana intubasi adalah satu kemestian telah di bahagikan kepada 2 kumpulan berasingan di mana masing-masing akan menerima sama ada lignocaine intravena 1.5 mg/kg berat badan (Kumpulan 1, n=25) atau pun menerima intravena magnesium

kepekatan 50% pada kadar 40 mg/kg berat badan (Kumpulan 2, n=25). Personel yang terlibat di dalam pembahagian kumpulan dan penyediaan ubatan yang berkenaan tidak terlibat di dalam pemberian ubat berikut secara intravena dan juga tidak terlibat di dalam merekod perubahan hemodinamik yang di perhatikan.

Teknik pembiusan adalah di seragamkan kepada satu standard dan di gunakan kepada kedua-dua kumpulan yang terlibat. Saluran darah vena di kanulasikan secara pemberian bius setempat dan aliran cecair di pasangkan. Tanda-tanda vital di rekodkan sebelum bermulanya induksi bius yang mana ini juga di ambil kira sebagai tanda vital asas sebelum perubahan hemodinamik di lihat berlaku.

Induksi bius di teruskan dengan pemberian sodium thiopentone pada kepekatan 2.5% sehingga tanda refleks kelipan mata tidak lagi di kesan , ubat yang telah di jadualkan untuk kajian di berikan ke dalan vena pesakit dan cubaan intubasi dari hanya seorang doktor bius yang sama sepanjang tempoh kajian di jalankan selepas 3 minit ubat penghalang neuromuskular di berikan.

Pembiusan di teruskan dengan penggunaan pembiusan gas isoflurane pada kepekatan ekspirasi MAC 1% dan oksigen : nitrous oksida pada 1:2 kadar aliran gas dan pengekalan kelumpuhan pesakit adalah dengan pemberian ubat atracurium.Setelah selesai pembedahan yang di jalankan, pesakit di sedarkan dan diberi neostigmine 2.5 mg dan atropine 1 mg.

Data yang di kumpulkan terdiri dari kadar denyut nadi, tekanan darah sistolik, tekanan darah diastolik, dan kadar tekanan darah aterial purata (MAP) pada

jangkamasa yang berlainan iaitu sebelum induksi, selepas ubatan standard induksi di berikan, selepas ubat kajian di berikan dan selepas percubaan intubasi selesai.

Perolehan keputusan hasil dari kajian yang di jalankan dalam membandingkan kedua-dua kumpulan menunjukkan bahawa walaupun kelihatan peningkatan dalam tekanan darah sistolik, diastolik dan kadar tekanan darah purata serta kadar denyut nadi di dalam kedua-dua kumpulan pesakit tetapi peningkatan ini adalah tidak penting dari segi statistik.

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TABLE OF CONTENTS

Acknowledgements	i
Abstract	ii
Abstrak	v
Table of contents	ix
List of tables	xi
List of figures	xii
INTRODUCTION	1
OBJECTIVES	7
3. LITERATURE REVIEW	8
3.1 Endotracheal anesthesia	8
3.1.1 Historical Development	8
3.1.2 Early Contributors To Endotracheal Anesthesia	10
3.2 The Respiratory System	13
3.2.1 The Pharynx	13
3.2.2 Innervation Of The Pharynx	14
3.2.3 The Larynx	17
3.3 Funtional Neuroanatomy	20
3.3.1 Afferent System	20
3.3.2 Efferent System	21
3.3.3 Laryngeal Reflexes	21
3.3.4 Glottic Closure Reflex	21
3.4 The Stress Response-Endocrine And Metabolic Alterations	23

