LOW DOSE SUCCINYLCHOLINE TO FACILITATE LARYNGEAL MASK AIRWAY INSERTION

This dissertation is in partial fulfillment of the requirement for the M.D. Degree (Branch X) Anaesthesiology Examination of The Tamil Nadu Dr. M. G. R. Medical University, Chennai, to be conducted in April 2013.

C E R T I F I C A T E

This is to certify that the dissertation entitled '**Low dose Succinylcholine to facilitate Laryngeal Mask Airway Insertion'** is the bonafide original work of Dr. Leah Maria Raju, towards the M.D. Branch-X (Anaesthesiology) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai, to be conducted in April 2013.

Signature of the Guide

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Ref: 11/2011

March 8, 2012

The Treasurer
C.M.C.

Dear Mr. Denzil,

Sub: **FLUID Research grant project NEW PROPOSAL:**
Low dose succinylcholine to facilitate laryngeal mask airway insertion.
Dr Leah Maria Raju (Emp. No. 28871), Anaesthesia, Dr Sarah Ninan, Anaesthesia, Dr Anita Shirley, Anaesthesia.

Ref: IRB Min. No. 7661 dated 18.11.2011

The Institutional Review Board at its meeting held on November 18, 2011 vide Min. No 7661 accepted the project for 1 year at a total sanction of ₹ 35,000/- (Rupees Thirty five thousand only). Kindly arrange to transfer the sanctioned amount to a separate account to be operated by Drs. Leah Maria Raju and Sarah Ninan.

Thank you.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr Leah Maria Raju, PG Registrar, Department of Anaesthesia, CMC
Dr Sarah Ninan, Anaesthesia, Professor, Department of Anaesthesia, CMC
File

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TITLE OF THE ABSTRACT: Low dose Succinylcholine to facilitate Laryngeal Mask Airway insertion

DEPARTMENT: Anaesthesiology

NAME OF THE CANDIDATE: Dr. Leah Maria Raju

DEGREE AND SUBJECT: MD, Anaesthesiology

NAME OF THE GUIDE: Dr Sarah Ninan

OBJECTIVES:

1) To prove that low dose Succinylcholine facilitates Laryngeal Mask Airway insertion.

2) To ascertain the lowest acceptable dose of Succinylcholine that is needed for smooth LMA insertion.

3) To ascertain if use of Succinylcholine, decreases Propofol consumption.

4) To compare haemodynamics, in the three groups.

METHODS: clinical and statistical

This is a prospective, double blinded, randomized control trial of 283 patients randomized into three groups- placebo, 0.1mg/kg and 0.25mg/kg of Succinylcholine. Patients excluded were ASA > II, age < 20 or > 65, BMI > 30, oral surgeries and difficult airways. Patients were induced with 2mg/kg of Propofol, after 2µgms/kg of Fentanyl. The study drug was given. After 60 seconds a classic LMA was inserted by the standard method by a single investigator. Jaw relaxation, coughing, gagging, movement, laryngospasm, ease of insertion, number of attempts, Propofol usage and haemodynamics were assessed. Statistical methods used were ANOVA with Bonferroni's t test, chi square test and Fischer's test. p value <0.05 was considered statistically significant.

RESULTS:

There was equal distribution of patients in all three groups. Demographically age, weight, height and BMI were equally distributed, though males were more than females. Jaw relaxation was significantly better in the 0.25mg/ kg Succinylcholine group. There was no significant difference in coughing and

gagging in the groups, but patient movement was more in the Placebo group. Two patients in the placebo group experienced partial laryngospasm. Overall insertion conditions were significantly better in the 0.25mg/kg group compared to the other two groups. Propofol consumption was significantly more in the placebo group. The study concludes that 0.25 mg/kg Succinylcholine facilitates insertion of the Laryngeal Mask Airway.

AIM

The aim of this study is to prove that low dose Succinylcholine facilitates Laryngeal Mask Airway insertion.

OBJECTIVES

1) To prove that low dose Succinylcholine facilitates Laryngeal Mask Airway insertion, leading to lesser attempts at insertion.

2) To ascertain the lowest acceptable dose of Succinylcholine that is needed for smooth LMA insertion, avoiding its side effects. Comparing placebo, 0.1mg/kg of Succinylcholine and 0.25mg/kg of Succinylcholine.

3) To ascertain if use of Succinylcholine, decreases Propofol consumption.

4) To compare haemodynamics, in the three groups.

INTRODUCTION

Ambulatory surgery is upcoming in all parts of the world as life becomes more fast pace and time is a limited commodity. In this setting general anaesthesia using the Laryngeal Mask Airway is widely used. Laryngeal Mask Airway insertion is accomplished using Propofol as it helps blunt the laryngeal reflexes well, when compared to other induction agents. (1)

Often though it has been seen that Propofol as a sole agent is not sufficient to prevent patient movement, coughing and gagging.(2) Additional doses of Propofol are required to prevent these undesirable airway reflexes and multiple insertion attempts needed. These can be associated with adverse haemodynamic changes and airway trauma.

Numerous adjuvants have been studied and proven to aid insertion of the Laryngeal Mask Airway eg: Midazolam,(3) low dose Rocuronium,(4) Fentanyl(5) and Remifentanyl(2); thus reducing the Propofol requirements and avoiding the adverse haemodynamic changes that can occur with large doses of propofol. These also aid in smooth Laryngeal Mask Airway insertion, avoiding unnecessary airway trauma.

Succinylcholine is a quick onset, short acting depolarizing muscle relaxant. It is a time tested drug, easily available and cost effective. The use of Succinycholine to aid insertion of the Laryngeal Mask Airway is advantageous as it avoids depression of the respiratory centre and has no influence on consciousness, unlike opiods and benzodiazepines. Use of Succinylcholine to facilitate Laryngeal Mask Airway insertion has been studied in the past. Succinycholine has been

proven to facilitate Laryngeal Mask Airway insertion, with and without(6) an additional agent such as Fentanyl or Midazolam. Most of these studies used a single arbitrary dose and did not compare two doses to get an ideal dose. (7),(8), (3). This study compares two doses of Succinylcholine and placebo and aims to identify the ideal dose of Succinylcholine required to facilitate Laryngeal Mask Airway insertion.

REVIEW OF LITERATURE

The review of literature is divided into the following topics:

A) Ambulatory surgery-history, current standing, advantages,

B) The Laryngeal Mask Airway- history, description, classification -types, Laryngeal Mask Airway verses the Endo Tracheal Tube, Laryngeal Mask Airway in ambulatory surgery, systemic changes

C) Use of the Laryngeal Mask Airway- size, checking the LMA and prepration of the mask, indications, contraindications, induction, insertion, cuff inflation and assessment of position and function, complications

D) Succinylcholine- history, pharmacokinetics, pharmacodynamics, mechanism of action, Dibucaine number, clinical uses and side effects

E) Studies on various adjutants to aid Laryngeal Mask Airway insertion

A) AMBULATORY SURGERY

Ambulatory surgery or day care surgery is clinical admission for a surgical procedure, with discharge of the patient on the same working day.

History

The first ambulatory surgery centre was started in Arizona, USA in 1970, by two physicians who felt the need for timely, convenient and comfortable surgical services for patients. Ambulatory surgery existed in 1960s, but in conjunction with hospitals. In 1973 the American Society of Anaesthesiologists released the "Guidelines for Ambulatory Surgical Facilities," a list of nine criteria approved by the ASA House of Delegates. In the 1970's and 80's there was rapid growth and numerous centres opened up.

Current standing

Currently two thirds of surgeries performed are in the ambulatory setting.(9) In the year 1998-1999, statistics showed that 65% of elective surgery was performed in the ambulatory setting in the United Kingdom, and 70% of the same in the United States of America.(10) In developing countries too ambulatory surgery is fast becoming the preferred procedure. In India with the ever expanding load of patients, low doctor to patient ratio and need for more beds; ambulatory surgery is fast becoming the preferred

choice. “The day care market in top 10 cities of India is expected to grow from `1,800 Cr in 2010 to `4,600 Cr in 2015 at a CAGR of 20 percent”, according to the CEO of Patni Health Care.

The advantages

The concept of ‘Day Care’ Surgery was welcomed by patients, nurses, surgeons and anaesthesiologists.

For the patient it meant lesser duration of hospital stay, early return to normal daily activities, less leave from work, and most importantly less costs incurred.
For the nurses it meant dealing with less morbid patients and visualizing quick post operative recovery. For the surgeon too quick recovery was satisfying and the fast pace, challenging. For the anaesthesiologist it meant modifying the techniques and drugs that were routinely used in the past, to ensure that same day discharge was a reality.

Ambulatory surgery has become so specialized today that specialized ambulatory surgery teams have been proven to contribute to decreased surgery recovery room length of stay(11).

Early recovery is aimed at by the entire team, the surgeons altering their technique and the anaesthesiologist altering theirs too accordingly. In this light the Laryngeal Mask Airway came to be one of the answers to what anaesthesiologists were looking for to enhance early recovery. Though the Laryngeal Mask Airway was first brought about with the difficult airway in mind, it’s use as an alternative to the endotracheal tube in the ambulatory setting was a discovery that was welcomed. Numerous studies were done in the early nineties proving that the use of the Laryngeal Mask Airway enhanced early recovery (12)(13)(14)(15). This study was done in the ambulatory surgery centre of

this hospital. It included general surgical procedures like Examination Under Anaesthesia and Lay Open Fistulae, haemorroidectomies, lipoma, breast lump excisions, Orthopaedic procedures like implant exits and knee arthroscopies, Urological procedures like cystoscopies, circumcisions; and ENT procedures like tympanplasties.

B) THE LARYNGEAL MASK AIRWAY

History

First designed by Dr. A I I Brain, the Laryngeal Mask Airway was made to combat the difficult airway. The first skill taught to any inspiring anaesthesiologist is how to handle the airway. Upper airway obstruction is the most common complication of general anaesthesia and can be life threatening if not overcome(16). The art of holding the face mask using the head tilt, chin lift and jaw thrust is life saving in many situations. The Guedel's oral airway improves patency. These methods though can be associated with aspiration of gastric contents, and can be difficult in patients with beards, obesity, facial deformities, those who are edentulous etc. As these methods also required the anaesthesiologist's hands to be 'tied', endotracheal tube insertion came as a breakthrough. It was first introduced in 1878(16). Yet this too has problems of its own. Muscle relaxation is needed, noxious airway reflexes can be stimulated and the incidence of sore throat and injury to the laryngeal apparatus is higher(17). Securing the endotracheal tube in the correct position in patients with difficult airways is not always easily accomplished.

With all this in mind Archie Brain devised the Laryngeal Mask Airway; a mask that was smaller than the face mask and could slip into the mouth and be positioned comfortably over the laryngeal apparatus, providing a conduit for air, oxygen and anaesthetic gases to pass into the trachea and lungs(16). He made plaster casts of the cadaveric pharyngeal space to understand it's anatomy. He realized the space was boat shaped and improvised with the Goldman dental mask, detaching the black rubber cuff and drawing it into the shape of an inflatable rubber boat. The proximal end was attached to a tube to complete what then became the Laryngeal Mask Airway.

THE GOLDMAN DENTAL MASK

Archie Brain went through long hours of work trying to bring about an acceptable device. He was born in Japan, during the World War 2, when his father was the British consul in Kobe. Similar to how Thomas Alwa Edison described his invention, the invention of the Laryngeal Mask Airway was "1% inspiration in 1981 and 99% perspiration over the next ten plus years"(18). Contrasting Edison who had numerous co workers, Archie Brain singlehandedly worked in a small workshop, developed different prototypes and tested them on his patients. It probably would be much harder today considering the strict and regulated research environment that currently exists (18).

The first prototype Laryngeal Mask Airway was used in 1981, in a forty year old male who underwent an elective inguinal hernia repair(19). Gradually the Dunlop Rubber Company made some latex and later on silicon masks. The first independent clinical trial was carried out in 1987 in the Northwick Park Hospital and in a year's time the design was finalized and different sizes available(20).

Description

The classic Laryngeal Mask Airway consists of three main parts 1) a shaft proximally 2) an elliptically shaped inflatable mask distally which lodges over the pharynx and the larynx and 3) a mask inflation line. The mask is an inflatable cuff and has a pilot balloon to ensure the same.

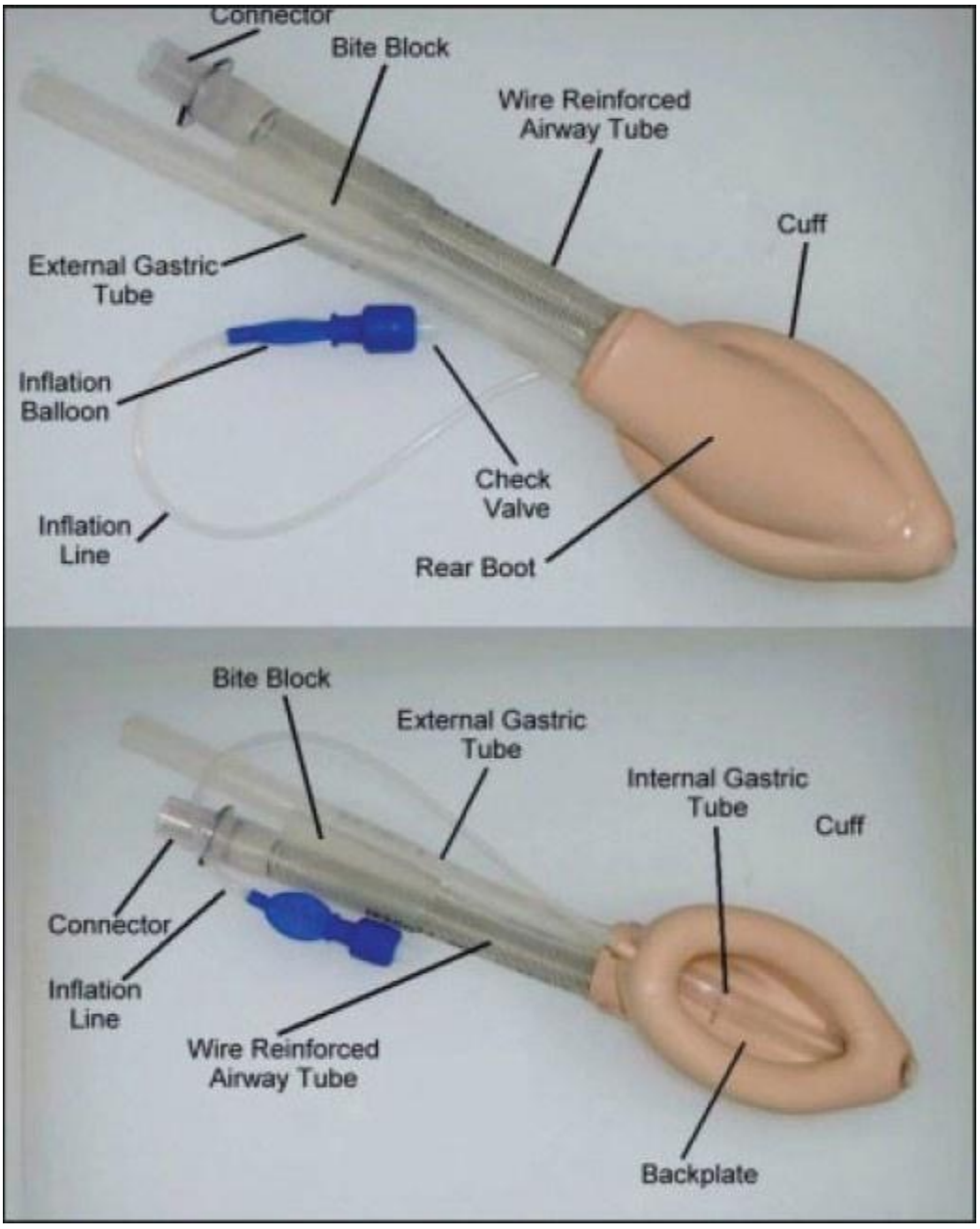
The shaft is slightly curved, so that it stays aligned with the axis of the airway, semirigid so that it does not bend on itself and semitransparent so that secretion or regurgitant material can be visualized immediately. There is a black line along the posterior border of the shaft that allows orientation of the position of the tube. The aperture at the distal end of the tube that opens into the lumen of the mask is protected by two flexible vertical rubber bars, which prevent the epiglottis from obstructing the airway.

The inflatable mask is elliptical in shape. It has a broader, rounded proximal end and a narrower distal end. The mask is semi rigid, concave, and is attached to a shield like backplate. The concave aspect of the mask is called the bowl.

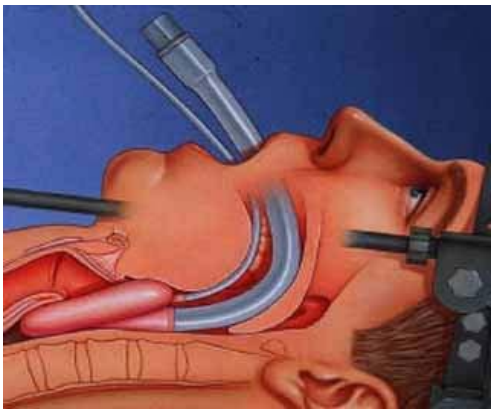
The mask inflation line attaches to the proximal part of the mask in the midline and has four parts, the inflation line, inflation balloon or pilot balloon, a metallic valve and a syringe port. The valve is made of polypropylene and it has a stainless steel spring(21).

On inflation the cuff conforms to the anatomy of the upper airway. The bowl of the cuff faces the space between the vocal cords. Thus it acts as a device to connect the artificial airway to the upper end of the respiratory tract in an end to end fashion. A face mask seals against the face and the endotracheal tube penetrates too deep into the respiratory tract. Dr Brain

wrote in his diary in May 1981, "Better, use a loop fitting into the anatomical loop of space surrounding the larynx, with a projection downwards into the oesophagus, which could be hollow, to drain regurgitant fluid"(16)



THE CLASSIC LARYNGEAL MASK AIRWAY



THE LARYNGEAL MASK AIRWAY IN POSITION

Types

Various types of Laryngeal Mask Airways are available. The term Supraglottic Airway refers to a family of devices that enable ventilation and oxygenation without an passing through the vocal cords, such as the Laryngeal Mask Airway. They can be broadly classified based on the mechanism of laryngeal sealing or by the evolution of the device(22).

CLASSIFICATION OF SUPRAGLOTTIC AIRWAYS BASED ON SEALING MECHANISMS

- Perilaryngeal sealers: The LMA family, i-gel, air-Q Intubating Laryngeal Airway (airQ ILA)
- Pharyngeal sealers: Combitube, the Streamlined Liner of the Pharynx Airway (SLIPA), the Laryngeal Tube
- Both: The Cobra Perilaryngeal Airway (CobraPLA)

CLASSIFICATION OF SUPRAGLOTTIC AIRWAYS BASED ON EVOLUTION

- First-generation devices: Simple airway tubes-

The laryngeal mask airway [classic LMA (cLMA)], flexible LMA (fLMA), unique LMA (ULMA) and The Cobra Perilaryngeal Airway (CobraPLA)

- Second-generation devices: With addition of Drainage tube-

Proseal LMA (PLMA), i-gel, Laryngeal tube, LMA Supreme, Streamlined Liner of the Pharyngeal Airway (SLIPA)

Laryngeal Mask Airway verses the endotracheal tube

After so many years of use of both the Laryngeal Mask Airway and the endotracheal tube; the preference of each in different situations has now been comfortably delineated, though interchangeability depending on the user's comfort and experience does exist.

In ambulatory surgery

Early recovery and fewer side effects are the main aim of an anaesthesiologist during ambulatory surgery. When ambulatory surgery started gaining popularity the beneficial use of the Laryngeal Mask Airway in this setting was identified. Studies were done to prove the same. It was seen that the endotracheal tube was associated with a greater haemodynamic response to insertion, skin incision and removal. The overall use of morphine was therefore more with the endo tracheal tube. There was less coughing with the Laryngeal Mask Airway(12). Considering that overall use of Morphine was less with the Laryngeal Mask Airway, one can deduce that awakening was better and post operative nausea and vomiting too were less.

