"A PROSPECTIVE, RANDOMIZED CONTROLLED STUDY TO COMPARE THE INTUBATING CONDITIONS ACHIEVED WITH SUXAMETHONIUM AND ROCURONIUM BROMIDE"

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CERTIFICATE

This is to certify that the dissertation entitled **"A PROSPECTIVE, RANDOMIZED CONTROLLED STUDY TO COMPARE THE INTUBATING CONDITIONS ACHIEVED WITH SUXAMETHONIUM AND ROCURONIUM BROMIDE"** is a bonafide work done by **Dr. RAJAMANIKANDAN.S**, Post Graduate Student, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai - 600 003, in partial fulfillment of the University Rules and Regulations for the award of MD Branch – X Anaesthesiology, under our guidance and supervision, during the academic year 2012 - 2015

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DECLARATION

I solemnly declare that the dissertation entitled **"A PROSPECTIVE, RANDOMIZED CONTROLLED STUDY TO COMPARE THE INTUBATING CONDITIONS ACHIEVED WITH SUXAMETHONIUM AND ROCURONIUM BROMIDE"** is done by me at Madras Medical College, Chennai -3 under the guidance and supervision of **Prof. Dr.B.KALA., M.D., D.A.,** to be submitted to The Tamilnadu Dr. M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D Degree In Anaesthesiology Branch-X.

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LIST OF ABBREVIATIONS USED

m.mol/lit	-	millimol/ litre
mV	-	millivolt
EPP	-	End plate potential
MEPP	-	Miniature end plate potential
SD	-	Standard deviation
NMJ	-	Neuromuscular junction
ICU	-	Intensive care unit
IV	-	Intravenous
GA	-	General anaesthesia

CONTENTS

ABSTRACT

BACKGROUND AND OBJECTIVES:

Endotracheal intubation is required for giving general anaesthesia for which adequate muscle relaxation is necessary. Suxamethonium is still used as a relaxant for endotracheal intubation . Rocuronium ,a non depolarising muscle relaxant was compared here for tracheal intubating conditions.

METHODS:

100 patients of ASA I and II were divided randomly into 2 groups undergoing elective surgeries:

Group I - Suxamethonium

Group II - Rocuronium.

RESULTS AND INTERPRETATIONS:

The intubating conditions were excellent in group I Suxamethonium as against Group II Rocuronium in 60 secs.

CONCLUSION:

Rocuronium can be used as alternative when suxamethonium is contraindicated for rapid intubation but not if anticipated difficult airway is present.

INTRODUCTION

Endotracheal intubation is necessary for giving general anaesthesia.

It is important for anaesthesiologist to reduce the airway injuries associated with tracheal intubation. Good intubating conditions are produced by adequate depth of anaesthesia and muscle relaxation.

Suxamethonium is often used in surgeries as it provides excellent intubating conditions and early establishment of patent airway thereby reducing airway injuries and aspiration. Still the side effects it may produce may range from post operative myalgia to life threatening complications like dysrhythmias, hyperkalemia, malignant hyperthermia.

To give good intubating conditions and early establishment of airway patency in patients with risk of complications with Suxamethonium, Rocuronium a newer steroidal non depolarising muscle relaxant was introduced which has rapid onset of action comparable to Suxamethonium.

This study compares the intubating conditions achieved with Suxamethonium and Rocuronium.

OBJECTIVES

OBJECTIVES

This study is to compare the intubating conditions achieved in patients undergoing elective surgeries under General Anaesthesia with Suxamethonium or Rocuronium in 60 secs and complications in both groups.

REVIEW OF LITERATURE

HISTORY

The arrow poison used for hunting by the native people of South America has been known for centuries. Shortly after the first Spaniards arrived in the New World in the sixteenth century accounts of the mysterious poison began to appear. Among the more spectacular personalities reporting on the poison was **Sir Walther Raleigh (1552-1618)**, he described the poison in 1596, and it was one of his captains who named the poison "Ourari". Among others, the French scientist **Charles-Marie de la Condamine (1701-1774)** and the English scientist **Edward Bancroft (1744-1821)** brought back to Europe samples of the curare poison. For many years these samples were the basis for experiments in different parts of Europe.