3.4.1 Perioperative Stress 24

3.4.2 Neuroendocrine And Metabolic Manifestations 26

3.5 Pathophysiologic Responses To Intubation 29

3.5.1 Cardiovascular Responses 30

3.5.2 Central Nervous System 31

3.5.3 Respiratory 32

3.6 Lignocaine 33

3.6.1 Local Anesthetic 33

3.6.2 Structure Of lignocaine 35

3.6.3 Administration And Dosage 36

3.6.4 Metabolism 37

3.6.5 Preparation And Clinical Uses 38

3.6.6 Toxicity 39

3.6.7 Obtundation Of Hemodynamic Response 39

3.7 Magnesium: Physiology, Pharmacology, And Its Therapeutic Uses 43

3.7.1 Physiology And Metabolism 43

3.7.2 Magnesium Therapy 47

3.7.3 Magnesium In Obstetrics 49

3.7.4 Magnesium And Phaechromocytoma 51

3.7.5 Magnesium And Cardiovascular Anesthesia 52

3.7.6 Magnesium And Tracheal Intubation 53

4. METHODOLOGY 55

5. RESULTS 58

6. DISCUSSION 67

7. CONCLUSION 73

REFERENCES 74

LIST OF TABLES

3.2.1	Somatic Innervation Of The Larynx	16
3.3.2	Somatic Innervation Of The Pharynx	16
5.1	Demographic Characteristics Of The Two Study Group	59
5.2	Hemodynamic Changes Systolic, Diastolic, Mean Arterial Pressure, Pulse Rate At Preinduction And At 1 Minute Postintubation	60

LIST OF FIGURES

3.2.1 Divisions of The Pharynx 15

3.2.2 View of The Larynx At Laryngoscopy 15

3.2.3 Nerve Supply Of The Larynx 15

5.1 Systolic Blood Pressure Changes Over Time 61

5.2 Diastolic Blood Pressure Changes Over Time 62

5.3 Mean Arterial Pressure Changes Over Time 63

5.4 Pulse Rate Changes Over Time 64

1. INTRODUCTION

The pressor response to laryngoscopy and endotracheal intubation has been recognized since the early 1950's. It has been described as a symphatatic reflex provoked by stimulation of the epipharynx and laryngopharynx (Tomori Z et al 1969). The increases in hemodynamic variables such as blood pressure and pulse rate are usually transitory, variable, and unpredictable (King BD et al 1951; Forbes AM et al 1970; Siedlecki J et al 1975). Hypertensive patients are more prone to have significant increases in blood pressure whether they have been treated beforehand or not (Prys-Roberts C et al 1971). Transitory hypertension and tachycardia are of probably little consequences in the healthy individuals but either undesirable hemodynamic complications or both may be hazardous to those with hypertension, myocardial ischemia disease, or cerebrovascular insufficiency.

The frequent occurrences of cardiovascular reactions to laryngoscopy and tracheal intubation has attracted the attention of anesthetists the world over for many, many years (Burstein CL, Lo Pinto et al 1950; Burstein CL, Woloshin G et al 1950; Noble MJ et al 1959; DeVault M et al 1960; Wycoff CC et al 1960; Takeshima K et al 1964; Sagarminga J et al 1963; Gibbs JM et al 1967; Dottori O et al 1970; Forbes AM et al 1970; Prys-Roberts C, Greene LT et al 1971; Prys-Roberts C, Foex P et al 1973). The reason for this particular interest is the occasional report of sudden death following immediately on intubation (Gibbs JM et al 1967) and increasing awareness that the common appearance of hemodynamic variables such as tachycardia, hypertension, and arrhythmia after this routine procedure of modern anesthesia may be potentially hazardous to the patient population. This is especially

true in patients with a premorbid status of suffering from hypertension (Forbes Am et al 1970) and in patients with cardiovascular compromise and cerebral vascular insufficiency (Dalton B et al 1972). An array of preventive measures recommended includes among others deep anesthesia, intravenous lignocaine, beta-blockers, and administration of topical anesthesia. However all the measures mentioned are only partially effective and each may have its own set of undesirable side effect.

A study done by Robert K Stoelting in 1977 specifically looking into the aspect of the duration of performing the laryngoscopy sequence and completing the endotracheal intubation step had observed that the implementation of the various pharmacological attempts to attenuate these blood pressure and heart rate elevations (although partially successful) may be negated due to fact of prolonged laryngoscopy attempt.In this study it was shown that there were progressive increases in the mean arterial blood pressure above baseline levels and that these increase of mean arterial blood pressure were maximal after the first 45 seconds of laryngoscopy, and that prolonging the act of intubation to 60 seconds produced less than a 5 mmHg increase in mean arterial blood pressure above the value obtained after 45 seconds.

Studies of anesthesia in relation to the hemodynamic consequences of induction and endotracheal intubation done by Prys-Roberts et al in 1971 had observed that most of the patients experienced three episodes of circulatory instability that is: during induction, during and after tracheal intubation, and during the immediate period surrounding the awakening from the effects of anesthesia phase.