A prospective, randomized multicentric study was done three years following the previous study comparing use of the endotracheal tube and Laryngeal Mask Airway in the ambulatory setting(15). There were close to two hundred patients in each group. The duration of stay in the post anaesthesia care unit and the time to ambulation was significantly shorter in the Laryngeal Mask Airway group. Intra operative Fentanyl used in the Laryngeal Mask Airway group was less, though it was not found to be statistically significant. There was no difference in the incidence of post operative nausea and vomiting, or in the need for rescue antiemetics. The study however did show a significantly higher incidence of post operative sore throat in the endotracheal tube group.

Laryngeal Mask Airway tolerates lighter planes of anaesthesia

One of the major advantages of the Laryngeal Mask Airway that is particularly beneficial in the ambulatory setting is that it causes very little stimulation and it tolerates lighter levels of anaesthesia (LMA User's Manual, Intavent International). This is beneficial as it provokes fewer episodes of coughing, breathholding and laryngospasm during emergence, when compared to an airway like the endotracheal tube that requires deeper planes of anaesthesia. Lighter planes of anaesthesia also causes less cardiovascular depression and has shorter recovery times(23).

Laryngeal Mask Airway is associated with a lower risk of airway complications

A systematic review of randomized prospective controlled trials was done in 2010 to compare the airway complications associated with the Laryngeal Mask Airway and the

endotracheal tube(24). 29 trials were included. It was found that there was a clinically and statistically significant difference in the incidence of laryngospasm during emergence, coughing, hoarseness of voice and sore throat; the endotracheal tube being associated with a higher incidence of these complications. There was no statistically significant difference in the incidence of nausea, vomiting, risk of regurgitation, or success of insertion on first attempt between the two groups.

Systemic changes- cardiovascular, neurovascular, intraocular- a comparison

Cardiovascular- Haemodynamic changes to insertion of the Laryngeal Mask Airway have been studied and often compared to the endotracheal tube. Mizrak et al looked at the heart rate, mean arterial blood pressure, P wave dispersion and QT dispersion in 75 patients(25). The comparisons were, made between insertions of the endotracheal tube, double lumen tube and laryngeal mask airway. Recordings were made immediately before insertion and at 1, 3, 5, 10, 15, 20, 25 and 30 minutes after insertion. All the patients were induced with Etomidate 0.3mg/kg and Fentanyl 1µgm/kg, and maintained with nitrous oxide, oxygen, Sevoflurane and Rocuronium 0.5mg/kg. It was found that there was no change in the heart rate, mean arterial blood pressure or P wave dispersion, during or after placement of the Laryngeal Mask Airway. There was QT dispersion though after placement. The heart and mean arterial blood pressure were significantly higher in the first minute, in the endotracheal tube group, when compared to the Laryngeal mask airway group.

Neurocirculatory- Heart rate, mean arterial blood pressure and muscle sympathetic nerve activity were compared between the Laryngeal Mask Airway and endotracheal tube(26). Muscle sympathetic nerve activity was checked using an electrode in the peroneal nerve. It

was found that the endotracheal tube group had a 27% increase in heart rate and a 42% increase in mean blood pressure compared to 12% and 23% increase respectively in the laryngeal mask airway group. The muscle sympathetic nerve activity increased 600% in the endotracheal tube group compared to 66% in the Laryngeal Mask Airway group. The time to return to baseline values of heart rate and mean arterial blood pressure were also higher in the endotracheal tube group. The Laryngeal Mask Airway is thus useful in situations where heart rate and blood pressure should be stable.

Intraocular- The ocular hypertensive response to manipulation of the airway can cause considerable rise in intraocular pressure. This has been shown to be significantly less with insertion and removal of the Laryngeal Mask Airway when compared to the endotracheal tube(27).

C) USE OF THE LARYNGEAL MASK AIRWAY

Size

The appropriate sized Laryngeal Mask Airway is to be chosen. A size smaller and larger must always be handy. Laryngeal Mask Airways are available in eight sizes. The smallest size can be used in neonates. The cuff is 15% larger as each size increases (21). The following table describes the appropriate Laryngeal Mask Airway for the weight and the amount of air that needs to be inflated in the cuff. This is for the classic LMA. This is to be used as a guide to selecting the appropriate size and clinical judgment must not be ignored taking patient anatomy also into consideration. When in doubt it is safer to use a larger rather than a smaller Laryngeal Mask Airway for the first attempt(28).

Table 1 (21)

Mask size	Patient weight in kg	Maximum volume of air inflated (ml)
1	Neonates/infants <5	4
1.5	Infants between 5-10	7
2	Infants/children between 10-20	10
2.5	Children between 20-30	14
3	Children 30-50	20
4	Adults 50-70	30
5	Adults 70-100	40
6	Adults >100	50

Checking the Laryngeal Mask Airway and preparation of the mask

Airway mishaps can be averted by a simple step such as checking the Laryngeal Mask Airway. Visual inspection- Discolouration of the shaft should be looked for, as fluid in the tube may be missed if the shaft has darkened. Cuts and tears should be checked for and the spiral wires should not be kinked. The cuff must not have any foreign particles lodged in it, as these can lead to obstruction. The bars at the mask aperture should be gently probed to ensure that they are not damaged and to there are no particulate matter between the two bars. The connector should be checked for cracks and should fit tightly into the shaft(28).

Deflation/ Inflation- The cuff should be fully deflated by withdrawing air from it with a syringe so that the walls are flattened. The syringe should be removed and the cuff should stay flattened. If it reinflates it indicates a faulty valve or leaking cuff. The cuff should then be inflated with 50% more air than the maximum recommended for that size and cuff should hold pressure for at least two minutes. If there is deflation, thinning of the wall or herniation at any point, the Laryngeal Mask Airway must be discarded. The pilot balloon should be elliptical in shape. If it appears wider than it should, or spherical, it indicates weakness and chances of rupture exist. This test is mandatory and major accidents can be averted, if this is diligently done prior to induction (28).

Prepration of the mask

The cuff should be fully deflated. A cuff deflating tool may be used , which increases the

life span of the Laryngeal Mask Airway. It could otherwise be deflated by pressing the concave side of the cuff on a clean, hard and flat surface. After complete deflation the cuff should be wrinkle free. A lubricant should be applied on the posterior surface of the cuff. Care must be taken to avoid spillage to the anterior surface. A water soluble jelly should be used. Analgesic containing gels should be avoided as return of protective reflexes may be delayed, and some patients may develop an allergic reaction to these gels. A gel that contains silicone may cause the mask to soften and swell (29).

Indications and Contraindication

Prior to planning on the use of a Laryngeal Mask Airway, the contraindications must be carefully thought of, and the its use indicated.

Indications

1) Short surgical procedures, including head and neck procedures(30). It's use in adenotonsillectomy, adenoidectomy and tonsillectomy is still gray. A retrospective review of 1199 records (2002-2006), showed the incidence of Laryngeal Mask Airway failure to be 6.8%. Patients undergoing adenoidectomy has lesser failure rates than adenotonsillectomy or tonsillectomy. Airway obstruction following insertion and placement of the mouth gag was the most common reason for complications. The ability of the surgeon to work around the Laryngeal Mask Airway played a major role in preventing airway complications. Male sex, younger patients, patients with co

morbidities and controlled ventilation also had higher incidence of complications. This review concluded that use of the Laryngeal Mask Airway for paediatric adenotonsillectomy was associated with higher incidence of complications compared to the endotracheal tube(31). Yet, another contemporary review of published articles in Pubmed, Medline and conference proceedings, showed the Laryngeal Mask Airway to be safe and efficacious in otorhinolaryngology and many head and neck procedures, including adenotonsillectomies. The Laryngeal Mask Airway can be used in the supine, prone, lateral, oblique, Trendelenberg and lithotomy position(32). Recommended duration by the manufacturer is 2-3 hours(31).

2) Cannot ventilate cannot intubate scenario, if the problem is supraglottic in nature. In 1996, the American Society of Aaesthesiologists added it in the Difficult Airway Algorithm in five different places as a method to ventilate and also as a conduit for intubation(21).
3) Cardiopulmonary resuscitation

Contraindications (21)

1) Patients with mouth opening less than 1.5cms
2) Poor lung compliance
3) Airway pressures of more than 20cms of water
4) Patients who are at risk of aspiration of gastric contents (full stomach, hiatus hernia with significant gastro oesophageal reflux, intestinal obstruction, delayed gastric emptying,

poor history, opiate medication prior to fasting(33))(32).

5) Morbidly obese patients(33)
6) Glottic or subglottic surgery(32)

Anaesthetic induction

Sufficient depth of anaesthesia is needed for insertion of the Laryngeal Mask Airway; as much as for an oropharyngeal airway, but not as much as for endotracheal intubation. No response to a jaw thrust is a good indicator of adequate depth. To date Propofol is the best induction agent. It has the added advantage of blunting laryngeal reflexes.

Insertion(33)(21)

There are many methods of inserting the Laryngeal Mask Airway. The standard insertion method is what was first described. Any method is acceptable as long as the Laryngeal Mask Airway is lodged correctly and ventilation is adequate.

Standard Insertion Method (pictures attached)

Gloves must be worn.

1) The plane of anaesthesia should be deep enough. Absence of response to a jaw thrust is method of checking adequacy of depth.
2) The head should be extended and the neck flexed as for laryngoscopy and intubation.

3) This can be done with the left hand, if insertion is being done with the right hand.

4) The mask is held like a pen, with index finger lodged between the junction of the cuff and shaft, anteriorly. The mouth is opened and the tip is pressed against the hard palate and lies against the palate as it is slid into the pharynx. The index finger is slid along with the Laryngeal Mask Airway, into the mouth, maintaining backward pressure against the palate.

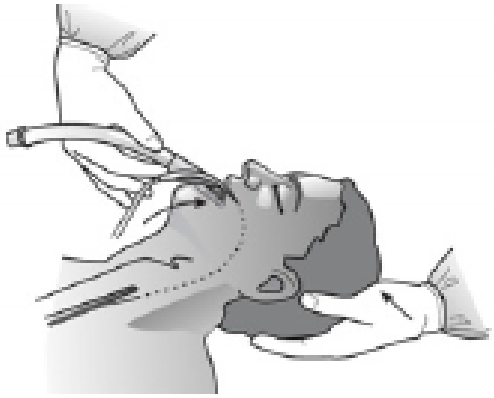
5) As it is pushed further downwards, backward pressure is maintained against the posterior pharyngeal wall to avoid collision with the epiglottis. During this time the ventral surface of the entire index finger should lie against the shaft of the Laryngeal Mask Airway.

6) Once resistance is felt it means the airway is in place. By then the entire length of the index finger should be in the mouth. The remaining fingers should be outside the mouth. As the index finger is being withdrawn, the other hand supports the shaft of the airway preventing it from coming out as the index finger is being withdrawn.

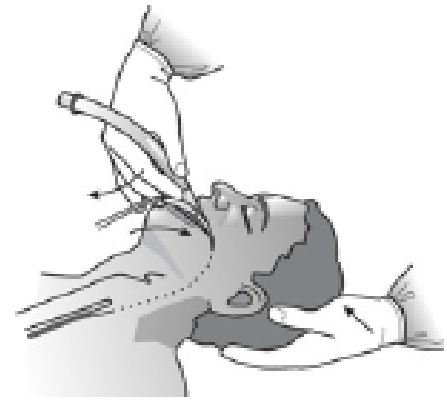
7) The black line on the shaft should face the upper lip.

8) The cuff should now be inflated with just enough air to seal. Cuff pressure must not exceed 60 cms of water. During inflation the shaft must not be held. The Laryngeal Mask Airway will rise slightly. This allows it to settle in a correct position. After this The gas supply can be connected to the airway. Care must be taken not to over inflate the cuff.

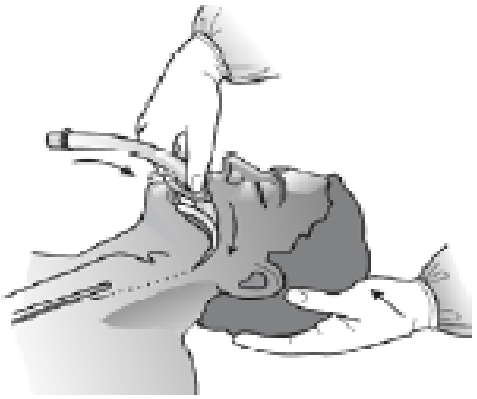
9) While connecting to the gas supply the shaft must be firmly held to prevent dislodgement. On ventilation of the lungs, adequate chest rise is looked for. A bite block, made of rolled gauze should be placed by the side of the shaft. The Laryngeal Mask Airway is then secured well, ensuring rotation and cranial movement is prevented.



STEP 1



STEP 2



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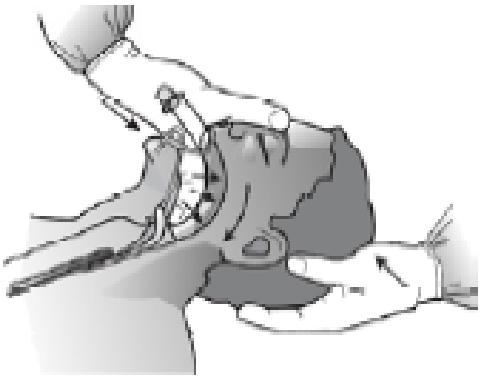
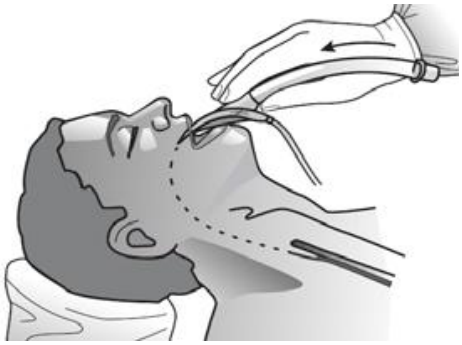


STEP 4

Thumb insertion method (33)

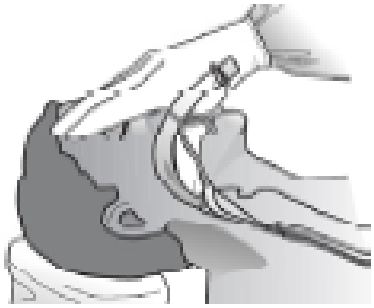
Here the Laryngeal Mask Airway is inserted with the anaesthesiologist facing the patient. It is useful in situations where access to the head end of the patient is difficult, for example during cardio pulmonary resuscitation. The thumb is placed between the proximal end of the cuff and the shaft, just how the index finger was placed in the classic method. The tip of the cuff is placed against the front teeth and

the cuff slid into the mouth against the palate using the thumb just as the in the classic method. As the cuff goes deeper into the mouth, the other four fingers are placed over the face and also help in extension. Flexion of the neck is provided by the pillow under the head. Once the thumb is pushed in maximally, the airway should be in place. As the thumb is taken out, the other hand holds the Laryngel Mask Airway in place.



STEP 1

STEP 2



STEP 4

STEP 5

180- degree technique(29)

Commonly used in paediatrics, here the Laryngeal Mask Airway is inserted with the aperture facing cephalad. It is rotated 180 degrees once it reaches the hypopharynx. A discrete give may be felt. It has been believed that this method can cause dislocation of the aretynoids.

Partial inflation technique (28)

In this technique the cuff is partially or fully inflated. It is useful for beginners, though malposition is common. Partial inflation may be associated with less sore throat.

Trouble shooting (28)

If initial insertion is not satisfactory there are many maneuvers that can help.

- Inserting the airway from the side of the mouth
- Pulling the tongue forward
- Jaw thrust
- Repositioning the head
- Applying continuous positive airway pressure (CPAP)
- Minimal lateral rotation
- Partial inflation of the cuff
- Inserting finger behind the mask, as a guide
- Using a laryngoscope
- Using a stylet or forceps

Position of a properly inserted mask is as follows. The mask rests on the floor of the hypopharynx. The sides of the mask face the pyriform fossa. The upper border of the cuff is behind the base of the tongue. The tip of the epiglottis may be within the bowl of the mask or under the proximal part of the cuff. Even though position may not be perfect, satisfactory function can be achieved.

Cuff inflation and assessment of position and function

The cuff must be inflated with air, the maximum amount not exceeding what is specified for a particular size. It should be inflated over 3-5 seconds. The shaft must not be held during inflation, a slight movement upwards occurs, and a small bulge becomes visible in the neck. The cuff must not be visible in the mouth. The maximum volume of air for a particular cuff is rarely needed. The cuff pressure should be approximately 60 cms of water. The cuff pressure monitor is the best means of assessing this. Feeling the tension in the pilot balloon is a subjective way of assessing the same. A spherically shaped pilot balloon would mean too much gas in the cuff. If greater than recommended volumes are apparently needed, it is often a smaller size cuff that has been used. In such a situation it is better to use a larger sized Laryngeal Mask Airway, rather than inflate larger volumes of air, as this tends to worsen the seal of the cuff against the larynx. The ideal way of filling the cuff would be to inflate it with half the maximum volume of air that is required, determine the oropharyngeal leak and inflate more air if needed. Adequate chest rise to squeezing the bag, normal breath sounds, and a good end tidal CO2 trace are reliable signs of proper position and function. Other elaborate ways of checking position are by passing fiberscope or rigid endoscope through the Laryngeal Mask Airway, this also helps rule out airway obstruction (28).

If the airway is obstructed, common causes are

- Incorrect mask position
- Downfolded epiglottis
- A closed glottis sphincter
- An overinflated cuff

Often removing and reinserting the mask solves the problem.

If spontaneous ventilation is being used, the leak pressure should be more than 10 cms of water and if positive pressure ventilation is being used, the leak pressure should be more than 20 cms of water.

Methods of determining airway sealing pressure

1) Bourdon pressure gauge
2) Listen for a leak with a stethoscope placed lateral to the thyroid cartilage
3) Listen over the mouth for a noise when the bag is squeezed
4) A sample line in the oral cavity may detect CO2 if a leak is present
5) Determine a steady airway pressure after closing the adjustable pressure valve in the circle system.

Complications (32)

1) Gastrooesophageal reflux and aspiration

2) Laryngospasm, coughing, gagging, retching, bronchospasm

3) Sore throat (0-70%, approximately 10%), hoarseness (4-47%), dysphagia (4-24%)

4) There have been reports of nerve injury. Pressure neuropraxia is the most common

cause. 26 cases were reported as of Sept 2006. Nerves injured were hypoglossal, recurrent laryngeal and lingual nerves. Onset of symptoms was from emergence to 48 hours after surgery. Spontaneous recovery occurred in all cases except one. Recovery occurred in 1hour to 18 months.

D) SUCCINYLCHOLINE

Muscle relaxants interrupt transmission of the nerve impulse at the neuromuscular junction. They are broadly divided into depolarizing neuromuscular blocking drugs that mimic the action of acetylcholine, and nondepolarizing neuromuscular blocking drugs that interfere with the action of acetylcholine. Succinlycholine is a depolarizing neuromuscular blocking drug(34).

History of muscle relaxants (35)(34)

Close to 500 years ago explorers who returned from South America first spoke of a poisoned arrow that was used in hunting and in war. This was curare. It fascinated man to further study this poison that killed immediately. The first mention of poisoned arrows though dates way back further in time and was mentioned by Homer (Odyssey, 1, 260) and Virgil (Adeneid, 9, 772).

One of the first persons to report on this intriguing drug was Sir Walter Raleigh (1552-1618). His first lieutenant Laurence Keymis, coined it 'ourari', in an attempt to make it sound like the Macusi Indian pronunciation of the drug. The drug was brought to Europe and extensive research was done on it in the 18^{th} century. Yet for close to 175 years there was no clinical use of the drug. There was a report in 1912, of the drug facilitating closure of the abdomen, but this was ignored.