Benjamin Brodie (1783-1862) and his assistant **Edward Nathaniel Bancroft (1772-1842; son of Edward Bancroft)**, showed that the poison paralysed the respiratory muscles, and that an animal given curare could be kept alive if ventilated. In 1856, Claude Bernard (1818-1878) published his classic experiments on frogs, and he found that curare acted peripherally, causing paralysis of the muscle by its effect at the Acetylcholine receptor site in NMJ. In the **1930s H.H.Daie, W. Felberg and M. Vogt** proved that Acetylcholine, the chemical neurotransmitter of the NMJ acted on skeletal muscle. Since then the NMJ has been the most studied junction in the body.

The basic concept of Acetylcholine as the chemical transmitter, being synthesized in the nerve endings and acting on postsynaptic receptors, has not been changed over the years. However, in recent years important advances in modern technology, not least in electron microscopy, electrophysiology, immunology and DNA technology, have much increased our knowledge of the transmission process.

In **1942 Griffith and Johnson** reported that D-Tubocurarine is a safe drug to use during surgery with good muscle relaxation. Later, Cullen reported that D-Tubocurarine had been given to 131 patients under general anaesthesia to produce additional skeletal muscle relaxation greater than that provided by the Volatile anaesthetic agents alone.

During subsequent years, as the clinical pharmacology of the neuromuscular blocking drug has been refined, and as the drugs themselves have been improved, the use of muscle relaxant has become a vitally important aspect of modern anaesthesiology practice. The development of new synthetic relaxants had greatly increased the clinicians options for providing skeletal muscle relaxation.

Suxamethonium, introduced by **Thesleff and Foldes et al in 1952,** revolutionized anaesthetic practice by providing intense neuromuscular blockade of very rapid onset and ultra short duration, thereby greatly easing the maneuver of tracheal intubation,

The synthetic and semisynthetic nondepolarizing drugs, such as Gallamine, Dimethyl tubocurarin, and Alcuronium, introduced over the next decade, were alternative to D-Tubocurarine. They were not considered as replacements for D-Tubocurarine because they all produced cardiovascular side effects, showed long duration of action similar to that of D-Tubocurarine.

Baird and Reid in 1967 reported on the clinical administration of the aminosteroid Pancuronium.

In the early 1980s two more newer muscle relaxants of intermediate duration of action namely Atracurium and Vecuronium was introduced into the clinical practice. These drugs revolutionized the performance of balanced general anaesthesia by providing very good muscle relaxation of faster onset and at the same time more rapid measurable faster recovery, without depending on kidneys solely for their metabolism.

Their faster onset and shorter duration of action property is more comparable with Suxamethonium which encouraged tracheal intubation for the use of non depolarising relaxants.

At the same time the property of faster measurable recovery and complete antagonism of the residual blockade by Anticholinesterases made it convenient to provide paralysis by continuous infusion of these non depolarising relaxants.

Along with introduction of Pipecuronium, Doxacurium, Mivacurium and Cisatracurium, the early 1990 witnessed the introduction of a steriodal compound “Rocuronium” of intermediate duration, with an onset of action that is faster than that of vecuronium.

Rocuronium is the first non-depolarizer considered to be an acceptable substitute for Suxamethonium in facilitating rapid intubation of the trachea.

Rocuronium is a step forward in the development of improved neuromuscular blocking agents and is indeed a new milestone in the clinical practice of anaesthesioiogy.

REVIEW OF LITERATURE

Puhringer F.K.etal., (1992)[35] conducted a study to assess the intubating conditions achieved with Suxamethonium and Rocuronium under iv anaesthesia with propofol, alfentanil and Nitrous oxide in 100 patients. The neuromuscular effects of both drugs were quantified by recording the indirectly evoked twitch response of adductor pollicis muscle after ulnar nerve stimulation. Patients were given either 0.6 mg/kg Rocuronium or 1 mg/kg Suxamethonium intravenously. Sixty seconds after the administration of the muscle relaxant, the trachea was intubated and the intubating conditions were scored by a "blinded" assessor. Intubating conditions were not different between Rocuronium and Suxamethonium groups. They concluded that in spite of the pharmacodynamic differences between sucamethonium and Rocuronium, the intubating conditions after administration of both compounds are similar and developed at the same rate.