Reflex cardiovascular response to mechanical stimulation of the upper airway respiratory tract have been described in cats by Tomori and Widdicombe in 1969 and to the aspiration of secretions from the trachea in patients with normal cardiovascular reflexes (Corbett; Prys-Roberts et al 1969) and in patients with exaggerated cardiovascular reflexes due to autonomic over activity (Corbett et al 1969). The predominant response in man is the tachycardia produced clinically and arterial hypertension, the latter being as a result of increased cardiac output rather than increase in systemic vascular resistance (Corbett et al 1969). That these reflex responses were attributed to and mediated by increased symphatatic nervous activity is based on circumstantial evidence in man although in has been shown in cats by Tomori and Widdicombe 1969.

They observed that mechanical stimulation of four areas of the upper respiratory tract, the nose, the epipharynx, the laryngopharynx, and the tracheobronchial tree, induced reflex cardiovascular responses associated with enhanced neuronal activity in the symphatatic nerve fibres.

The cardiovascular responses, tachycardia and arterial hypertension, and the enhanced symphatatic neuronal activity were most pronounced during stimulation of the epipharynx whereas those arising from the mechanical stimulation of the tracheobranchial tree were the least marked.

Once the endotracheal tube was in position and the laryngoscope withdrawn the hypertension and tachycardia quickly subsided but the dysryhthmia tended to persist for up to 2-3 minutes.

The introduction of a foreign object into the upper respiratory has been almost always associated with cardiovascular disturbances (Siedlecki et al 1975). As mentioned before the commonly encountered responses are arterial hypertension, tachycardia and cardiac dysrhythmias. Although these cardiac manifestations during anesthesia are recognized there is little documented evidence on the mechanism giving rise to its production. Alpha and Beta-adrenergic receptor blockade have been used to minimize these changes and successful results have been reported following ganglion blockade (Siedlecki 1975).

The basis for adrenergic blockade is the assumption that increases in plasma catecholamine concentrations could contribute to the cardiovascular changes seen during intubation. A study done by Russel WJ 1981 and a replication study by Derbyshire DR et al 1983, with variations in the collection of blood sample sites, and the use of differing neuromuscular blocking agents revealed that there were increases in the arterial pressure and plasma norepinephrine concentrations although the serum levels of epinephrine and dopamine did not change significantly. On this basis it can be postulated that intubation is associated with a significant increase in symphatatic neuronal activity.

Studies of young normotensive subjects (Takeshima, Noda, and Higaki, 1964; Forbes and Dally, 1970) have established that the mean increase in arterial blood pressure due to laryngoscopy and intubation was of the order of 20-25 mmHg, with maximum changes of about 40-45 mmHg.Hypertensive patients whether treated or not, are prone to much greater changes in arterial blood pressure than normotensive patients within the same age group.Dingle (1966), in a series of 19 hypertensive patients, found a mean increase in systolic arterial pressure of 35 mmHg.

The endeavor to perform this comparative study between the use of intravenous lignocaine 1.5 mg/kg which has been shown by a number of studies to be able to obtund the hemodynamic consequences of intubation and the possible alternative of using intravenous magnesium 40 mg/kg in attenuating the pressor response, to endotracheal cannulation stems from the fact that a myriad of pharmacological methods had been studied and advocated in minimizing the cardiovascular reflex response but none appears to be satisfactory. Although lignocaine is advocated widely (also being practiced in the Anesthetic Department of University Sains Malaysia) and was chosen as the standard agent for the attenuation of the pressor response, its effectiveness has been questioned in more severe cases (Connell H et al 1980) and may be harmful to the fetus in the pregnant lady (Ralston DH et al 1978); with the opioids there the risk of fetal depression: the vasodilators may produce serious hypotension; and the beta blockers may produce fetal hypoglycemia.

The properties of intravenous magnesium among others that is the ability to inhibit catecholamine release (Lishajko F 1970) and to control both catecholamine release and pressor response make it a potential alternative in our continuing efforts to find the most ideal agent to minimize the hemodynamic response to tracheal intubation.