In 1935 the active compound from the plant *Chondodendron* was isolated and called D-tubocurarine. Its main use was to control muscle spasms in patients with tetanus. Richard Gill had an interest in primitive medicine and set up fort in Ecuadore. He unfortunately developed a

painful, spastic muscle disorder. This though is what led him to acquire 11kgs of a dark tar like paste- crude curare from the Indians, who were willing to share their secret material with him as he had won their rust. Squibb and Sons, Inc prepared a sterile injectable solution of D-tubocurarine and called it Intocostrin. This was first used by Bennett, a psychiatrist for electro convulsive therapy in 1940. Squibb and Sons along with an anaesthesiologist, Wright were convinced that "the true home for curare was with the anaesthesiologist" They were right and it was first used by Harold R. Griffith in 1940 during general anaesthesia. A breakthrough was made and many began to use the muscle relaxant during general anaesthesia. Of course the problems of inadequate reversal gradually came to light and the concept of using a peripheral nerve stimulator came about in 1952.

Numerous other muscle relaxants were introduced and the methonium compounds, from plant alkaloids were one among them. The parasympathomimetic effects of Succinylcholine were already being studied in 1906, this masked the neuromuscular blocking properties of the drug. Succinylcholine's neuromuscular blocking effects were identified in 1949, and the drug was introduced by Thesleff, Foldes an d colleagues in 1952. Daniel Bovet won the Noble Prize in 1957, for the discovery of the same. This rapid onset, ultrashort acting drug was a seen as a boon to anaesthesiologists, and changed anaesthetic practice drastically as rapid endotracheal intubation became possible. D-tubocurarine and Succinylcholine were the most commonly used muscle relaxants in the 1950s to 60s. Steroid based neuromuscular blocking agents like Pancuronium, Vecuronium and Rocuronium were identified in the 1960s to 1990s. Their improved safety profile, compared to older drugs like curare and gallamine was well welcomed. Foldes and colleagues stated that "the use of muscle relaxants not only revolutionized the practice of anaesthesia but also started the modern era of surgery and made possible the explosive development of cardiothoracic, neurologic, and organ transplant surgery."

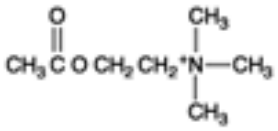
PHARMACOLOGY OF SUCCINYLCHOLINE

Structure- activity relationships

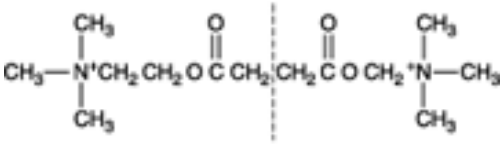
It is a quaternary ammonium compound and is structurally similar to acetylcholine. The positive charges get attracted to the alpha subunit of the muscle and neuronal type nicotinic acetylcholine receptors at the neuromuscular junction. The neuronal type nicotinic receptors are also present in autonomic ganglia, along with at least five different kinds of muscarinic receptors. Neuronal nicotinic and muscarinic receptors are also present prejunctionally at the neuromuscular junction.

Succinylcholine consists of two molecules of acetylcholine attached together through the acetate methyl groups. It is a long, thin and flexible molecule. It stimulates the cholinergic receptors and opens the ion channel in it.

Acetylcholine



Succinylcholine (diacetylcholine)



Pharmacokinetics and Pharmacodynamics

Succinylcholine is still the only muscle relaxant which has a rapid onset and ultra short

duration of action. Its ED_{95} is 0.51- 0.63 mg/kg, that is, the dose required for desired effect in 95% of the population. 1mg/kg of Succinylcholine gives adequate muscle relaxation for intubation within 60 seconds. Considering that different patients respond differently, a dose of 1-1.5mg/kg is appropriate for complete neuromuscular blockade. Recovery to 90% of muscle strength occurs in 9 to 13 minutes in those with genotypically normal butyrylcholinesterase (also knowm as plasmacholinesterase or pseudocholinesterase).

Succinylcholine gets hydrolysed rapidly by butyrylcholinesterase, which is present in the plasma, to succinylmonocholine and choline. Butyrylcholinesterase has enormous capacity to hydrolyse Succinylcholine and hydrolyses it before it reaches and after it diffuses away from the neuromuscular junction. Because of this only 10% of the administered drug actually reaches the neuromuscular junction. Butyrylcholinesterase thus affects the onset and duration of action of Succinylcholine. Succinylmonocholine is a weaker neuromuscular blocking agent and gradually gets metabolized into succinic acid and choline. The elimination half life of Succinylcholine is around 47 seconds.

Mechanism of action(35)(34)

Structure of the nicotinic acetylcholine receptors and the adjacent Na channels

It is a pentameric complex, which consists of two α subunits and one each of β, δ and ε subunits. These subunits form a transmembrane channel. Acetylcholine, as well as muscle relaxants bind to the α subunit. Mature receptors have a short burst duration and higher conductance for Na, K and Ca ions. Fetal receptors on the other hand differ in structure with the ε subunit being replaced by a γ subunit; functionally they have a prolonged open channel time and are a low conductance channel. The receptor just described is present at the end plate.

Adjacent to the end plate, perijunctionally are the sodium ion channels. These channels open in response to a transmembrane change in voltage. These too form a transmembrane channel. Structurally they have two gates, the upper one being voltage gated and the lower one being time gated. Depending on whether these gates are open or closed, the sodium channel exits in three states. 1) The resting state where the voltage dependent gate is closed and time dependent gate is open, 2) the active state where both channels are open and the flow of Na ions occurs and 3) the inactive state where the voltage dependent gate is open and the time dependent gate is closed.

When acetylcholine binds to the receptor, the membrane depolarizes. The adjacent sodium channels sense the voltage change and the voltage dependant gate opens. Since the time dependant gate is already open, sodium flows into the cell. After some time the time dependant gate closes. The voltage gate stays open as long as it senses a change in voltage around it (depolarization). It does not close until the depolarization disappears. The time gate on the other hand cannot open again until the voltage gate closes. This is the basis of the mechanism of action of Succinylcholine.

Succinylcholine is a partial agonist and mimics the action of acetycholine at the nicotinic acetycholine receptors. It attaches to one or both of the alpha subunits and causes depolarization of the postjunctional membrane. Normally when acetylcholine attaches to the receptor it gets hydrolysed fast because acetylcholinesterase is present in the neuromuscular junction itself. Succinylcholine gets hydrolysed much slower leading to a sustained depolarization (opening) of the ion channel, with the voltage gate being open and the time gate being close, ie) the sodium channels stay in the inactive state, till the relaxant is removed. Thus the membrane cannot

respond to subsequent release of acetylcholine and neuromuscular blockade develops. This depolarizing block is called **Phase I block**. This sustained opening of the ion channel leads to leakage of potassium ions out of the cell and increase serum levels by 0.5mEq/L.

A single large dose of Succinylcholine (>2mg/kg), repeated doses or an infusion can lead to what is known as the **Phase II block**. The junction gets depolarized initially, the membrane potential gradually returns to normal, even though the drug is still attached, but neuromuscular transmission does not occur. A conformational change occurs in the receptor, not allowing it to open. Many reasons for this exist. A) Repeated channel opening causes a continuous efflux of potassium and influx of sodium, leading to abnormal electrolyte balance and thus abnormal response of the junctional membrane. B) Calcium that enters the cell causes a disruption of the receptors. C) Desensitization- refers to receptors that have bound to agonists but do not open. The exact mechanisms are not known. Normally binding of Succinylcholine leads to only a transient state of desensitization. But when large doses, repeated doses or an infusion is given the receptor gets trapped in a desensitized state.

Dibucaine number and butyrylcholinesterase activity

Butyrylcholinesterase is produced in the liver. The activity of the enzyme is depicted by the number of substrate molecules (μmol) hydrolysed per unit of time. This can be expressed as IU (International Units). Since the normal enzyme is highly active, significant decreases in its activity result in only a modest increase in duration of action of Succinylcholine, which is clinically not very significant. Factors that lower butyrylcholinesterase activity are liver disease, old age, malnutrition, burns, pregnancy, malignancies and drugs like oral contraceptive pills, MAO inhibitors, cytotoxic drugs, echothiophate, anticholinesterases, metoclopramide, esmolol

and bambuterol, the prodrug of terbutaline.

What was found to be clinically significant though was if there was an abnormal genetic variant of butyrylcholinesterase. Dibucaine is a local anaesthetic that inhibits butyrylcholinesterase. It was found that it inhibits the normal enzyme to much larger extent than the abnormal enzyme. Thus the concept of Dibucaine number came about, as a test to determine the genetic makeup of an individual with respect to butyrylcholinesterase. Dibucaine number indicates the percentage of enzyme inhibited. It is a qualitative test and not a quantitative test. Dibucaine inhibits the normal enzyme by around 80% and the abnormal enzyme by around 20%. Dibucaine resistant varieties are of most significance. The following table shows us the relationship between Dibucaine number and the duration of Succinylcholine neuromuscular blockade.

Genetic type of butyrylcholinesterase	**Incidence**	**Dibucaine number**	**Response to Succinylcholine**
Typical- homozygous	Normal	70-80%	Normal
Atypical- heterozygous	1/480	50-60%	Lengthened by 50-100%
Atypical- homozygous	1/3200	20-30%	Prolonged to 4-8 hours

Since the Dibucaine number is not a quantitative test, it does not measure the concentration butyrylcholinesterase, nor does it estimate the efficiency of the enzyme to hydrolyse Succinylcholine. These can be acquired by measuring the butyrylcholinesterase activity.

The molecular biology of butyrylcholinesrase has been extensively researched and well understood. Most often genetic variants are due to single amino acid substitution or sequencing

errors, at or near the active site of the enzyme.

Clinical uses

Despite Succinylcholine having been discovered way before other currently being used non depolarizing agents, its use in clinical practice has still not been displaced. This is due to its rapid onset, profound depth and short duration of action. It is the agent of choice in rapid sequence intubation and proves beneficial above all neuromuscular blocking agents in an anticipated difficult airway (35). Conventionally 1mg/kg of Succinylcholine is used for intubation, in 60 seconds. A prospective, randomized double blinded study done on 200 patients, and published in 2003, relooked into the intubating dose of succinylcholine and concluded that intubation conditions similar to 1mg/kg Succinylcholine were achieved within 60 seconds with 0.3 and 0.5mg/kg of Succinylcholine. Quicker return of spontaneous respiration and airway reflexes was the stated advantage (36).

Side effects(35)

1) Cardiovascular
2) Hyperkalemia
3) Increased intraocular pressure
4) Increased intragastric pressure
5) Increased intracranial pressure
6) Myalgias
7) Masseter spasm

1) Cardiovascular

The cardiovascular effects of Succinylcholine are because it stimulates all the cholinergic receptors in the body, which include the nicotinic receptors in the sympathetic and

parasympathetic ganglia, as well as the muscarinic receptors in the sino atrial node of the heart. At low doses Succinylcholine induces a negative ionotropic and chronotropic effect, but at higher doses it induces tachycardia (37). The common arrhythmias it induces are sinus bradycardia, junctional rhythms and ventricular dysrhythmias.

Sinus Bradycardia- This is due to stimulation of cardiac muscarinic receptors in the sinus node. It is more predominant in children due to their higher vagal tone. Prior administration of Atropine can blunt this bradycardia. In adults it commonly occurs approximately five minutes after a second dose of Succinylcholine. Other than stimulation of sinus node muscarinic receptors, direct myocardial effects and ganglionic stimulation may also contribute to the bradycardia, as drugs like thiopental, atropine, ganglion blocking drugs and non depolarizing agents too help prevent the bradycardia. Also since bradycardia is more after the second dose, the breakdown products of Succinylcholine, Succinylmonocholine and choline may be implicated in sensitizing the heart to a second dose.

Nodal/ junctional rhythms- These are also common after Succinylcholine, particularly the second dose. It may be due to excessive stimulation of the nodal muscarinic receptors causing their suppression. This leads to firing from the AV node.

Ventricular dysrhythmias- These can certainly be alarming. There is an increased release of catecholamines with administration of Succinylcholine and also a decreased threshold of the ventricles to catecholeamine induced arrhythmias. The hyperkalemia induced by Succimylcholine further aggrevates arrythmogenicity. Other autonomic stimuli induced by endotracheal intubation, hypercarbia, hypoxia and the stress of surgery itself can add on to arrythmogenicity. There can be ventricular escape beats due to severe suppression of the sinus

and AV node.

2) <u>Hyperkalemia</u>

Normally there can be a rise in serum potassium values by 0.5mEq/l. This occurs due to depolarization of the muscle membrane by Succinylcholine and subsequent efflux of potassium due to the influx of sodium. Patients with renal failure are no more susceptible to this release in potassium, but if potassium levels are already high, Succinylcholine is better avoided to prevent further rise in potassium.

Patients with severe metabolic acidosis and hypovolemia can have an exaggerated hyperkalemic respose to Succinylcholine. They have higher resting potassium too. This potassium release is apparently from the gastrointestinal cells rather than muscle cells. Some amount of correction of the acidosis with sodium bicarbonate and hyperventilation can be instituted prior to administration of Succinylcholine. In case hyperkalemia does occur it should immediately be corrected with 1-2gms of Calcium chloride intra venously to stabilize the membranes, hyperventilation, 1mg/kg sodium bicarbonate, 10U regular insulin in 50ml of 50% dextrose in adults and 0.15U/kg of regular insulin in 1ml/kg of 50% dextrose. It has been found that in patients with severe abdominal infections particularly those lasting for more than a week have high chances of hyperkalemia with Succinylcholine, potassium values rising by around 3.1mEq/L. This can pose a serious risk of cardiac arrest in these patients.

After massive trauma a patient is susceptible to hyperkalemia even 60 days following the trauma or until the damaged muscles have healed completely. Potassium can rise by up to 3.6mEq/L, which can cause cardiac arrest. It was found that prior administration of d-

tubocurarine can negate this.

Hyperkalemia following administration of Succinylcholine to those who have developed extrajunctional receptors can also be life threatening. Examples are post burns, post cerebrovascular accident leading to hemiplegia or paraplegia etc, Guillain- Barre syndrome, muscular dystrophies etc. This occurs because these extrajunctional receptors have increased permeability to potassium.

3) Increased intra ocular pressure

Succinycholine increases the intraocular pressure. This occurs within 1 minute of giving the drug, it peaks in 2-4 minutes and subsides by 6 minutes. The mechanism is probably due to contraction of tonic myofibrils. Nifedipine was found to decrease this increase in pressure and therefore a possible vascular mechanism like transient dilatation of choroidal vessels was postulated. The exact mechanism is still not clear. Though Succinylcholine causes this rise in intraocular pressure, it still can be in ophthalmic surgery, except when there is open injury to the globe. Varying studies are available regarding precurarization with a small dose of non depolarizing agent to decrease this raise in intraocular pressure. Other stimuli like endotracheal intubation itself or bucking on the tube too cause a raise in intra ocular pressure so what is more important is a smooth induction and sufficient plane of anaesthesia intraop. Now that agents such as Rocuronium are available, Succinylcholine may be replaced in this setting.

4) Increased intragastric pressure

A raise in intragastric pressure occurs with Succinylcholine, which is quite variable. It is probably due to fasciculations of the abdominal wall muscles and varies with the intensity of the

fasciculations. Prior administration of a non depolarizing agent prevents the fasciculations and thus the raise in intragastric pressure too. The pressure can rise up to 120cms of water. The cholinergic effects of Succinylcholine itself can add to the rise in intragastric pressure.

Increased intragastric pressure would be significant if it causes incompetence of the lower gastrooesophageal sphincter. This requires a pressure of more than 28 cms of water. However in conditions such as pregnancy, gross ascitis, intestinal obstruction and hiatus hernia, the normal oblique angle of entry of the oesophagus to the stomach is altered. In these conditions an intragastric pressure of even less than 15 cms of water can cause incompetence. Therefore special precaution needs to be taken in these situations when Succinylcholine is being given, such as a defasciculating dose of non depolarizing agent.

Infants and children do not have much of a raise in intragastric pressure, probably because they do not experience as much fasciculations.

5) <u>Increased intracranial pressure</u>

Succinylcholine causes a transient raise in intracranial pressure. The exact mechanism is not known. It can be prevented with mild hyperventilation or a small dose of non depolarizing agent.

6) <u>Myalgia</u>

Incidence of myalgia due to Succinylcholine varies from 0.2- 89%. It has been found to occur more in women, and more often after minor surgery such as those done in the ambulatory setting(38). It is more in ambulatory rather than bed ridden patients. The myalgia is probably due

to the damage produced in the muscles due to unsynchronized contraction of muscles, during the fasciculations and prior to the paralysis. It was found that serum creatine kinase increased and myoglobinemia occurred after administration of Succinylcholine. Numerus reasons for post operative myalgia have been postulated, such as type and location of surgery, patient position during surgery, intubation trauma, post operative ambulation and post operative requirement of analgesics; and it is now thought to be multi factorial, succinylcholine being only one of the reasons(38). Though Naguib et al(39) found that pretreatment with lysine acetyl salicylate decreased post operative myalgia, suggesting that there may an inflammatory component to the myalgia more recent studies by Schreiber at al disprove this in two of his studies (40)(41), stating that pre treatment with paracoxib and dexamethasone do not decrease myalgia. Myalgia was found to be less in those who are physically fit(42). Numerus agents have been studied and are still being studied to prevent Succinylcholine induced fasciulations and myalgia. It has been found that prevention of fasciculations does not necessarily prevent post operative myalgia. Lately it has also been found that post operative myalgia occurs after ambulatory surgery even in the absence of Succinylcholine. Thus other factors may contribute to myalgia. A study done by Joshi et al found that pretreatment with Rocuronium and d Tubocurarine decreased fasciculations, better than Cisatracurium, but incidence of post operative myalgia was not affected by pre treatment in the ambulatory setting(43). Menke at al also found that pre treatment with Rocuronium decreased fasciculations but did not decrease incidence of post operative myalgia, and was asscociated with more muscle weakness prior to induction(44). Other drugs found to decrease Succinylcholine induced fasciculations are Remifentanyl 1.5µgm/kg(45), though it did not decrease myalgia, Lidocaine 1.5mg/kg decreased myagia at 48 hours better than Rocuronium(46), Magnesium 40mg/kg decreases fasciculations and myalgia(47), Propofol 3.5mg/kg decreases fasciculations and myalgia(48), and more recently the role of gabapentine is being studied in decreasing fasciculations and myalgia(49).

Most data suggest that onset of myalgia is within the first 24 hours in 60 to 90% of patients(38).

7) <u>Masseter spasm</u>(35)

Increased tone of the masseter muscle can occur with Succinylcholine. This is most probably due to an exaggerated contractile response at the neuromuscular junction. It may be a sign of malignant hyperthermia, but isolated incidences of masseter spasm with Succinylcholine does not negate the use of “non triggering agents” .

E) STUDIES ON ADJUVANTS TO AID LARYNGEAL MASK AIRWAY INSERTION

Numerous adjuvants have been tried to aid insertion of the Laryngeal Mask Airway. Studies continue to be done on the same. It has been found that the Laryngeal Mask Airway is easier to insert and has a quicker learning curve(50),(51),(52). Despite the ease in insertion it can still be associated with patient movement, coughing, gagging and other adverse patient responses. Hence; the need for an adjuvant. The following is a review of the various adjuvants that have been and continue to be studied, in chronological order.

From when the use of the Laryngeal Mask Airway became popular, the search for an ideal adjuvant has been rampant. Beginning with the days of Etomidate and Thiopentone, where insertion was not smooth(6), Succinylcholine was studied to facilitate insertion of the Laryngeal Mask Airway. Yoshino et al found that 0.5mg/kg of Succinylcholine was required to blunt adverse airway reflexes associated with Laryngeal Mask Airway insertion. The induction agent he used was Thiopentone. Unfortunately this dose was also coupled with more myalgia and a longer duration of apnoea(6).

Ho and Chui compared 0.1mg/kg Succinylcholine and placebo, with 2.5mg/kg of Propofol and found it to be better, with lesser insertion attempts and smoother insertion. Propofol requirement was less, thus there was less hypotension. The duration of apnoea was not found to be different. Myalgia though was more(7).