2. OBJECTIVE OF THE STUDY

The aim of this study was:

1. To compare the effectiveness between intravenous magnesium sulphate 50% at a dose of 40 mg/kg and intravenous lignocaine hydrochloride at a dose of 1.5 mg/kg in attenuating the hemodynamic responses to endotracheal intubation.

It is hoped that this study would be helpful in eliciting the clinical use of magnesium in terms of its ability to obtund the pressor response to the manipulation of the upper respiratory tract during the act of endotracheal intubation.

Development of the endotracheal technique was stimulated by the need for providing of safe anesthesia during operations of the neck, head, and oral cavity particularly manifested by European surgeons and the controls of respiration during thoracic surgery at time coming in particular from surgeons from the United States.

The first period of development (1900-1910) was largely influenced by the work of Franz Kahn who used a tube of coiled flat metal 12 to 15 cm in length that he inserted into the trachea with a curved introducer by the sense of touch. After insertion of the tube Franz Kahn used gauze soaked in oil to pack of the passage of the pharynx.

The second period of endotracheal anesthetic development revolved around the so called insufflation method of anesthesia administration, which originated from the need to maintain an expanded lung during surgical pneumothorax. In New York in 1909 Meltzer and Auer advanced this technique and later showed when a catheter is inserted into the trachea as far as the bifurcation of the trachea and if air is blown into the catheter full oxygenation can be maintained and that the lung would remain expanded when the chest was opened. This was called a high pressure technique whereby gas exchange actually depended on the flushing principle.

A third period of development ensued with the break of World War I not only in technique but also in physiology. It was found that the insufflation technique obviously lacked a great deal in maintaining normal respiratory physiology and there was a return to true endotracheal reparation stimulated by the efforts of Magill and Rowbotham anesthetists for the British Army Plastic Unit. They inserted a wide bore

rubber tube into the trachea through which the patient not only inhaled but exhaled thus the anesthetic system employed was semi closed.

Until 1912 the development of endotracheal anesthesia proceeded independently of progress being made in the field of laryngoscopy especially so in the invention of the laryngoscope. The work of one named Chevalier Jackson revolutionized laryngologic and endoscopic procedures but the anesthesiologists had neglected the aid of the laryngoscope. In the same year of 1912 Elsberg reported his use of the Jackson's instrument in endotracheal anesthesia and laryngeal intubation and ushered in the modern endotracheal anesthesia. The laryngoscope now served to reduce the uncertainty inaccuracy and trauma of performing blind intubation.

3.1.2 Early Contributors To Endotracheal Anesthesia

1000-Avicenna.First reported human tracheal intubation (Arabian).

1543-A. Vesalius performed intubation of animal trachea.

1667-Robert Hooke demonstrated the technique of intubation to the Royal Society of London.

1792-Curry performed the first endotracheal intubation.

1858-John Snow used the tracheotomy technique in the rabbit with the wide bore tube and to and fro breathing from the reservoir bag.

1871-Friedrich Trendelunberg used Snows technique in humans but added an inflatable cuff to prevent aspiration of blood during the operations on the upper airway.

1880-William Mac Ewan performed endotracheal as it is known today. He inserted a metal tube through the mouth into the trachea by the sense of touch.

1887-J. O'Dwyer and G. E. Fell performed their classic work on oral intubation of the trachea for diphteria membrane obstruction and treatment of apnea from opium poisoning.

1893-V. Eisenmonger modified a metal orotracheal tube to have an inflatable cuff with a pilot balloon to indicate degree of inflation.

1895-R.Kristen originated the laryngoscope and the art of direct laryngosopy but the tactile method and insufflation prevailed until 1910.

1900-1910-Franz Kuhn of Cassel, Germany a surgeon used a flexible coil of metal to provide an orotracheal airway for surgery of upper airway passages. He employed and taught most principles of inhalation endotracheal anesthesia but the insufflation technique remained the order of the day at that particular time.

1910-C. A. Elsberg of Mount Sinai Hospital, New York taught and practiced direct laryngoscopy and intubated the trachea with a metal endotracheal tube but continued the insufflation technique of anesthesia.

1910-G. M. Dorrence reintroduced the cuff. He constructed a metal tube with a cuff for treatment of injuries of the chest and lungs and used the inhalation anesthesia technique.