Once Propofol was discovered it was thought that the solution to problem was found, yet using Propofol alone was not sufficient. Nakazawa et al compared placebo, Midazolam and Fentanyl, in the attempt of trying to avoid a muscle relaxant. They found that the insertion conditions were significantly better in the Midazolam and Fentanyl group compared to the placebo group. The Fentanyl had more hypotension and hence concluded that Midazolam was better(53). Considering the use of the Laryngeal Mask Airway in the ambulatory setting, Midazolam would cause more clouding of consciousness when compared to an agent like Succinylcholine.

Cheam and Chui found that Fentanyl 1μg/kg and Mivacurium 0.04mg/kg were equally effective in facilitating Laryngeal Mask Airway insertion with Propofol 2mg/kg as the induction agent. The duration of apnoea was more, but with little clinical significance(54).

Alfentanyl 5μ/kg was compared with 10μ/kg and found to be better, as 10μ/kg was associated with more hypotension and longer duration of apnoea(55).

Wafaa et al compared Midazolam 0.04mg/kg and 0.1mg/kg of Succinylcholine and concluded that Midazolam was superior with better insertion conditions, less change in haemodynamics, shorter duration of apnoea and less fasciculations and myalgia(3).

Once Rocuronium came to the scene, different doses were tried to aid Laryngeal Mask Airway insertion. 100, 150 and 300μ/kg were compared and it was found that the optimal dose was 100μ/kg. These doses of Rocuronium need to be given before induction, thus the

chances of unpleasant effects of neuromuscular block are present(4).

Lee et al concluded that 0.25μ/kg of Remifentanyl provided excellent insertion conditions avoiding the hypotension that was present with 0.5μ/kg of the same(2).

Oral clonidine as premedication was found to decrease the Propofol required to insert the Laryngeal Mask Airway. But as with Midazolam or other opioids, it's sedative effects may not be acceptable in the day care set up(56).

Ganatra et al compared Sevoflurane induction and Propofol induction after Fentanyl and also looked at costs and found that though Propofol induction was faster, insertion conditions were similar in the two groups. Haemodynamic stability was with Sevoflurane but costs were more(57).

Hui et al compared Alfentanyl 10μ/kg and Fentanyl 1μ/kg and found that insertion conditions were better with Alfentanyl but duration of apnoea was significantly longer(58). Ang et al had also found the duration of apnoea with 10μ/kg of Alfentanyl to be signifantly long (55).

In an attempt to prevent apnoea and airway obstruction in children, particularly in those with a difficult airway, Jae- Hyon Bahk et al compared different doses of Ketamine and Lignocaine spray in the oropharynx with different doses of Propofol and looked not just at insertion conditions, but also apnoea, airway obstruction and secretions. They found that 3-

3.5mg/kg of Ketamine with Lignocaine spray provided satisfactory conditions. Most patients in the Propofol group experienced either apnoea or airway obstruction. Thus they concluded that in the difficult airway situation Ketamine and Lignocaine would be a safe option(59).

Liou et al looked at 1mg/kg of Succinylcholine with Etomidate as the induction agent comparing it with 2μ/kg of Fentanyl and found that Succinylcholine had a higher success rate of insertion, better jaw relaxation and shortened time to insertion(8).

Goh et al again looked into Ketamine to maintain haemodynamics and prevent apnoea. They found that 0.5 mg/kg of Ketamine with Propofol as the induction agent provided insertion conditions similar to the Fentanyl 1μ/kg group and better than the placebo group, maintaining haemodynamics and less prolonged apnoea(60).

Chari et al compared Butorphanol and Thiopentone with Fentanyl and Thiopentone and found that the Butorpanol group had better insertion conditions compared to the Fentanyl group(61).

Etomidate being cardio stable was studied again. Its main disadvantage is that it does not blunt laryngeal reflexes like Propofol does. A study by Uzun et al though found that addition of Remifentanyl to Etomidate did not improve insertion conditions(62).

As studies continue to be done, the α 2 agonist Dexmeditomidine was studied by

Uzumcugil. One group received 1μ/kg Fentanyl with Propofol and the other 1μ/kg Dexmeditomodine with Propofol. They found that insertion conditions were similar to Fentanyl and respiratory function and haemodynamics were preserved better. Time to emergence though was more prolonged with Dexmeditomidine, making its use in the day care setting again, doubtful(63).

Baik et al found that intravenous injection of Lignocaine 1.5mg/kg prior to Propofol target controlled infusion improved insertion conditions.

In 2012 now, Gabapentine is the latest agent to be studied to reduce the fasciculation and succinycholine induced myalgia as succinylcholine is still one of the best agents to facilitate Laryngeal Mask Airway insertion.

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MATERIALS AND METHODOLOGY

This is a double blinded randomized control trial done on 283 patients. The study was predominantly done in the day care theatre, as this is where most number of Laryngeal Mask Airways are used in a day. The required sample size to show a difference in the insertion conditions was found to be 92 in each group with an anticipated proportion of insertion conditions as 30%, 10% and 15% respectively with 80% power and 1% level of significance (this is done for three group comparisons).

$$n = \frac{\left(Z_{\alpha/2} + Z_{1-\beta}\right)^2 2 * PQ}{d^2}$$

Required sample size for each arm was 92. Values were taken from the 'overall insertion conditions' table in the study " A comparison of Midazolam and mini dose Succinylcholine to aid Laryngeal Mask Airway insertion during Propofol anaesthesia" by Wafaa Taha Salem(3).

Patients were not premedicated. All cases were in the elective setting. Surgeries requiring general anaesthesia using the Laryngeal Mask Airway were included, such as exploration under anaesthesia and lay open fistulae, lipoma excision, wide local excision of breast lump, implant removal, skin grafting, cystoscopy, circumcision, tympanoplasty etc. Patients included were ASA I and II, age between 20 and 65 requiring general anaesthesia using a Laryngeal Mask Airway. Patients excluded were ASA > II, age < 20 or > 65, BMI > 30, difficult airways, oral surgery.

Informed consent was taken from all patients. Patients were preoxygenated with 100%

oxygen. 2mg/kg of Propofol was given over a constant rate over 30 seconds after 2µg/kg of Fentanyl. Adequacy of anaesthesia was assessed by loss of eye lash reflex. If this dose of Propofol was not adequate further boluses of 0.25mg/kg were given every 15 seconds till depth was adequate. The study drug was given after the eyelash reflex was abolished.

A computer block randomization was used to allocate patients into three groups, Placebo (groupI), 0.1mg/kg (groupII) and 0.25mg/kg (group III) of Succinylcholine. The method of allocation concealment was using opaque envelopes with serial numbers. The person administering the drug would choose the appropriate syringe out of three which was loaded by the anaesthetist; according to what was mentioned in the envelope.

The classic Laryngeal Mask Airway was inserted 60 seconds after the study drug was given using the standard method of insertion. Patients were assessed for jaw relaxation, coughing, gagging, laryngospasm and overall insertion conditions. Number of attempts at insertion and total Propofol consumption were also recorded, as were duration of apnoea, haemodynamics, presence of fasciculations and post operative myalgia. Pre induction heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and saturation were recorded. The same were recorded post induction and post insertion.

If insertion was not possible at the first attempt, anaesthesia was maintained with 2% of Isoflurane, an additional dose of 1mg/kg of Propofol was given and insertion attempted 30 seconds later. 1mg/kg of Propofol was repeated as and when necessary.

Patients were monitored using standard methods of monitoring with the electrocardiogram, non invasive blood pressure, pulse oximetry and end tidal carbon di oxide.

Intra operative anaesthesia was maintained using oxygen and nitrous oxide 50:50, and Isoflurane 1%. Intraoperative use of analgesics was standardized. 0.1mg/kg of Morphine intra venous and 1gm of Paracetamol intra venous was administered to all patients. If the anaesthesiologist felt that the patient required additional analgesia either intra operatively or post operatively, it was administered, and noted down in the data collection form. Patients were examined for myalgia at two hours and four hours post operatively. Post operative myalgia on the following days could not be assessed as this was in the day care setting.

Assessment was made using different standard criteria(3). Jaw relaxation was according to the criteria of Young et al- namely good, incomplete and poor. Coughing and gagging- none, mild, moderate, severe; laryngospasm-none, partial, total; patient movement- none, mild, moderate, severe, according to Nimo et al. Overall insertion conditions were assessed according to the modified scheme of Lund and Stovner- excellent- insertion easy, no gagging, coughing, movement or laryngospasm; good-insertion resulting in mild to moderate coughing, gagging, movement with no laryngospasm; poor- insertion possible but resulting in moderate to severe coughing, gagging, patient movement with no laryngospasm; and unacceptable- severe coughing, gagging, movement or laryngospasm. Scoring of Laryngeal Mask Airway insertion was performed only for the first attempt at insertion.

Statistical analysis was performed using analysis of variance (ANOVA) with Bonferroni's t test and Chi square test to compare groups and calculate duration of apnoea. Fischer's exact test was used to assess insertion conditions, fasciculations and myalgia. A p value of < 0.05 was considered significant.

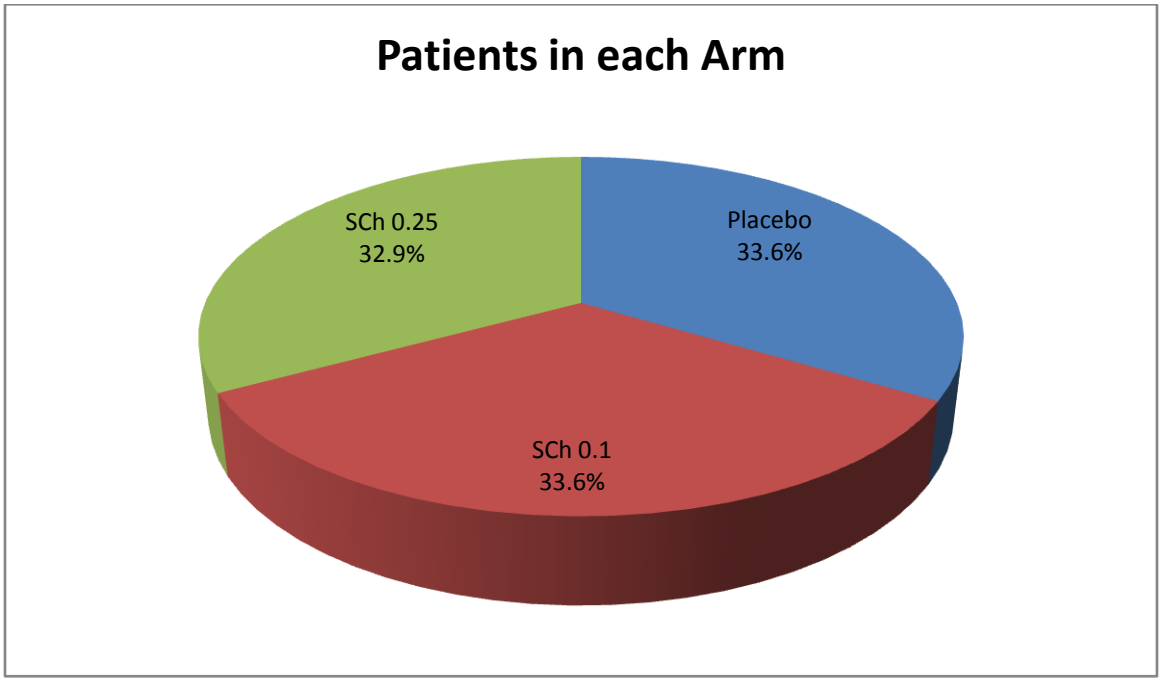
RESULTS

The following results were obtained from the study. Group I refers to placebo which was saline, Group II refers to 0.1mg/kg of Succinylcholine and Group III refers to 0.25mg/kg of Succinylcholine.

1) Adequate **sample size** was attained with a total of 283 patients. Informed consent was taken from all patients. Group I and II had 95 patients each, and Group III 93 patients. All patients were ASA I or II. None of the patients had a difficult airway.

Demographic Data

	Placebo- saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
No Of Patients- n (%)	95 (33.6%)	95 (33.6%)	93 (32.9%)

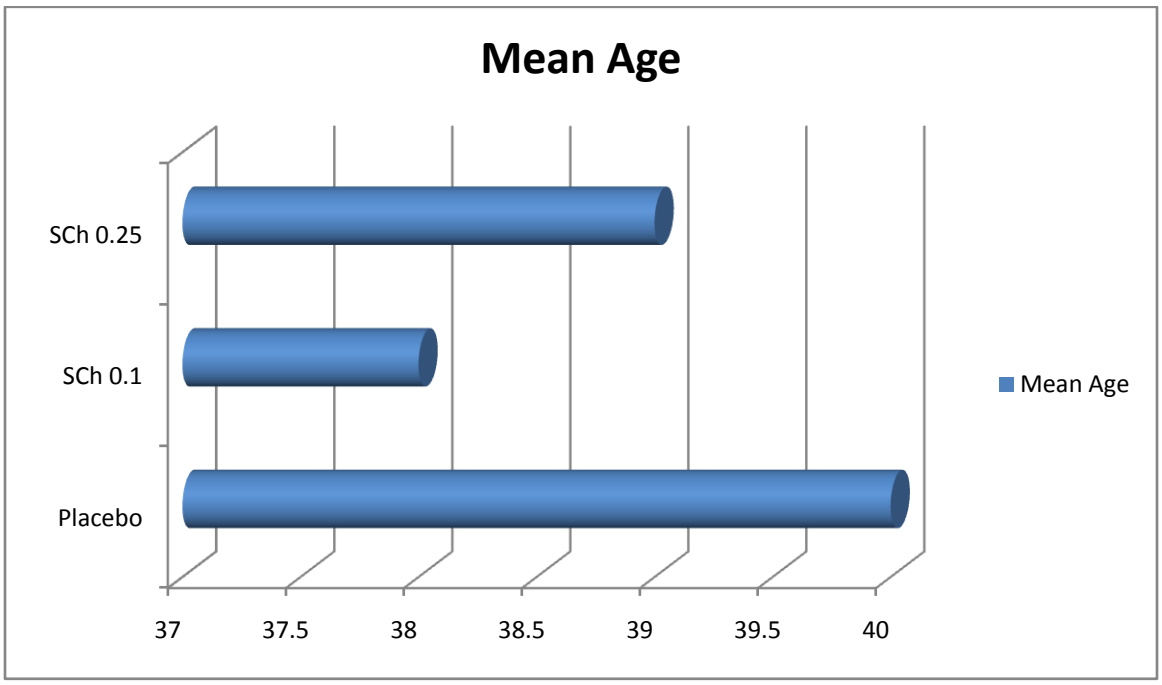


2) **Demographically** all groups were equally distributed in terms of age, weight, height and BMI.

Age

	Placebo- saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
Age(yr) - mean(+/- SD)	40 (12)	38 (12)	39 (12)

Mean age was 37 to 40 and was equally distributed in all three groups.

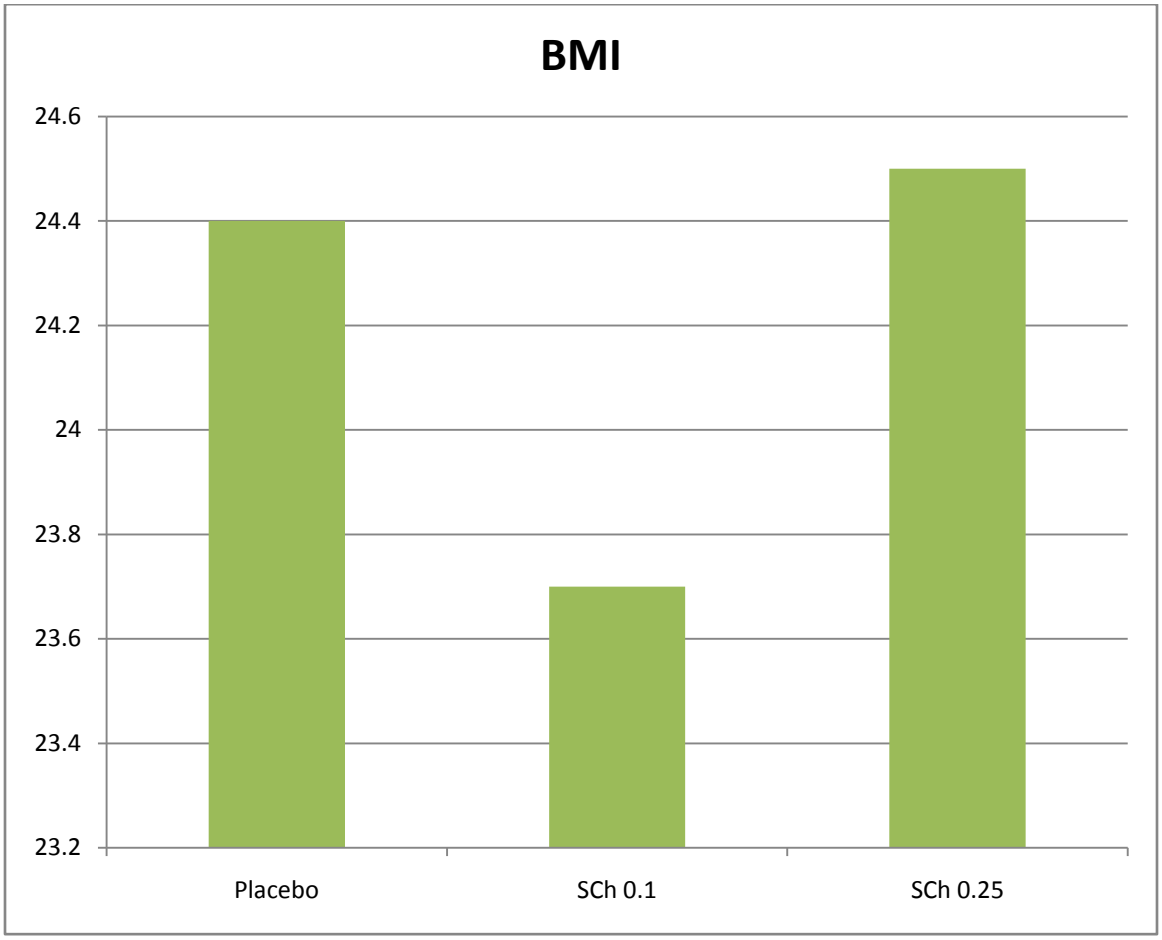


Demography

Weight, height and BMI

	Placebo- saline (groupI)	0.1mg/kg Succ innylcholine (groupII)	0.25mg/kg Succinylcholine (groupIII)
Weight(kg)– mean(+/- SD)	66 (12)	64 (13)	64 (11)
Height(cms)– mean(+/- SD)	163 (9.5)	164 (9.3)	162 (9.1)
BMI – mean(+/- SD)	24.4 (4)	23.7 (4.5)	24.5 (3.7)

The average BMI in all three groups was 23- 24.