1911-Paluel Flagg developed a coiled metal spiral endotracheal tube covered with a sheath of penrose drain. He developed a laryngoscope for anesthetist for direct laryngoscopy. The inhalation technique as we know it today in contrast to the insufflation technique prevailing was described in his text "The art of Anesthesia". Subsequently the insufflation technique was displaced by the inhalational technique.

1914-1918-I. W. Magill and E. S. Rowbotham developed a single wide bore endotracheal tube and the technique of blind nasotracheal intubation for the British Army Plastic Unit during the World War I.Magill originated an intubating forceps to guide the tubes into the trachea.

1928-A. Guedel and R. Waters designed an endotracheal tube and a balloon cuff with a piolet tube to seal off the trachea from the upper airway.

3.2 THE RESPIRATORY SYSTEM

The respiratory system is separated into an upper airway tract and a lower respiratory tract with the former consisting of two main anatomical structures namely the nose and the pharynx and the latter consisting of the larynx, trachea, and the lungs.

3.2.1 The Pharynx

The pharynx is a midline, funnel shaped structure, longitudinal, muscular tube whose dual function is to convey air to and from the larynx and ingested food to the oesophagus.

It extends from the base of the skull above, passes down behind the nose, mouth, and the larynx and becomes continuous with the oesophagus at the level of the sixth cervical vertebra.

The roof of the pharynx is limited above by the body of the sphenoid and the basilar region of the occipital bones. The posterior wall is separated from the anterior surfaces of the bodies of the upper 6 cervical vertebrae by the retropharyngeal space and prevertebral fascia, which permits free movement during deglutition and phonation. The anterior wall is deficient, with openings into the nasal cavity, oral cavity and the larynx.

The pharynx is topographically and functionally separated into thirds- an upper nasopharynx, a middle oropharynx, and a lower laryngopharynx.

3.2.2 Innervation Of The Pharynx

The principal innervations of the pharynx are via the pharyngeal plexus, which is formed on the external surface of the middle constrictor muscle, opposite the greater horn of the hyoid bone. It arises from the pharyngeal branches the cranial nerves IX, X, and XI along with branches from the superior cervical symphatatic ganglion. From this plexus, branches penetrate into the substance of the pharynx and are responsible for much of the innervations to this region. The glossopharyngeal (IX) is the principal sensory nerve, and the cranial part of the accessory (XI) via the vagus (X) is the main motor supply. The symphatatic component is largely vasomotor in nature.

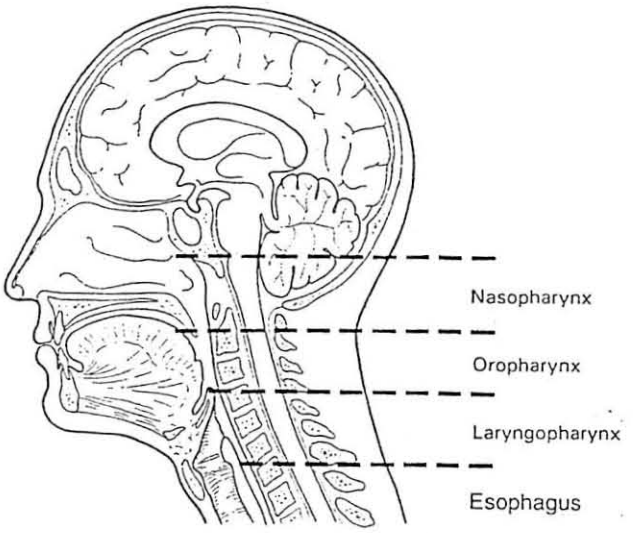

Figure 3.2.1 Divisions of the pharynx

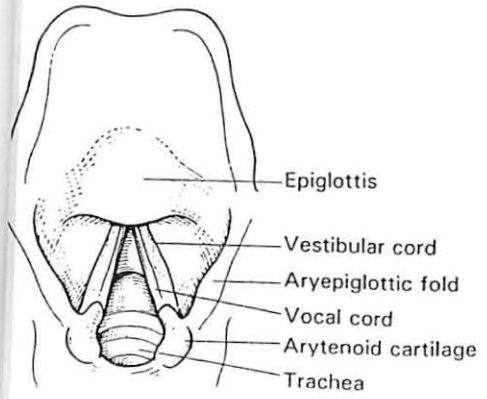

Figure 3.2.2 View of the larynx at laryngoscopy

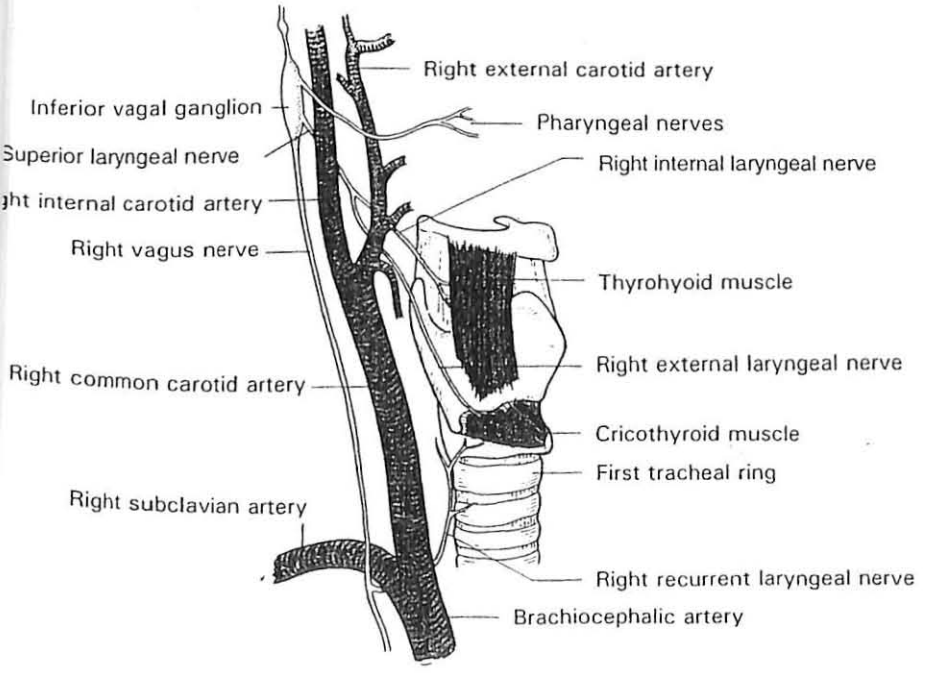

Figure 3.2.3 Nerve supply of the larynx

SOMATIC INNERVATION OF THE PHARYNX	
Nasopharynx	
Sensory	Trigerminal (V) via pterygopalatine ganglion
	Glossopharyngeal (IX) to lower regions
Oropharynx	
Sensory	Glossopharyngeal (IX)
Taste	Glossopharyngeal (IX) to region of palatoglossal and oropharynx
	Facial (VIII) and glossopharyngeal (IX) to soft palate
	Vagus (X) via branch of superior laryngeal nerve to region of epiglottis
Laryngopharynx	
Sensory	Glossopharyngeal (IX)
Motor Innervation	
Pharyngeal plexus to all muscles of pharynx and soft palate except:	
	Stylopharyngeus via glosopharyngeal (IX)
	Tensor veli palatini via trigerminal (V)

Table 3.3.2 Somatic innervation of the pharynx

SOMATIC INNERVATION OF THE LARYNX	
Sensory	Vagus (X) via the internal laryngeal nerve to mucosa above vocal folds and recurrent laryngeal nerve-mucosa below vocal folds.
Motor	Accesory (XI) distributed through vagus (X) via recurrent laryngeal nerve to all Intrinsic muscles except cricithyroid (external laryngeal nerve to X)
Taste	Vagus (x) to epiglottis and back of tongue

Table 3.2.1 Somatic innervation of the larynx

3.2.3 The Larynx

The larynx is the first part of the lower respiratory tract and is formed from a complex arrangement of cartilages, muscles, ligaments and membranes. It is a midline structure, which extends the third and the sixth cervical vertebrae in the adult, although in the infant it may only extend as far as the inferior border of the fourth cervical vertebrae. It is superficial and readily palpated, as it is covered only by skin, by the platysma muscle and superficial and deep layers of the fascia.