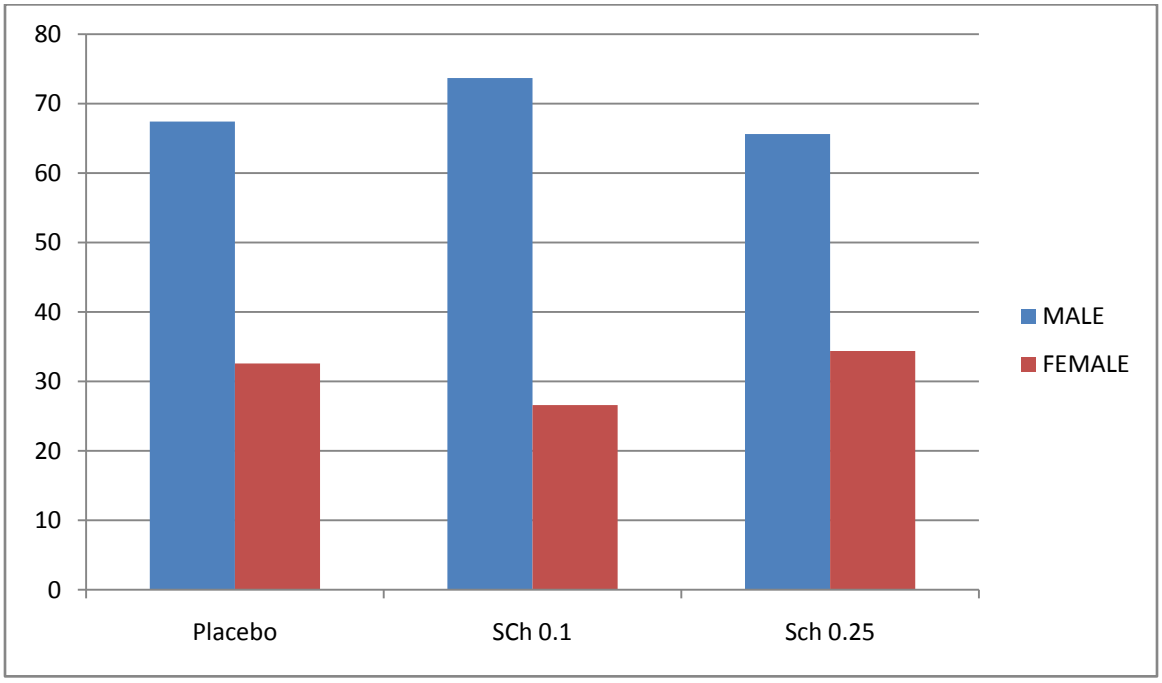


3) **Sex ratio**

	Placebo- saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
Sex- M:F n (%)	64:31 (67.4%:32.6%)	70:25 (73.7%:26.3%)	61:32 (65.6%:34.4%)

The male to female ratio was equal in all three groups, though there were more males than females in each group.

Sex ratio

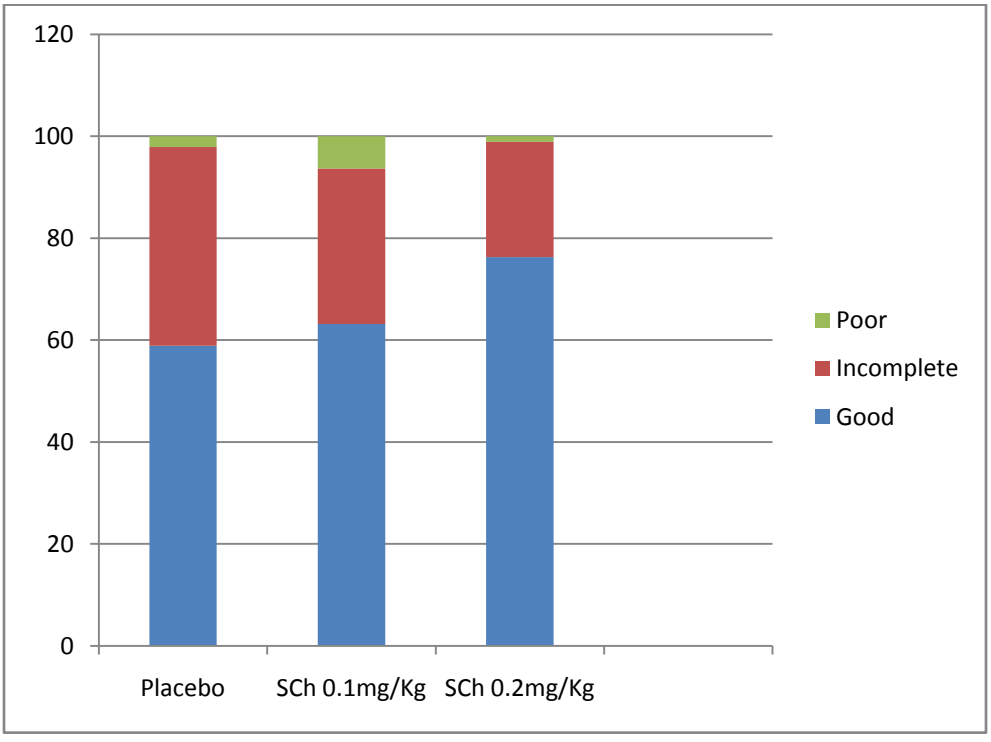


4) **Conditions during LMA insertion- jaw relaxation**

Conditions during LMA insertion-jaw relaxation

	Placebo- saline (groupI)	0.1mg/kg Succ innylcholine (groupII)	0.25mg/kg Succinylcholine (groupIII)
Jaw Relaxation (p-0.026)			
Good- n (%)	56 (58.9%)	60 (63.2%)	71 (76.3%)
Incomplete- n (%)	37 (38.9%)	29 (30.5%)	21 (22.6%)
Poor- n (%)	2 (2.1%)	6 (6.3%)	1 (1.1%)

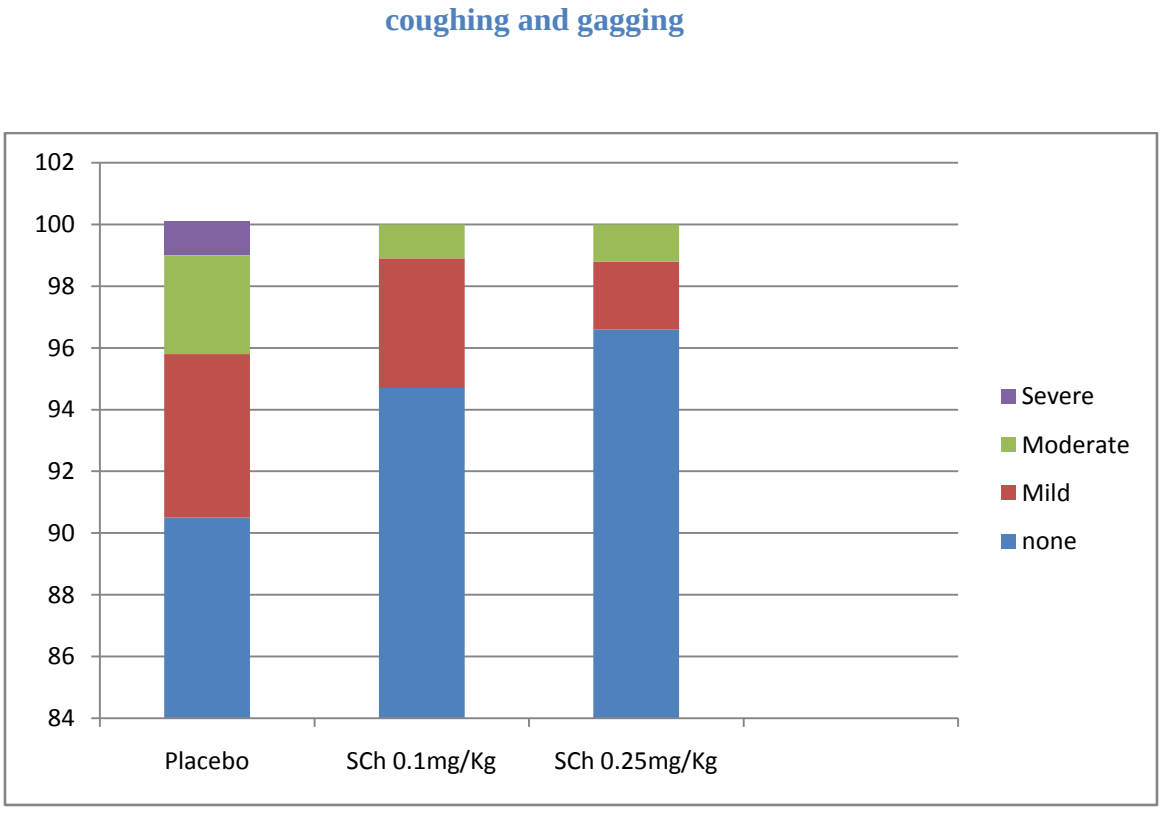
On looking at **conditions during Laryngeal Mask Airway insertion**; **jaw relaxation** was significantly better in Group III, with a p value of 0.026. It was also seen that jaw relaxation was incomplete in close to 40% of the patients in the 0.1mg/kg Succinylcholine group.



5) **<u>Conditions during LMA insertion- coughing and gagging</u>**

Gagging, Cough (p-0.59)			
None- n (%)	86 (90.5%)	90 (94.7%)	90 (96.6%)
Mild- n (%)	5 (5.3%)	4 (4.2%)	2 (2.2%)
Moderate- n (%)	3 (3.2%)	1 (1.1%)	1 (1.1%)
Severe- n (%)	1 (1.1%)	0 (0.0%)	0 (0.0%)

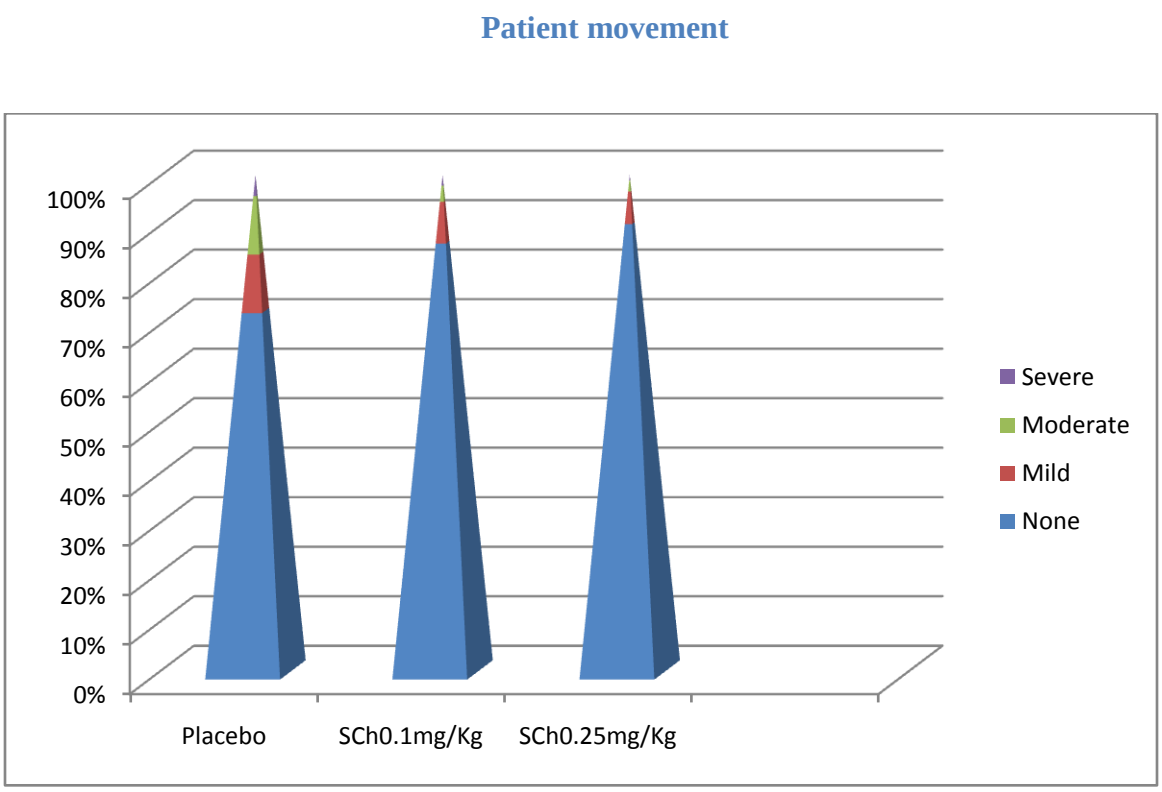
There was no statistically significant difference in the incidence of **coughing and gagging** between all three groups, though clinically there was more in the Placebo group.



5) **Conditions during LMA insertion- patient movement**

Patient movement (p- 0.018)			
None- n (%)	69 (72.6%)	83 (87.4%)	84 (90.3%)
Mild- n (%)	11 (11.6%)	8 (8.4%)	6 (6.5%)
Moderate- n (%)	11 (11.6%)	3 (3.2%)	2 (2.2%)
Severe- n (%)	4 (4.2%)	1 (1.1%)	1 (1.1%)

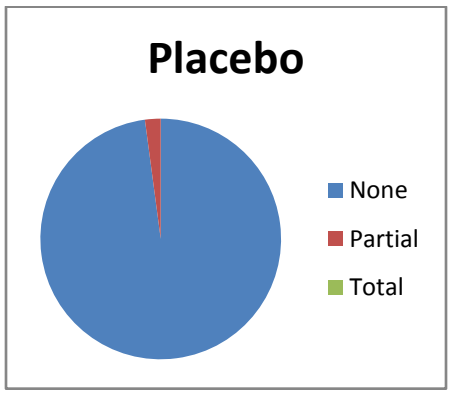
There was significantly more **patient movement** in the Placebo group, with a p value of 0.018. Group II and III had similar values.

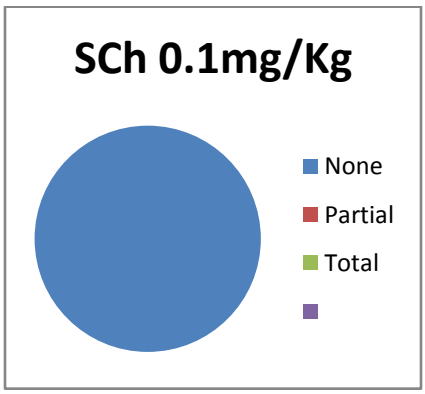


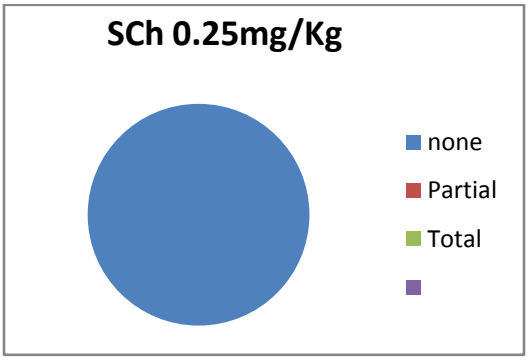
6) Only two patients in the Placebo group experienced partial **laryngospasm**. None of the other patients had laryngospasm.

Laryngospasm (p-0.136)			
None- n (%)	93 (97.9%)	95 (100%)	93 (100%)
Partial- n (%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
Total	0 (0.0%)	0 (0.0%)	0 (0.0%)

Laryngospasm



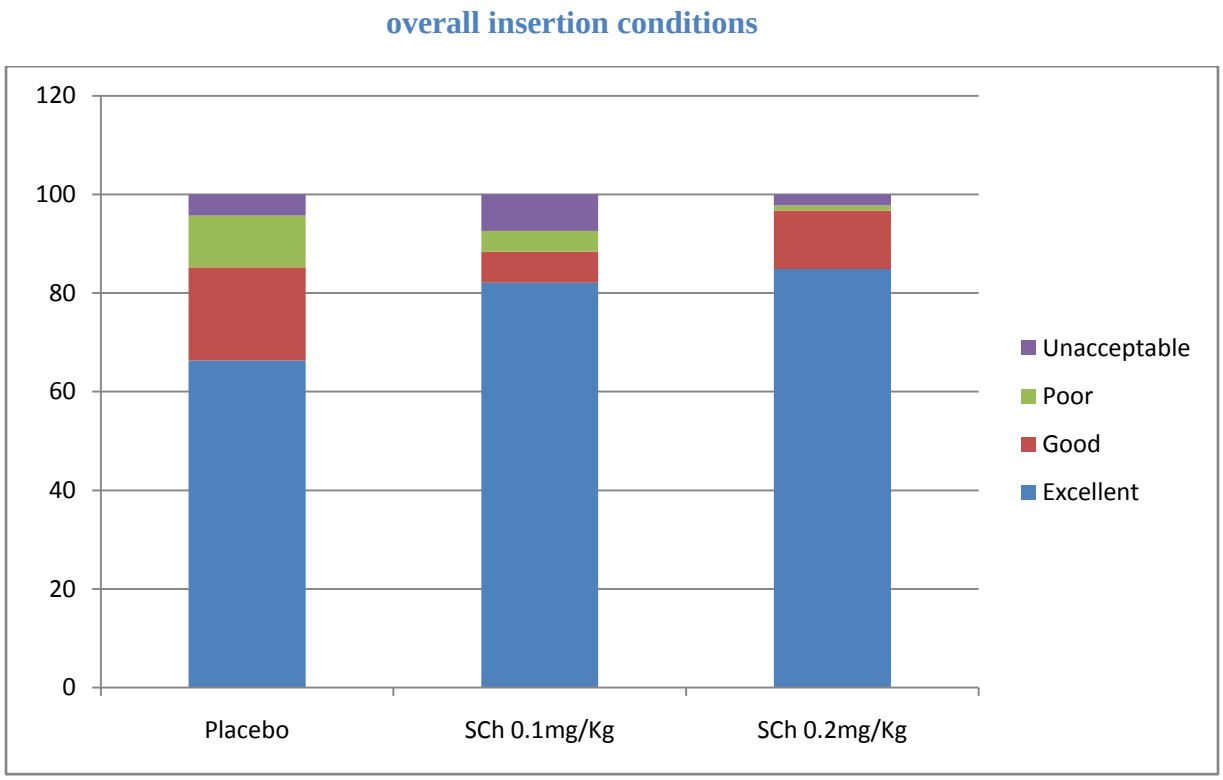




7) Overall insertion conditions

OVERALL INSERTION CONDITIONS (p- 0.003)			
Excellent	63 (66.3%)	78 (82.1%)	79 (84.9%)
Good	18 (18.9%)	6 (6.3%)	11 (11.8%)
Poor	10 (10.5%)	4 (4.2%)	1 (1.1%)
Unacceptable	4 (4.2%)	7 (7.4%)	2 (2.2%)

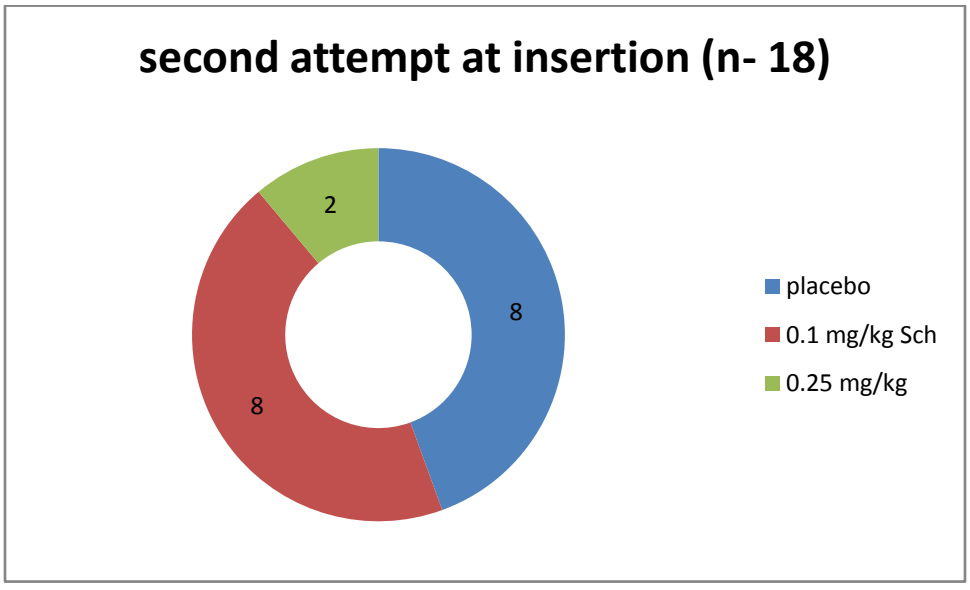
Overall insertion conditions were evidently better in Group III with a p value of 0.003. Though excellent insertion conditions were seen in 82% of Group II, this group had a higher number of unacceptable insertion conditions, compared to Group I. This helps us conclude that 0.1mg/kg of Succinylcholine is not sufficient to aid smooth insertion of the Laryngeal Mask Airway.



8) **Insertion attempts-** In most patients the Laryngeal Mask Airway was inserted in the first attempt, 264 out of 283 patients. Only 18 patients required two attempts and only one patient required three attempts. Thus statistically there was no difference in number of insertion attempts. Most often the Laryngeal Mask Airway was inserted, there would be patient reaction, and an additional dose of Propofol would be given. Most cases would settle with the Laryngeal Mask Airway well in place, not requiring a second attempt at insertion. Out of the 18 patients that required a second attempt, there were 8 each from Group I and Group II, and only 2 from Group III.