Posteriorly it is separated from the cervical column by the pharynx and the thin prevertebral muscles. It communicates with the laryngopharynx behind and with the trachea below. Its rigid skeletal structure ensures that it remains patent at all times, which is essential for its primary role as a respiratory passage. It has also developed a protective valve mechanism at the inlet to prevent entry of foreign material from the laryngopharyngeal passageway.

In view of the complex function of the larynx it is not surprising that its anatomy is somewhat intricate and highly specialized. The larynx has had to compromise between the need for rigidity for its respiratory purpose and the need for mobility to fulfil its function as a valve and the mechanism for phonation.

The larynx itself is formed from 9 cartilages, 3 of which are midline and singular and 6, which come in pairs and are more laterally placed. The 3 midline cartilages are the epiglottis (elastic), the thyroid (hyaline), and the cricoid (hyaline), and the 3 more lateral pairs are the arytenoids (hyaline and elastic), the cuneiforms (elastic), and the corniculate cartilages (elastic).

The **thyroid cartilage** is the largest of the laryngeal cartilages and is a midline structure composed of 2 quadrilateral laminae fused anteriorly in the midline to form the laryngeal prominence. The posterior border of each lamina is free and receives the fibres of the stylopharyngeus and the palatopharyngeus muscles. This border is extended upwards to form the superior horn and downwards to form the inferior horn. The superior border of the thyroid cartilage is connected to the superior border of the hyoid bone by the fibrous thyrohyoid membrane, which is pierced laterally by the internal laryngeal nerve and the superior laryngeal artery. The inferior horn of the thyroid articulates via synovial joints with the cricoid cartilage below.

The **cricoid cartilage** is somewhat smaller than the thyroid cartilage but is thicker, stronger and more fixed in position. It lies at the level of the 6 cervical vertebrae and is the only rigid region of the larynx. It articulates with the thyroid cartilage above and is connected below to the tracheal ring via the cricotracheal membrane. It is shaped like a signet ring with a broad posterior lamina and a narrower anterior arch. The upper border of the cricoid cartilage is connected to the thyroid cartilage by the cricothyroid membrane, which is also known as the conus elasticus and forms part of the important fibro elastic membrane of the larynx.

The **epiglottis** is shaped like a leaf or perhaps more realistically like a bicycle seat. It stands vertically behind the hyoid bone and the root of the tongue and overhangs the laryngeal inlet. It is broad superiorly with a free border, which tapers inferiorly to attached to the inner surface of the thyroid cartilage by the thyroepiglottic ligament. The anterior surface of the epiglottis is attached to the hyoid bone via the

hyoepiglottic ligament. The mucous membrane covering this surface is reflected onto the root and sides of the tongue as one median and two lateral glosso epiglottic folds and the depressions that form between them are the valleculae.

The **laryngeal cavity** is divided into 3 topographical regions:

1. An upper vestibule or supraglottic region, which extends from the laryngeal inlet to the vestibular folds or cords.
2. The ventricle or glottic region, which extends between the vestibular and the vocal folds.
3. An infraglottic region, which extends from below the vocal folds to the beginning of the trachea.

The **laryngeal inlet** is the opening into the larynx from the laryngopharynx. It is bounded anteriorly by the upper edge of the epiglottis, posteriorly by a membrane between the arytenoids cartilages, and laterally by the aryepiglottic folds containing the cuneiform and corniculate cartilages.

3.3 FUNCTIONAL NEUROANATOMY

Function of the larynx is dependant on the complex and timely interactions of all the structures described as above. This activity is mediated by the ever present central nervous system and the peripheral neurologic connections of the upper respiratory tract. The functional neuroanatomy of the larynx would be more placed into emphasis in the discussions below whereby its functions are profoundly affected by and are intimately associated with those of the entire upper aero digestive tract.

3.3.1 Afferent System

Sensation from the supraglottic structures reaches the central nervous system via the internal branch of the superior laryngeal nerve found on both sides of the normal human anatomy. Afferent impulses arising in the glottis and subglottic regions are transmitted by way of the recurrent laryngeal nerves. Proprioceptive and sensory nerve endings are situated most densely on the laryngeal surface of the epiglottis and less is to be found on the true vocal cords. More touch receptors are concentrated toward the posterior commissure than near the anterior and temperature control receptors are almost found in the supraglottic larynx. Information thus obtained reaches the central nervous system through the nodal ganglion to the tractis solitarius where further central and integrative connections take place.

3.3.2 Efferent System

Efferent nerve fibers destined for the larynx arise from the nucleus ambigus of the medulla. All the intrinsic laryngeal muscles are innervated via the recurrent laryngeal nerves. Only the interarytenoids muscles are bilaterally innervated. The cricothyroideus muscles, which are not intrinsic to the larynx, are innervated via the external branch of the superior laryngeal nerves.

3.3.3 Laryngeal Reflexes

The protective, respiratory and the phonatory functions as were mentioned above are mediated through several polysynaptic reflexes at the level of the brainstem. Whereas the glottic closure reflex, which is essential for the protection of the airway is entirely automatic, the other reflexes can at least be initiated , and to some degree be modified voluntarily.

3.3.4 Glottic Closure Reflex

Touch and chemical or thermal stimulation of the supraglottic mucosa subtended by the superior laryngeal nerves results in the involuntary forceful closure of the entire larynx. The sequence of events is anatomically the same as that described for effort closure. In man unilateral superior laryngeal stimulation does not result in

the contra lateral adductor activity seen in most lower animals. This may account for at least in part for the tendency of unexpected aspiration of saliva associated with unilateral superior nerve palsy. If the laryngeal closure reflex becomes overly sensitive laryngospasm may result. It is characterized by electrical activity in the adductor fibers long after instigating mucosal stimulus has ceased. It can be abolished by heavy sedation particularly with barbiturates and also decreases with hypoxia. This may explain why patients are rarely in danger of asphyxia since in very severe cases the patient in question simply faints from hypoxia at which the spasm breaks.

3.4 THE STRESS RESPONSE-ENDOCRINE AND METABOLIC ALTERATIONS

The human body naturally will try its very best to maintain its normal environment. Hormones mediate much of the body's homeostatic response to various stressful stimulus. Physical injury resulting in differing levels of tissue destruction and reduction in the circulating blood volume constitutes a threat to life and the outcome is dependent on the efficacy of the human body's defense mechanism. It was thought (Selye H 1950) that a number of different stimuli otherwise known as stressors induce similar homeostatic reactions with the sole aim of trying to maintain and contributing towards the maintenance of the 'milieu interieur'.The metabolic and hormonal response to trauma is an important component of the protective alarm reaction or the ''general adaptation syndrome''.

Recent studies have shown that it has become obvious that a complex interplay between the various systemic and local factors is taking place (Minnear et al 1983). Some of the many factors influencing quantitively and qualitatively the metabolic response and alterations seen in patients experiencing tissue trauma. The neuroendocrine activation induced by tissue trauma is considered the most important stimulus for the metabolic alterations (Brizio et al 1984).

As hormones play a much important role in mediating body's homeostatic response to stress the circulating concentrations of the so called flight or flight hormones norepinephrine (noradrenaline), cortisol, epinephrine (adrenaline) and growth hormone increase in response to most acute stress. The plasma levels and

activities of these and other minerals involved vary following different stressful situations. Although the stressors have existed for quite some time albeit for centuries the availability of sensitive and specific hormonal assays are relatively new. Apparently for this reason the endogenous stress responses continue to be defined.

Evidence is accumulating (Anad et al 1987) to support the concept that modulation of the various stress response may to an extent improve outcome from surgery. Newer anesthetic analgesic approaches have permitted a reduction in the perioperative experienced by most patients. In this study the stress response is used to mean the hemodynamic exhibition presented clinically as a result of the stress induced changes in the circulating hormone and mineral concentrations during the perioperative period.

3.4.1 Perioperative Stress

Perioperative anxiety, induction of anesthesia, endotracheal intubation, vascular cannulation, anesthetic related and surgically induced tissue trauma, visceral pain, and the process of recovering from surgery are each stressful in its own way and very much contributes to the responses as described below. In addition to the expected perioperative events the spectre of the unwanted complications such as sepsis, hemorrhage, hypothermia, pneumonia, pneumothorax and a number of other complications may also alter the measurable stress response.

The level or degree of each stressful component is probably central to the amount of the observed hormonal and metabolic changes observed. Higher grades of surgical and anesthetic stress are reflected perioperatively by increased circulating