Total insertion attempts

	Placebo - saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
No of insertion attempts mean(+/- SD) p- 0.27	1 (0.27)	1 (0.27)	1 (0.25)

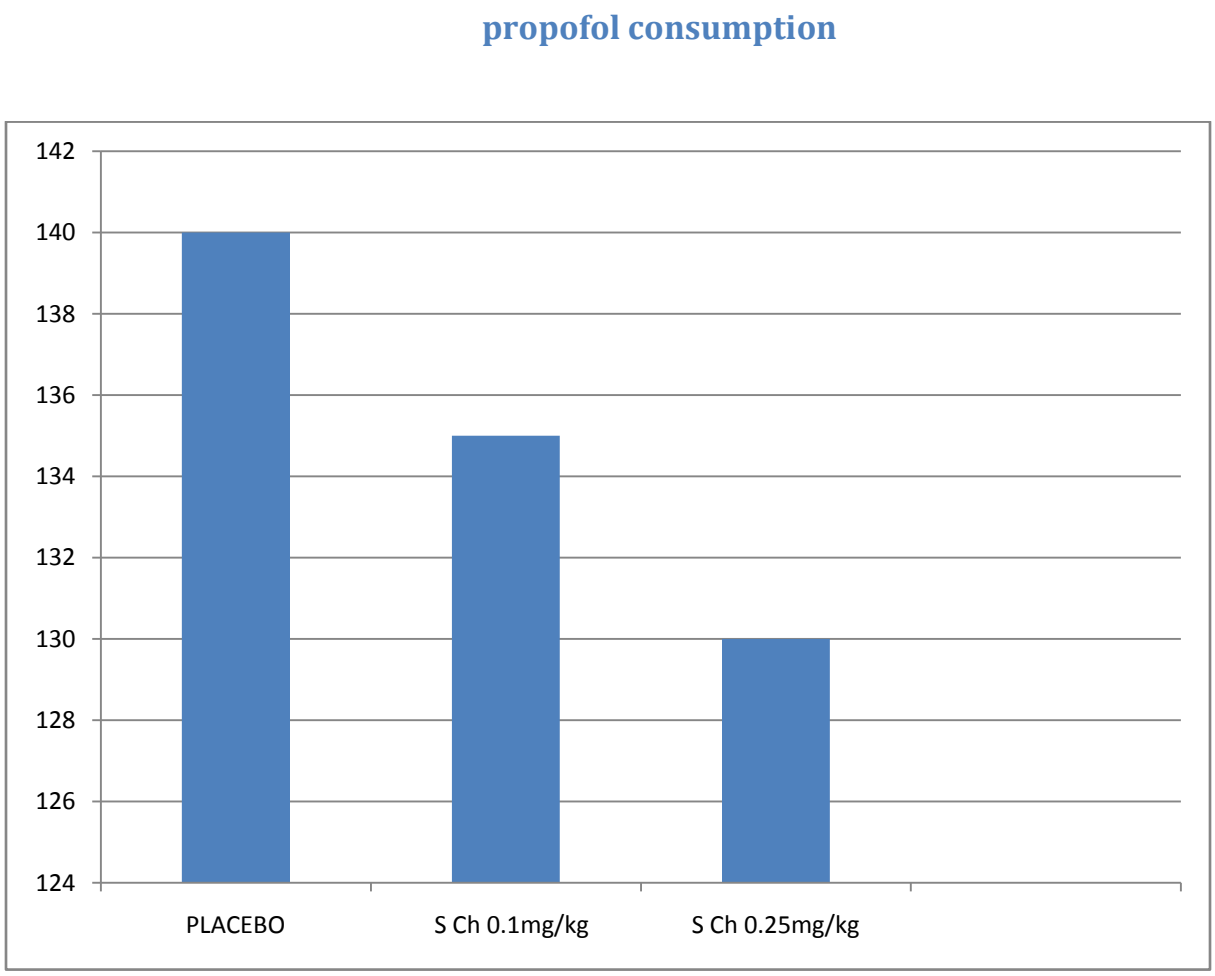


9) Total Propofol requirement

Total dose of Propofol in each group

	Placebo- saline (group I)	0.1mg/kg Succ innylcholine (groupII)	0.25mg/kg Succinylcholine (groupIII)
Total dose– median (IQR) p- 0.024	140 (120- 160)	135 (110-150)	130 (120- 145)

Significantly more in the Placebo group with a p value of 0.024.

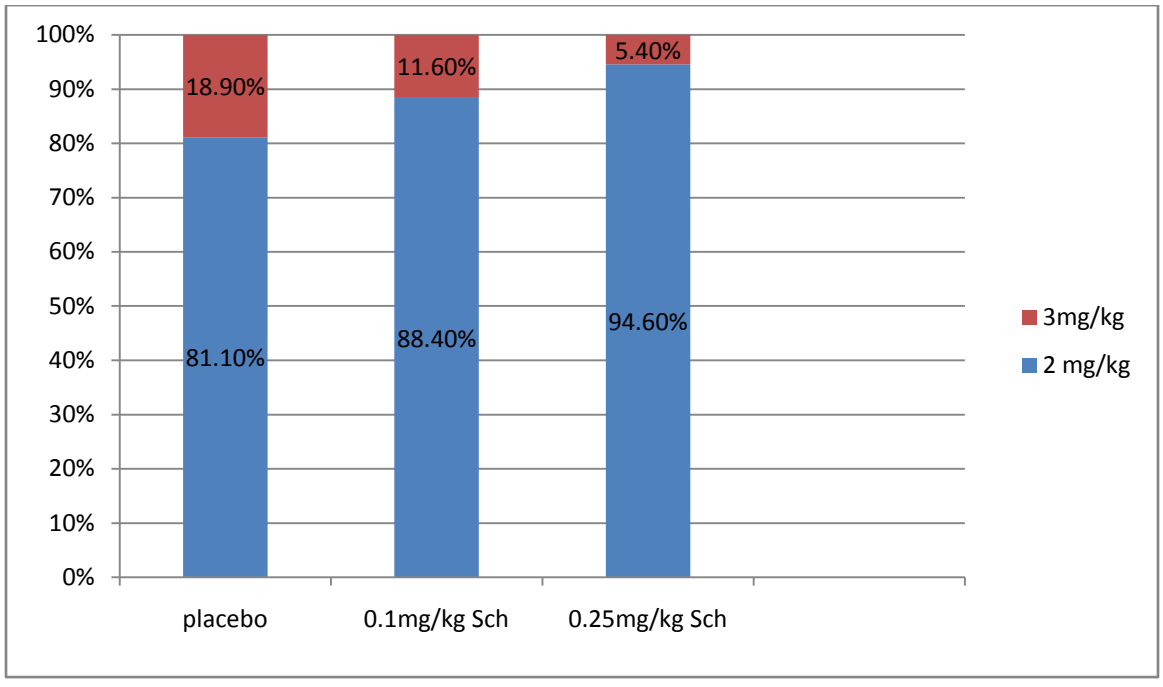


Propofol consumption in mg/kg

	Placebo- saline (group I)	0.1mg/kg Succinylcholine (groupII)	0.25mg/kg Succinylcholine (groupIII)
Propofol 2mg/kg n (%)	77 (81.1%)	84 (88.4%)	88 (94.6%)
Propofol 3mg/kg n (%)	18 (18.9%)	11 (11.6%)	5 (5.4%)

Most patients required 2mg/kg of Propofol, but out of those requiring 3mg/kg most were from the placebo and 0.1mg/kg Succinylcholine group. 249 patients of 283 required 2 mg/kg, and 34 needed 3 mg/kg.

Propofol consumption in mg/kg



10) Haemodynamics and Oxygen Saturation in each group

	Placebo- saline (groupI)	0.1mg/kg Succ innylcholine (groupII)	0.25mg/kg Succinylcholine (groupIII)
Systolic blood pressure (mm Hg) mean(+/- SD)			
Pre-Induction (p-0.205)	132 (21.1)	129 (15.9)	134 (18.3)
Post-Induction (p-0.019)	103 (15.2)	102 (13.9)	108 (16.3)
Post-Insertion (p-0.166)	101 (16.0)	97 (11.5)	99 (12.4)
Diastolic blood pressure (mm Hg) – mean(+/- SD)			
Pre-Induction (p-0.345)	77 (10.6)	75 (13.3)	78 (13.1)
Post-Induction (0.044)	61 (12.4)	58 (12)	63 (14)
Post-Insertion (p-0.303)	59 (11.5)	57 (11.30	56 (10.8)
Mean arterial blood (mm Hg) pressure – mean(+/- SD)			
Pre-Induction (p-0.226)	90 (11.1)	88 (12.4)	90 (12.8)
Post-Induction (0.013)	71 (12.5)	68 (11.6)	74 (13.5)
Post-Insertion (p-0.279)	69 (11.5)	66 (11)	67 (11.4)
Heart rate (bpm) – mean(+/- SD)			
Pre-Induction (p- 0.354)	84 (15.6)	85 (15.9)	87 (14.8)
Post-Induction (p-0.909)	77 (14.3)	77 (13.1)	78.3 (12.9)
Post-Insertion (p-0.789)	73 (12.0)	72 (12.0)	73 (12.8)
SpO2% – mean(+/- SD)			
Pre-Induction (p-0.845)	99 (1.1)	99 (1.1)	99 (0.9)
Post-Induction (p-0.332)	99 (0.3)	99 (0.9)	99 (0.5)

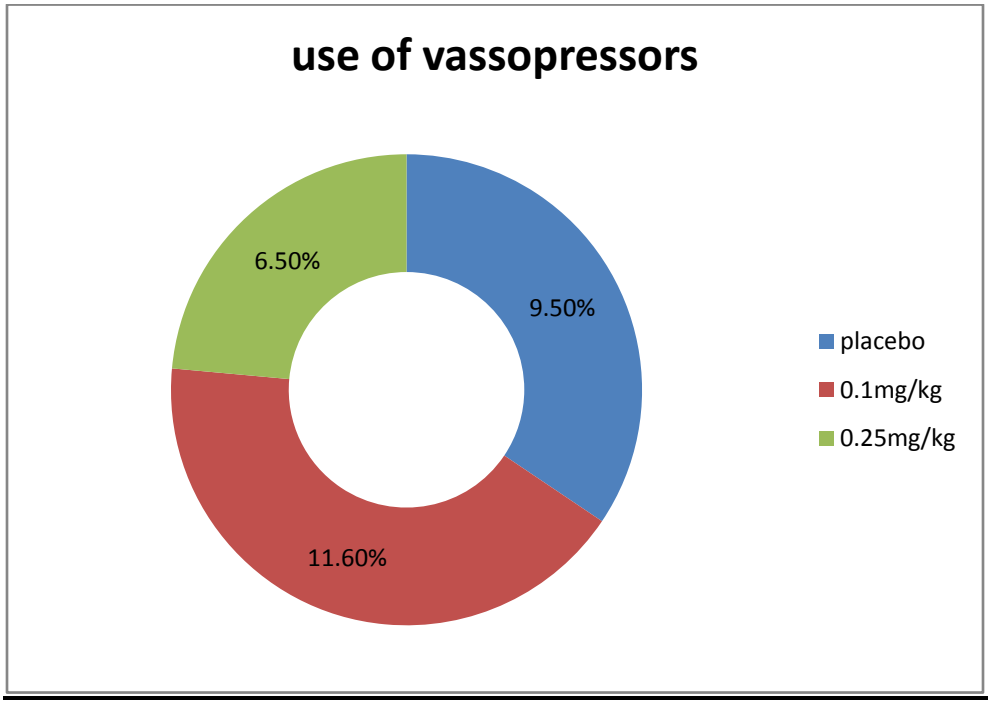
Post-Insertion (p-0.841)	99 (0.8)	99 (0.9)	99 0.7)

There were no statistically significant differences in haemodynamics between the groups.

11) As haemodynamics were not different, the **use of vasopressors** was not significantly different between the groups.

Use of Vasopressors

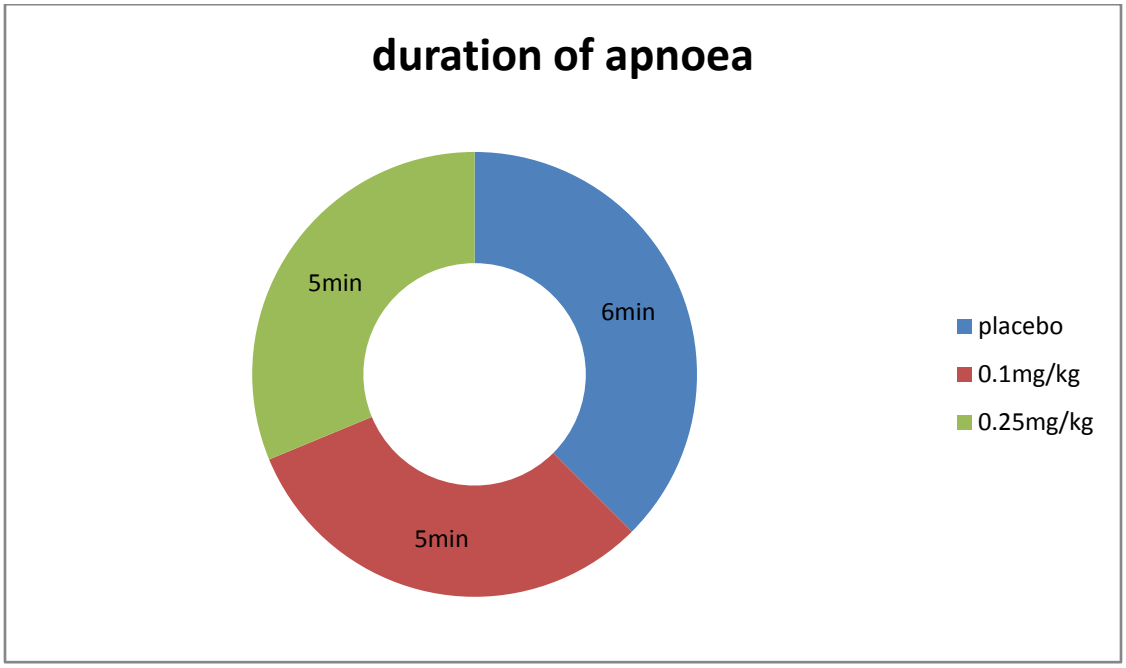
	Placebo- saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
n (%) p- 0.474	9 (9.5%)	11 (11.6%)	6 (6.5%)



12) **Duration of apnoea**- Average duration of apnoea was 5-6 minutes. There was no clinically significant difference in the duration of apnoea between the groups. This could be because the placebo group required significantly more Propofol.

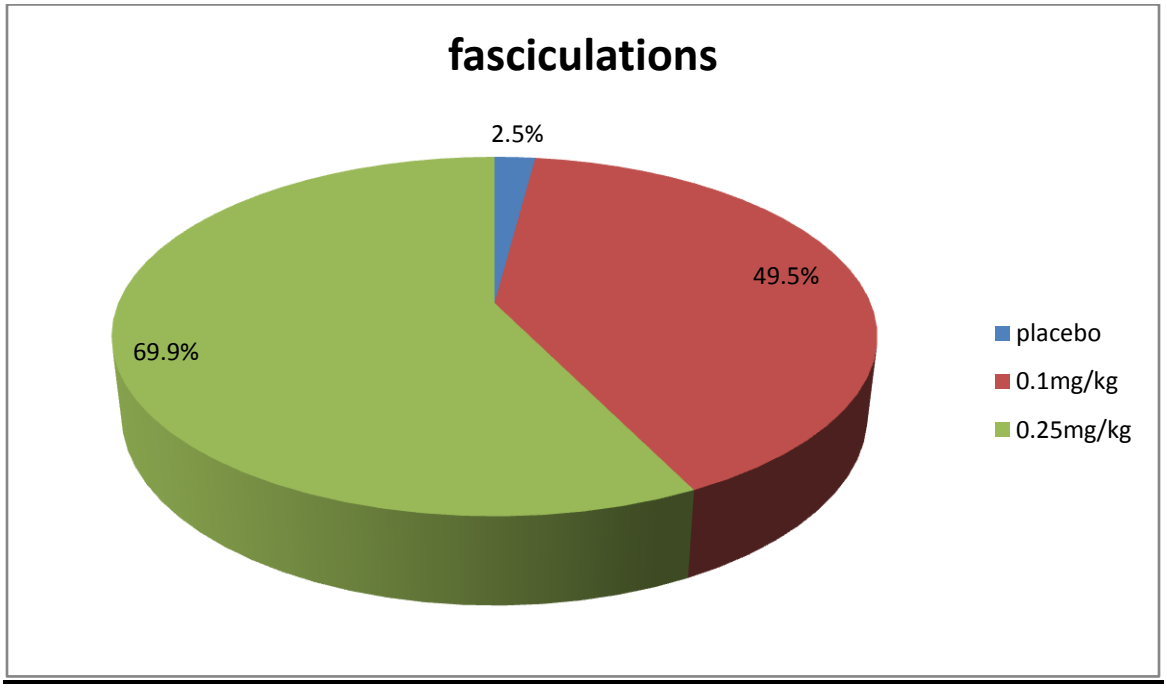
Duration of apnoea

	Placebo - saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
Apnea duration (min) Median (IQR) p- 0.502	6 (0-25)	5 (0-30)	5 (0-30)



13) Fasciculations were more in Group III.

	Placebo - saline (groupI)	**0.1mg/kg Succinnylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
n (%)	2 (2.5%)	47 (49.5%)	65 (69.9%)



14) Only one patient in Group II complained of **myalgia** after two hours. Two patients in

Group I complained of myalgia after four hours.

Myalgia after 2 hours

	Placebo - saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
n (%) p (0.37)	0 (0%)	1 (1.1%)	0 (0%)

Myalgia after 4 hours

	Placebo - saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
n (%) p (0.13)	2 (2.1%)	0 (0%)	0 (0%)

15) **Intraoperative analgesia** was standardized for all patients so that it would not confound results of post operative myalgia. If the anaesthesiologist felt the patient required more analgesia it was given and recorded. There was no statistically significant difference in the amount of additional analgesia given. Hence it was not a confounding factor towards postoperative myalgia.

Intraoperative analgesia

	Placebo - saline (groupI)	**0.1mg/kg Succ innylcholine (groupII)**	**0.25mg/kg Succinylcholine (groupIII)**
n (%) p	15 (15.8%)	19 (20%)	11 (11.8%)

DISCUSSION

Christian Medical College is a tertiary level teaching centre that caters to 5000 out patients a day, and has 2600 inpatient beds. Surgical specialties do 2000 surgeries a month. Our ambulatory surgery center was set up in the year 2000. There are two operating theatres, each comprising of a well set up anaesthesia work station. On an average 350- 400 cases are done in a month. The departments of general surgery, vascular surgery, endocrine surgery, hepatobiliary surgery, colorectal surgery, orthopaedics, urology and otorhinolaryngology operate every week. Most of these are under general anaesthesia using the Laryngeal mask Airway as regional or neuraxial anaesthesia is asscociated with slower recovery and discharge(64). The main theatre complex in this hospital has thirty two operating theatres. Here too the Laryngeal Mask Airway is used in several surgeries. In fact around the world the use of the Laryngeal Mask Airway is becoming more and more common for numerous different surgeries. Hence the relevance of this study.

Propofol is the induction agent of choice in Laryngeal Mask Airway placement as it blunts the laryngeal reflexes (33). The disadvantage of using Propofol alone is excessive patient movement and coughing and gagging. This leads to additional Propofol usage and thus hypotension and prolonged duration of apnoea. Wafaa et al found that failed insertion attempts of Laryngeal Mask Airway placement were due to coughing and gagging in 75% of patients when only Propofol was used (3). Successful insertion at first attempt was only 60%.

Numerous adjuvants have been and are still being studied to facilitate Laryngeal Mask Airway insertion. Benzodiazepines are known to reduce upper airway reflexes(65). Midazolam has been studied more than once (3), (66). Wafaa found that 0.04mg/kg of Midazolam helped

reduce the Propofol dose by 40%. Thus there was less hypotension and more cardiovascular stability. The disadvantage of Midazolam is its sedative effect and particularly in the ambulatory setting this may cause delayed discharge.

Other agents that have been studied like Clonidine(56) and Dexmeditomidine(63) all which have some benefit but sedation would be an issue in the ambulatory surgery setting and costs and availability too need to be looked into.

Relatively newer Opioids such as Alfentanyl, Remifentanyl and Butorphanol are also being studied but duration of apnoea, hypotension, post operative nausea, vomiting and availability are issues to be dealt with(55)(58)(62)(61).

Ketamine provided stable haemodynamics and less duration of apnoea and was found to be more useful in the difficult airway setting(59)(66)(60).

. Since relaxation of the muscles of the airway is what would enable smooth insertion, a muscle relaxant would be the best agent to serve this purpose. The ideal muscle relaxant for use in the ambulatory setting is still in search(67),(68),(64). Muscle relaxants avoid side effects like hypotension and sedation.

Non depolarizing muscle relaxants like Mivacurium and Rocuronium have been studied(4)(54). The effects of residual neuromuscular blockade always remain a concern with non depolarizing agents, especially in the day care setting. The use Neostigmine and the nerve stimulator are implicated if non depolarizing agents are being used. Use of Neostigmine can be associated with increased incidence of post operative nausea and vomiting. . Suggamedex as the answer to the problem is being hoped for.

Depolarizing agents like Succinylcholine are still widely used because of its quick onset, short duration, and excellent intubating conditions(68). It is easily available, inexpensive, a time tested drug, and has no sedative side effects. The usual induction dose is 1- 2 mg/kg (7). Side effects include apnoea, anaphylaxis and myalgia. Lower doses have less of these side effects. 0.1 mg/kg of Succinylcholine is known to relieve laryngospasm (69) and does not cause increased duration of apnoea. To date none of the studies done on low dose Succinylcholine compare two different doses to estimate the ideal dose for smooth insertion of the Laryngeal Mask Airway. Yoshino et al did such a study comparing 0.25mg/kg and 0.5mg/kg Succinylcholine, with Thiopentone as the induction agent. 0.5 mg/kg Succinylcholine had higher incidence of side effects like fasciculations, myalgia and apnoea (6). Most studies compare another agent such as Midazolam, or Fentanyl with Succinylcholine. In our study we look at 0.1 mg.kg and 0.25mg/kg of Succinylcholine. Most studies have a sample size of 60-150. In this study 283 patients were included.

283 patients were equally distributed in all three groups- Placebo, 0.1mg/kg of Succinylcholin and 0.25mg/kg of Succinylcholine. There were 95 patients each in the placebo and 0.1mg/kg group, and 93 patients in the 0.25mg/ kg group. This was adequate to power the study well as according to the sample size calculation each arm required 92 patients. Demographically patients were equally distributed in terms of age, weight, height and BMI. Overall there were more males than females. This is probably because patients coming for Urological procedures were mainly male. Anorectal rectal disorders are more in males than females with ratio of 70%:30% (70). A lot of patients included in the study came for anorectal procedures. This is also one of the reasons for males than females.

Jaw relaxation was clearly better in Group III. Group II had quite a high incidence of incomplete and poor jaw relaxation. This helps us infer that 0.1mg/of Succinylcholine is probably not sufficient and 0.25mg/kg is better for adequate jaw relaxation. There was no significant difference in the incidence of coughing and gagging between all three groups. Clinically there were more numbers in the Placebo group, though not statistically significant. Patient movement was significantly more in the Placebo group. This was the most common reason for additional Propofol requirement. Laryngospasm was not experienced by any patient; there was partial laryngospasm in only two patients in the Placebo group. This is probably because of the uniform use of 2mg/kg of Propofol which blunts laryngeal reflexes.

Overall insertion conditions were clearly better in the Group III, both clinically and statistically. Group II had similar values to Group III in the 'excellent' insertion conditions group, and had 6.3% and 4.2% of patients who had 'good' and 'poor' insertion conditions respectively. Surprisingly Group II had more patients in with 'unacceptable' insertion conditions, due to inadequate jaw relaxation and patient movement; 7.4% compared to even the Placebo group, which had only 4.2%. One explanation could be that there was more patient movement in the Placebo group during attempts to open the jaw hence an additional dose of Propofol was given before attempting insertion itself. In the Group II the first signs of inadequate dose were during insertion of the Laryngal Mask Airway itself and that is probably why this group had a higher number of unacceptable insertion conditions. We infer again that 0.1mg/kg of Succinylcholine is not sufficient to facilitate smooth insertion of the Laryngeal Mask Airway.

Number of insertion attempts was not statistically significant, most requiring one attempt. The number of patients requiring more than one insertion attempt was 19, of which 18 needed

two attempts. Of these there were eight each from Group I and II, showing us that number of insertion attempts was clinically more in these groups, though not statistically significant.

Total Propofol consumption was significantly more in the Placebo group. Most patients in the study required 2mg/kg of Propofol, but 12% required 3mg/kg of which 60% were from the placebo group and 32% from the 0.1mg/kg group. This again shows us that clinically more patients in these groups required more propofol, though statistically not significant.

Haemodynamic stability was similar in all groups. Though a large drop in blood pressure was expected in the placebo group because they required more Propofol, they were found to be stable. Only 26 in the entire 283 patients required a vasopressor, Ephedrine 6mg to restore the blood pressure, most often after insertion of the Laryngeal Mask Airway.

Duration of apnoea was the same in all groups. The Placebo group though expected to have a shorter duration of apnoea had duration similar to the Succinylcholine groups. This is probably because of the increased Propofol consumption.

Fasciculations were more in the Group III. Some patients in the 0.1mg/kg group did not have fasciculations. There were two patients in the Placebo group who had ‘fasciculations’, these were probably involuntary movements that can occur with Propofol, and were interpreted as fasciculations.

The incidence of myalgia was very low. Lately it has been observed that myalgia is common after ambulatory surgery and the causes are multifactorial. The incidence of myalgia is highest in the first 24 hours, but does occur even afterwards (38). One study by Yoshino et al

showed a higher incidence of myalgia on the third post operative day. In this study myalgia patients were checked for myalgia 2 hours and 4 hours post operatively as they were discaharged on the same day. Myalgia was seen in one patient in Group II after 2 hours and two patients in the Placebo group after 4 hours. This too may advocate the multifactorial cause of myalgia.

CONCLUSIONS

This study concludes that a low dose of Succinylcholine does facilitate insertion of the Laryngeal Mask Airway. The ideal dose is 0.25mg/kg of Succinylcholine. 0.1mg/kg is not sufficient and is associated inadequate jaw relaxation and does not always provide smooth insertion conditions. There is decreased Propofol consumption with use of Succinylcholine. Haemodynamics were not affected adversely. Duration of apnoea is not unduly prolonged and was the same in all groups. Fasciculations were more in the 0.25mg/kg group but there was no relation between fasciculations and myalgia, reinstating the multifactorial basis behind myalgia.

LIMITATIONS

1) Though the primary investigator was blinded, fasciculations was sometimes a confounding factor. All cases using Succinylcholine especially 0.1mg/kg did not have fasciculations, so it was not necessarily known whether Succinylcholine was used or not.
2) Myalgia was assessed only at two and four hours. There may have been more myalgia later than this period.

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APPENDIX

I) Patient information sheet

II) Patient consent form

III) Data collection sheet

IV) Data spread sheet

I) INFORMATION SHEET

This is a study that is validating the use of succinyl choline facilitating the LMA insertion.

The patient will be undergoing a surgical procedure requiring general anaesthesia which will be administered in this case by LMA (Laryngeal Mask Airway). This is a simple and safe procedure. Here the airway which looks like a tube is inserted through the mouth and oral cavity and rests over the respiratory passage. In normal conditions after induction (putting the patient into a deep sleep), the LMA is inserted directly without any muscle relaxant. However there can be some difficulty during the insertion of the LMA as the oral and pharyngeal musculature can be tight.

This study asseses the benefit of using Succiny choline in facilitating LMA insertion.

Succinyl choline is a drug which has been widely used in anaethetic practice. It is a muscle relaxant that is used to relax the pharyngeal (throat) and laryngeal (vocal chords) muscles. It is often used during general anaesthesia requiring endotracheal intubation. Here in this study the drug will be administered after putting the patient to sleep and soon after the LMA will be inserted. Vital parameters such as heart rate, blood pressure etc will be monitored during the surgery. Post operatively side effects will be assessed.

It is vital to note that as this is blinded study the patient may not receive the actual drug and might only receive a placebo (normal saline) injection. There are no associated risks with this. The common side effects of Succinylcholine are

fasciculations, postoperative body pain and it is not used in patients with burns and paralysis due to severe side effects.

The potential benefit of using SC can be easier insertion of the LMA, facilitating better anaesthesia, lesser soft tissue trauma, reduced post operative pain and voice problems.

The patient has every right to refuse participation in the study but cannot decide which drug he will receive (SC or NS).

Participation is voluntary and the patient can withdraw from the study at any time and refusal to participate will not involve any penalty or loss of benefits to which otherwise entitled.

All data and vital statistics obtained in this study will be confidential and will be maintained by the principal investigator.

There will be no compensation and/or treatment available to the subject in the event of a study-related injury

For any further queries:
Contact

Dr. Leah Maria Raju,

Dept of Anaesthesiology,

CMCH.

II) CONSENT FORM

Low dose Succinylcholine to facilitate LMA insertion

Date:

Patient's Name:

Patient's Initials:

Hospital No.

Date of Birth / Age:

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

DATA COLLECTION SHEET

Name- Surgery-

Hospital number-

Age-

Weight- Height- BMI-

ASA Grade-

Airway- Mallampati- Teeth- Neck extension

ASSESMENT

1) jaw relaxation-
2) coughing or gagging
3) patient movement-
4) laryngospasm-
5) overall insertion conditions-
6) total insertion attempts-
7) total Propofol requirement- ---------- mg (---------mg/kg)
8) haemodynamics

	pre induction	post induction	post insertion
Heart rate			
BP (MAP)			
SpO2			

Use of vasopressors- Drug- Dose-

9) apnoea duration-
10) fasciculations-
11) myalgia- 2hrs- 4hrs
12) additional analgesia- intra op post op

DRUG-

IV) DATA SPREAD SHEET

AUDIT

ADEQUACY OF INTRA OPERATIVE TIME OUT PROCEDURE

Dr Leah Maria Raju - Christian Medical College, Vellore

Dr Mary Korula
Head of Department of Anaesthesia

AUDIT- ADEQUACY OF INTRA OPERATIVE TIME OUT PROCEDURE

INTRODUCTION

One of the sentinel events in medical practice that can be wholly avoided is the predicament of wrong site, wrong procedure and wrong person surgery.Wrong-site surgery is defined as an operation conducted at the wrong site, on the wrong person, or resulting in the wrong procedure(1). Since the early nineties reports of wrong side, site, patient, procedure or implant have been reported. Such incidents continue to occur and numerous organizations have identified the problem and come up with protocols. The Second Global Patient Safety Challenge initiative by the WHO was Safe Surgery Saves Lives. This addressed the issue of safety of surgical care. The World Alliance for Patient Safety began work on this challenge in January 2007. The focus of the Challenge was the WHO Safe Surgery Checklist. The checklist was divided into three phases. The first, “sign in” is done before the induction of Anaesthesia, the second, “time out” is done just before the incision is made, and the third, “sign out” is done before the patient leaves the operating room. Our institution follows these guidelines. This audit was done on the first phase, “sign in”(2).

The American Joint Commission Board of Commissioners issued two Sentinel Event Alerts, one in 1998 and a follow up in 2001. As a reaction to numerous reports of wrong side, site, procedure and patient events, they hosted a Wrong Site Surgery Summit and along with many other key organizations came up with the Universal Protocol for Preventing Wrong Site, Wrong Procedure and Wrong Person Surgery in July 2003. This became effective in July 2004(3).

In 2003 the National Patient Safety Agency advocated side marking to avoid errors.

AUDIT SCOPE

Even in 2012 the search for methods to reduce the incidence of wrong site, side and patient are still on. The Urologists of University of Michigan Medical School, Ann Arbor came up with a radio opaque stickers labeled R or L that were stuck preoperatively and could be identified during intra operative fluoroscopy for upper tract endoscopic procedures(4).Mahar et al did a comprehensive electronic data base search and highlighted the findings of one interrupted time series (ITS) study(5). This study concluded that specific educational interventions which included a training session for junior staff, exposing them to reports of previous wrong side/ site surgeries and guidelines, helped reduce wrong site surgery. Wu et al published that scheduling errors also added to the risk of wrong side/ site surgery apart from increasing costs and disruption of operating room dynamics and delays (6).

These errors continue to occur at an alarming rate. It was the most frequently reported sentinel event in 2009 and the third most reported sentinel event in 2010. Though the exact incidence and prevalence is difficult to ascertain, the Joint commission estimated a national (USA) incidence as high as 40 per week (6). This is quite a disturbing number and indicates that the problem is a reality and there is scope for improvement. Methods to stop these mishaps should be taken seriously.

APPROACH AND METHODOLOGY

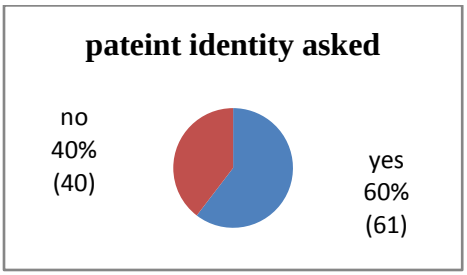
A data collection sheet was devised based on the institutions surgical safety checklist. This was distributed to anaesthesiologists in different operating rooms of various surgical specialties who observed if the “sign in” was done correctly or not. The surgeons and nurses

were not aware of this. This was done over a period of two weeks. 101 cases were entered and analyzed.

AUDIT FINDINGS

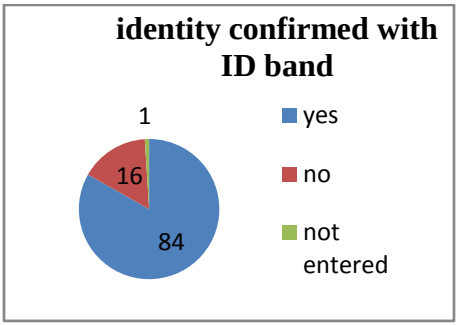
101 cases were included in the audit, from different specialties.

Was the patient asked his/her name?



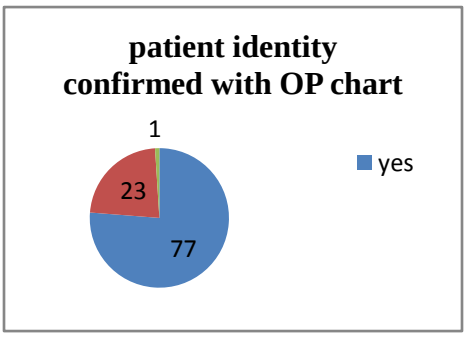
n = 101

Was the patient identity confirmed with the identity band?



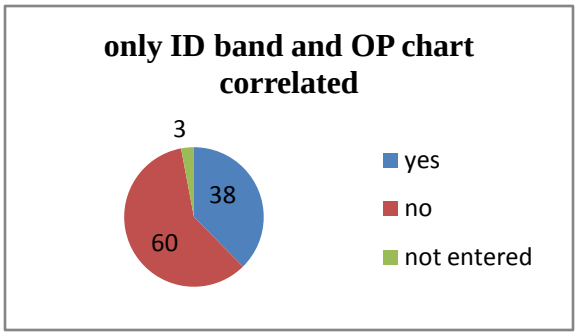
n = 101

Was the patient identity confirmed with the Out Patient chart?



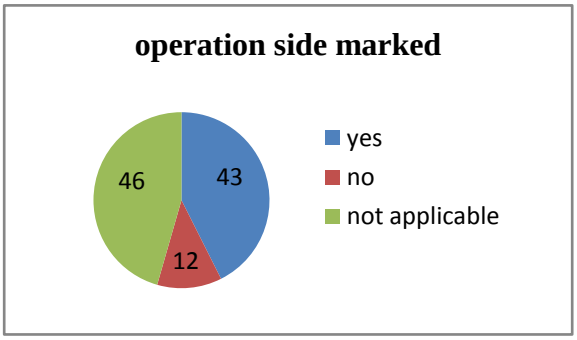
n = 101

Was the patient not spoken to and only the ID band and chart correlated?



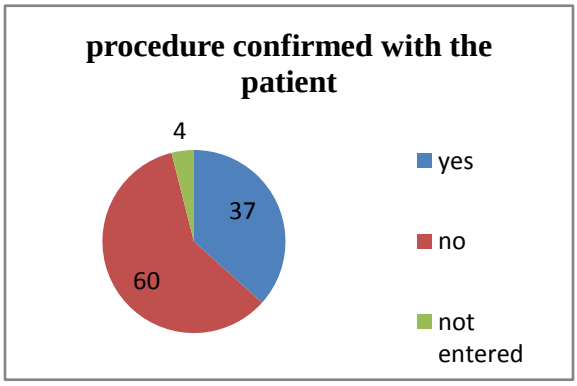
n = 101

Was the operation side marked ?



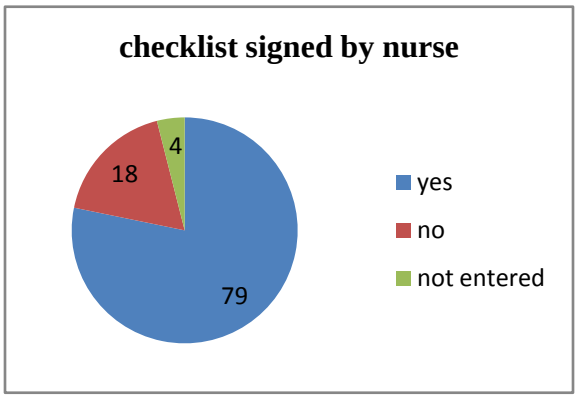
n = 101

Procedure confirmed with the patient?



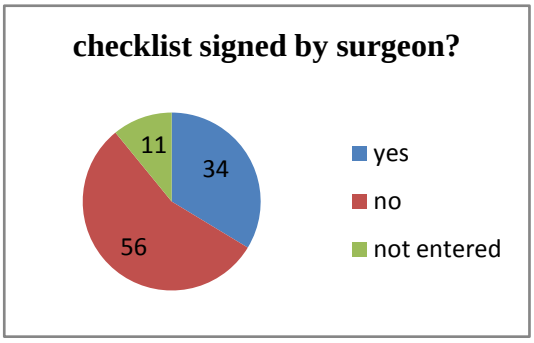
n = 101

Checklist signed by nurse?



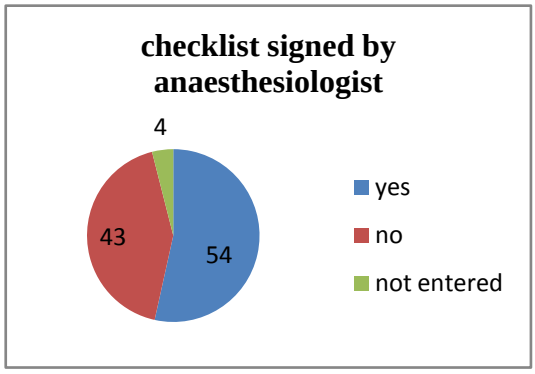
n = 101

Checklist signed by surgeon?



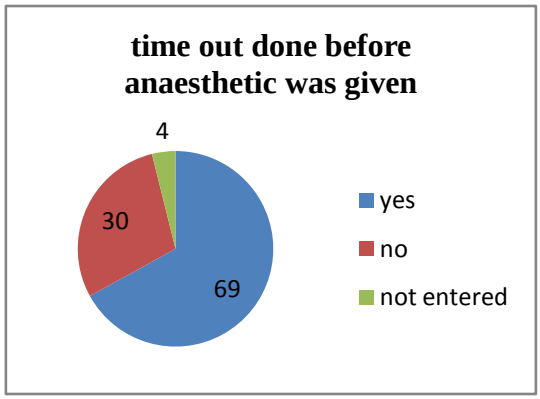
n = 101

Checklist signed by anaesthesiologist?



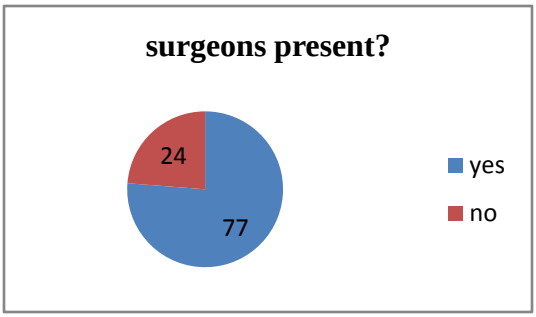
n = 101

Time out done before anaesthetic given?



n = 101

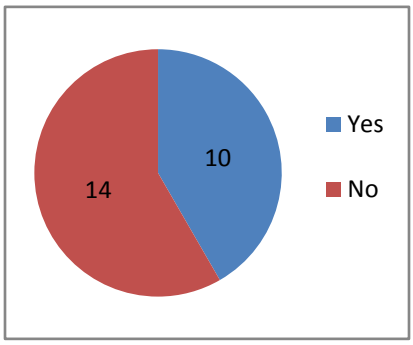
Were the surgeons present during time out?



n = 101

In cases where the surgeon was absent,

was it the first case or not?



n = 24

RECOMMENDATIONS

As seen in the audit findings, the patient is often not spoken to to confirm name and procedure. The nurses sign the check list in most cases though. The surgeons and anaesthesiologists lag in this field. Surgeons were present most of the time during the 'sign in', though when they were not it was the for the first case half the times.

We recommend that the importance of this check list be made known to all by regular training sessions that emphasise on mistakes made in the past. As an anaesthesiologist and a leader of the team, we may choose not to start a case until the 'sign in' is done in the correct manner, so that it becomes a habit for all. The findings of tis audit may be made known to the operatig room personnel and a reaudit can be done. During following audits if it is found that the checklist is not signed, it can be recommended that the concerned professional be penalised.

CONCLUSIONS

We conclude that presently the intra operative check list is not being followed in the correct manner. Patients are not being spoken to quite often and this can pose a great risk in the false identification of a patient. The surgeons, anaesthesiologists and nurses must each inculcate the habit and take upon the responsibility to ensure that this basic protocol is followed. This will also put the patient at ease and improve the overall functioning of the operating room.

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1	1	excision lip	1	1	1	1	1	1	
1	1	EUA LOF	2	1	1	1	1	1	
1	1	EUA LOF	1	1	1	1	1	1	
1	1	EUA LOF	1	1	1	1	1	1	
1	1	knee arthr	1	1	1	1	1	1	
1	1	hip biopsy	1	1	2	1	2	1	
1	1	suture rem	3	1	3	1	4	2	
1	1	STSG	1	1	1	1	1	1	
1	2	lt great toe	2	1	1	1	2	1	
2	2	RT BK STUI	2	1	1	1	1	1	
1	1		1	1	1	1	1	1	
1	1	OPEN BX K	1	1	1	1	2	1	
2	1	BX KNEE	1	1	1	1	1	1	
1	1		1	3	3	1	3	1	
1	1	BONE STAI	2	1	1	1	2	1	
1	3	EUA LOF	1	1	1	1	1	1	
1	1	EUA LOF	1	1	1	1	1	1	
1	1	RT MRM	2	1	1	1	1	1	
1	1	EXCISION F	1	1	1	1	1	1	
1	1	SYNOVIAL I	1	1	1	1	1	1	
1	1	K WIRE EXI	2	3	4	1	4	3	
1	1	tympanopl	1	1	1	1	1	1	
3	1	excision gra	1	1	1	1	1	1	
1	2	OCTR	1	1	1	1	1	1	
1	1	HAEMARRO	1	1	1	1	1	1	
1	1	EUA LOF	1	1	1	1	1	1	

1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	2	1	4	1	3	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	BIOPSY AN	1	1	1	1	1	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	STSG LEG	1	1	1	1	1	1
1	1	MRM RT	1	1	1	1	1	1
1	1	LT MRM	1	1	1	1	1	1
1	1	RT MRM	1	1	1	1	1	1
5	1	RESUTURIN	1	1	1	1	1	1
1	1	RT RADIUS	2	2	2	1	3	1
1	1	IMPLANT E	3	3	4	1	3	1
1	1	LT KNEE OF	1	1	1	1	1	1
1	1	EUA LOF	2	1	2	1	2	1
1	1	ANKLE SYN	1	1	1	1	1	1
1	1	KNEE SCOP	1	1	1	1	1	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	RT FIBROAI	2	1	1	1	2	1
1	1	LT BREAST	1	1	1	1	1	1
1	1	RT MRM	2	1	1	1	1	1
1	1	GANGLION	1	1	1	1	1	1
1	1	WRIST BIOI	1	1	1	1	1	1
1	1	B/L RADIUS	1	1	1	1	1	1
1	1	ANKLE BUR	2	1	1	1	2	2
2	1	LT INGUINA	1	1	2	1	2	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	R KNEE SCC	1	1	1	1	1	1
1	1	RT INGUINA	2	1	2	1	2	1
1	1	EVERSION (	1	1	1	1	1	1
1	1	RT MRM	1	1	1	1	1	1
1	1	RT FIBULOT	2	1	1	1	2	2
1	1	lt radius k v	1	1	1	1	1	1
1	1	RT HSD	1	1	1	1	1	1
1	1	LT BREAST	2	1	1	1	1	1
1	1	RT BREAST	1	1	1	1	1	1
1	1	WLE BREAS	1	1	1	1	1	1
1	1	BCS RT BRE	1	1	2	1	2	1
2,5	2	EXCISION L	2	1	1	1	2	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1

1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1		1	1	1	1	1	1
1	1	BG RT TIBI/	2	1	1	1	2	1
1	1	IMPLANT E	2	2	3	1	4	2
1	1	EXCISION L	2	1	1	1	1	1
1	1	HSD	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	LT INGUIN/	1	1	1	1	1	1
5	1	EUA LOF	2	1	1	1	1	1
1	1	EXCISION L	1	1	1	1	1	1
1	1	circumcisio	1	1	1	1	1	1
2	1	ILIZAZOV R	2	1	2	1	2	1
1	1	TSSA	2	1	2	1	3	2
1	1	TSSA	1	1	1	1	1	1
1	1	LT INGUIN/	2	1	1	1	1	1
1	1	RT HERNIO	1	1	1	1	1	1
1	1	B/L LUMPE	2	1	1	1	1	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	RT INGUNA	1	1	1	1	1	1
1	1	WLE RT BR	1	1	1	1	1	1
1	1	RT TIBIA OI	1	1	1	1	1	1
1	1	WLE RT BR	2	2	3	1	3	1
1	1	WLE RT BR	1	1	1	1	1	1
1	1	WLE RT BR	1	1	1	1	1	1
1	1	MRM RT BI	2	1	1	1	1	1
1	1	TYMPANOI	2	1	1	1	1	1
1	1	RT WRIST C	2	2	3	1	3	1
1	1	K WIRE EXI	2	1	1	1	1	1
1	1	K WIRE EXI	2	1	1	1	1	1
2	1	GANGLON	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	3	1	1	1	4	2
1	1	STSG	3	1	2	1	4	2
1	1	ANT ABD W	1	1	1	1	1	1
1	1	WLE RT BR	1	1	1	1	1	1
1	1	HAEMATOI	1	1	1	1	1	1

1	1	EXCISION L	1	1	1	1	1	1
1	1	LT INGUINA	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
4	1	LT HYDROC	1	1	1	1	1	1
1	1	IMPLANT E	3	1	1	1	4	2
1	1	OLECRANO	1	1	1	1	1	1
1	1	CURETTAG	2	1	3	1	2	1
1	1	RT TSSA	1	1	1	1	1	1
1	1	IMPLANT E	1	1	2	1	2	1
1	1	B/L TSSA	2	1	1	1	1	1
1	1	BX RT ELBC	1	1	1	1	1	1
1	1	STSG LT LE(	1	1	1	1	1	1
4	2	EUA LOF	1	1	1	1	1	1
1	1	UMBILICAL	1	1	1	1	1	1
4	1	RT INGUINA	1	1	1	1	1	1
4	1	B/L HYDRO	2	1	2	1	2	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	LT KNEE SC	1	1	1	1	1	1
1	1		1	1	1	1	1	1
1	1	RT FEMUR	1	1	1	1	1	1
1	1	WLE B/L BF	1	1	2	1	2	1
1	1	EXCISION R	1	1	1	1	1	1
1	1	WLE RT BR	1	1	1	1	1	1
4,5	1	RT MRM	1	1	1	1	1	1
1	1	LT HAND G	1	1	1	1	1	1
1	1	OCTR, 2 FIN	2	1	1	1	1	1
1	1	RT LUMPEC	1	1	1	1	1	1
1	1	EPIGASTRIC	1	1	1	1	1	1
1	1	SUBMENTA	1	1	1	1	1	1
1	1	LT INGUINA	3	1	1	1	4	2
4	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
5	2	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	LT FEMUR I	1	1	1	1	1	1
1	1	LT PROXIM	1	1	2	1	2	1
3	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	2	1	2	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
2	1	EUA LOF	1	1	2	1	2	1
1	1	LT KNEE SC	1	1	1	1	1	1

1	1	LT LYMPH I	1	1	1	1	1	1
1	1	INCISIONAI	1	1	1	1	1	1
1	1	STSG LT LL	2	1	2	1	2	1
1	1	LT FEMUR I	1	1	1	1	1	1
1	1	HSD LT SHO	1	1	1	1	1	1
1	1	LT ANKLE II	1	1	1	1	1	1
1	2	B/L RFA	1	1	1	1	1	1
1	1	RT FEMUR	2	1	1	1	1	1
1	1	TBW EXIT F	1	1	1	1	1	1
1	1	RT BREAST	2	1	1	1	1	1
1	1	INCISIONAI	1	1	1	1	1	1
1	1	INCISIONAI	2	1	1	1	1	1
1	1	LT KNEE SC	1	1	1	1	1	1
1	1	LT TYMPAN	2	1	1	1	1	1
1	1	RT BREAST	2	1	1	1	1	1
1	1	RT TYMPAN	1	1	1	1	1	1
1	1	LT TYMPAN	2	1	1	1	1	1
1	1	SCHWANO	3	1	1	1	4	2
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	3	4	1	3	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	2	1	2	1
1	1	STSG LT LE	1	1	1	1	1	1
1	1	RT FOOT C	1	1	1	1	1	1
1	1	BX RT THIG	1	1	1	1	1	1
1	1	BX RT FEM	1	1	2	1	2	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	LAS	1	1	1	1	1	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	RT KNEE SC	1	1	1	1	1	1
1	1	B/L HYDRO	2	2	2	1	2	1
1	1	LT FOREAR	1	1	1	1	1	1
1	1	RT KNEE OI	2	2	4	1	3	1
1	1	EUA LOF	2	1	1	1	1	1
1	1	LT HUMERI	1	1	1	1	1	1
1	1	LT HIP MAS	2	1	1	1	1	1

1	1	PARAUMBI	2	1	1	1	1	1
1	1	LT HYDROC	1	1	1	1	1	1
1	1	RT INGUIN/	2	2	3	1	4	2
1	1	EUA LOF	2	1	3	1	2	2
1	1	EUA LOF	2	1	3	1	3	2
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
2	1	K WIRE EXI	1	1	1	1	1	1
1	1	RT HIP BX	1	1	1	1	1	1
1	1	RT KNEE SC	2	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	RT MRM	2	1	2	1	2	1
1	1	LT MRM	2	1	2	1	2	1
1	1	RT MRM	1	1	1	1	1	1
1	1	WLE BREAS	1	1	1	1	1	1
1	1	OPEN BX R	2	1	1	1	1	1
1	1	DEBRIDEM	1	1	1	1	1	1
3	1	LT TSSA	1	1	1	1	1	1
1	3	RT RFA	3	1	1	1	4	2
1	1	B/L TSSA	1	1	1	1	1	1
1	1	INCISIONAI	2	1	1	1	1	2
1	1	LT FEMUR I	1	1	1	1	1	1
1	1		1	1	1	1	1	1
1	1	RT ANKLE S	1	1	1	1	1	1
1	2	CYSTOLTHL	2	1	1	1	1	1
1	1	MEATOPLA	1	1	1	1	1	1
1	1	CIRCUMCIS	1	1	1	1	1	1
1	1	RT HYDRCC	1	1	1	1	1	1
1	1	EIU	1	1	1	1	1	1
1	1	THYROGLO	1	1	1	1	1	1
1	1	STOMA CL(	1	1	1	1	1	1
1	1	SKIN TAG E	2	1	3	1	3	1
1	1	DJ STENT R	1	1	1	1	1	1
5	2	RT SUBMAI	1	1	1	1	1	1
1	1	IND KNEE	1	1	1	1	1	1
1	1	LT INGUIN/	2	3	3	1	3	1
1	1	IM NAIL RE	2	1	1	1	1	1
1	2	HYDROCOE	1	1	1	1	1	1
1	1	EXCISION L	1	1	1	1	1	1
1	1	ARTHROSC	1	1	1	1	1	1
1	1	ILIAC BONE	2	4	3	2	4	2
1	1	LIPOMA EX	1	1	1	1	1	1
1	1	ACL LT KNE	1	1	1	1	1	1

1	1	TBW LT WF	1	1	3	1	3	1
1	1	PUV FULGU	1	1	1	1	1	1
1	1	AXILLARY L	1	1	1	1	1	1
1	1	EUA LOF	1	1	2	1	2	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	B/L TSSA	2	1	1	1	2	1
1	1	RT INGUIN/	2	1	1	1	2	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	CYSTOLITH	1	1	1	1	1	1
1	1	IM NAIL EX	1	1	1	1	1	1
1	1	INCISIONAI	1	1	1	2	2	1
1	1	RT BREAST	2	1	1	1	1	1
1	1	ANKLE SCR	1	1	1	1	1	1
1	1	EUA LOF	1	1	1	1	1	1
1	1	DIAGNOSTI	1	1	1	1	1	1
1	1	TYMPANOF	1	1	1	1	1	1
1	1	CYSTSCOPY	2	1	1	1	1	1
1	1	INTRA TYM	1	1	4	1	3	1
1	1	REDO COR	2	1	2	1	2	1
1	1	EIU	1	1	1	1	1	1

tpropr	tpropr1	hrpreind	sbppreind	dbppreind	mappreimc	spo2prein	hrpostind	sbppostin
165	2	87	131	84	95	100	82	89
120	1	91	90	50	60	100	72	94
140	1	56	114	72	81	100	60	106
150	2	111	145	86	99	100	100	95
240	2	115	146	85	99	100	91	104
140	1	75	117	71	83	99	71	103
120	1	82			96	100	69	
100	1	91	116	59	72	100	83	120
160	1	76			86	97	70	
140	1	91	108	58	70	100	75	110
140	1	76	148	103	113	98	74	102
135	1	74	137	98	105	98	82	101
130	1	71	95	54	63	99	65	93
160	1	70	127	66	79	100	66	91
140	1	85	142	81	96	99	85	107
180	2	83	116	71	81	100	86	102
130	1	62	128	82	93	99	69	92
140	1	99	148	102	112	98	86	102
160	1	93	97	67	74	100	85	101
120	1	68	127	79	90	96	60	86
110	1	106	135	82	94	100	86	121
150	1	67	136	81	93	100	67	130
130	1							
120	2	142	122	76	88	100	100	94
110	1	102	132	81	91	99	99	113
110	1		168	78	101	97	102	157
110	1	106	125	72	86	95	109	120
110	1	94	131	77	89	100	96	110
110	1	70	181	88	113	100	47	120
85	1	81	120	58	73	100	70	101
135	2	111	132	80	91	100	97	98
150	1	82	154	110	120	100	82	101
170	1	86	148	80	92	99	77	112
165	1	63	102	58	68	100	64	128
170	1	89	137	70	86	96	86	130
120	1	99	112	63	75	100	79	79
170	1	90	160	63	80	100	88	90
190	2	84	133	91	99	100	76	100
120	1	64	132	84	97	100	67	96
140	1	68	101	52	63	98	71	106
150	1	84	172	87	104	98	71	118
90	1	77	147	58	79	100	68	81
125	1	73	112	54	73	100	65	97

180	1	85	119	79	87	100	77	95
150	1	80	121	76	86	100	78	88
190	2	105	112	71	81	100	100	107
140	1	76	106	72	82	100	68	118
120	1	86	153	70	90	100	64	84
90	1	103	100	60	73	100	92	85
110	1	89	132	85	95	99	82	87
130	1	68	131	73	86	100	78	108
130	1	97	112	100	103	99	96	99
130	1	64	162	76	96	100	58	114
130	1	97	109	56	67	99	90	118
130	1	94	181	75	96	97	77	110
140	1	80	143	88	101	99	77	118
150	2	83	129	71	85	99	80	93
195	2	106	139	93	103	100	107	138
100	1	83	126	70	86	100	79	104
100	1	72	113	65	77	99	69	91
130	1	86	121	77	88	99	84	101
140	1	117	103	61	71	100	75	109
130	1	72	148	69	86	100	68	94
90	1	84	138	85	99	100	84	99
115	1	79	149	93	106	100	74	109
120	1	70	135	76	89	98	70	128
110	1	102	121	63	77	100	102	99
140	1	84	134	92	102	100	72	98
110	1	66	141	60	77	100	66	139
150	1	70	138	75	90	99	61	92
120	1	59	137	78	93	100	57	121
170	1	78	153	66	85	100	77	106
160	1	90	173	56	81	100	76	107
100	1	64	109	68	78	100	61	94
170	1	70	136	92	102	100	66	82
130	1	93	149	71	90	100	79	100
160	1	60	133	77	90	99	61	93
130	1	66	176	82	105	99	69	125
120	1	99	181	78	103	97	72	123
90	1	79	108	72	80	100	72	96
120	1	116	126	46	65	100	96	92
125	1	95	144	67	86	98	91	117
115	1	104	141	68	85	100	85	119
160	1	90	162	91	109	100	80	95
110	1	100	136	81	93	100	79	107
150	1	92	132	78	90	100	68	102
130	1	88	119	79	89	100	88	118

200	1	64	133	78	91	100	63	103
135	1	88	121	75	87	100	72	118
140	1	82	137	88	99	100	82	92
140	1	90	121	75	87	99	82	118
120	1	96	134	84	96	99	91	102
186	2	64	152	64	84	100	71	93
140	1	95	180	84	108	99	54	97
140	1	90			105	100	78	
200	1	68	128	84	93	99	69	94
120	1	89	158	83	101	100	71	107
120	1	81	140	105	111	99	73	84
140	1	70	121	76	88	100	71	98
130	1	91	120	78	88	100	87	97
140	1	77	133	81	98	98	66	104
222	2	73	117	75	84	96	76	128
200	2	114	135	94	103	99	95	105
155	1	81	122	88	97	100	84	108
150	1	84	144	78	94	98	80	101
110	1	119	129	76	85	100	94	114
110	1	100	112	95	100	100	80	97
135	1	80	180	95	115	99	74	105
150	1	66	148	79	96	96	60	102
125	1	87	152	86	101	99	88	103
130	1	86	101	59	68	100	78	83
190	2	133	160	86	103	100	90	106
75	1	105	160	89	106	98	92	130
120	1	66	114	71	81	100	69	91
110	1	80	147	103	114	95	74	101
100	1	80	101	68	75	100	72	90
150	2	105	116	70	80	100	108	90
170	1	86	129	74	88	96	75	96
170	1	80	133	93	100	100	69	109
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pop	drug2	dose2	drug3
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