Cooper R. et al., (1992)[8] conducted the study assessing intubating conditions after administration of Org 9426 (Rocuronium) 600 ug/kg at 60 or 90s in groups of 20 patients anaesthetized with Thiopentone, Nitrous oxide in Oxygen and small doses of Fentanyl, and compared the data with those obtained after Suxamethonium 1 mg/kg in similar groups of patients. Intubating conditions after Org 9426 were found to be clinically acceptable

(good or excellent) in 95% of patients at 60s and in all patients at 90s and in all patients at both times after Suxamethonium.

Huizinga A.C. **et al., (1992)**[18] investigated the intubating conditions and neuromuscular blocking profile following 600 ug/kg Rocuronium. They were compared with conditions following 1.5 mg/kg Suxamethonium. Rocuronium produced good to excellent intubating conditions at 60 as well as 90 seconds after administration, even though there was only a partial blockade of adductor pollicis muscle. Intubating conditions following Suxamethonium were comparable with those after Rocuronium. Rocuronium may have a major advantage over existing non-depolarizing muscle relaxants due to the early presence of excellent intubating conditions.

Porte F. et al (1993)[14] studied the dose response relationship on diaphragm and adductor pollicis using Rocuronium. They concluded that the dose necessary to block the diaphragm is 1.5 to 2 times higher than that for the adductor pollicis. A dose of at least 0.5 mg/kg could be necessary to produce good intubating condition because such a dose is necessary to block the diaphragm.

Wicks T.C. (1994)[46] Rocuronium is a new non-depolarising neuromuscular blocking drug. Its onset of action is comparable to that of Suxamethonium, with good to excellent intubating conditions possible 1

minute after doses two times the ED95 (600 ug/kg). The ED95 of Rocuronium is essentially the same for children as for adults, Rocuronium is readily reversed with conventional doses of cholinesterase inhibiting drugs. A new agent, Rocuronium possesses a very stable cardiovascular profile and a rapid onset of action. It may be useful for rapid sequence intubation without unacceptable delays in the spontaneous recovery of neuromuscular function.

Feldman S.A. (1994)[15] studied the onset time and intubating conditions of Rocuronium. The rapidity of onset of Rocuronium in man appears to be due to an early presynaptic effect. Observations, which are difficult to explain, are that increasing the dose above about 2 x ED90 does not shorten the time of onset and 'priming' also has no beneficial effect. Although some studies have produced evidence that Rocuronium can produce smooth easy intubating conditions in 60s, 90s would appear to be close to the time when excellent conditions can be guaranteed.

Nilesh Kumar Patel et al., (1995)[33] compared Rocuronium Vs Suxamethonium for emergency surgery and rapid sequence intubation. There study suggests that 1) Rocuronium, 0.9 mg/kg provides comparable tracheal intubating conditions as Suxamethonium 1.5 mg/kg; 2) Suxamethonium, 1.5 mg/kg has a more rapid onset of complete block at the orbicularis occuli than does Rocuronium ; and 3) visual loss of TOF may not always be necessary to

ensure good- excellent tracheal intubating conditions.

The study comparing the intubating conditions as well as onset and clinical duration of 0.6 mg/kg (2 x ED95) with 1 mg/kg Suxamethonium (3 x ED95) by .**Latorre F. et al,, (1996)**[24] **showed** results the that intubating conditions assessed were clinically acceptable(excellent or good) after Rocuronium and Suxamethonium. They concluded that Rocuronium has an onset time of about 3 minutes and a clinical duration of relaxation of nearly half an hour. These data are supported by various studies, while others show shorter times, probably due to different monitoring techniques. In spite of the pharmacodynamic differences between Rocuronium and Suxamethonium, the intubating conditions after administration of both compounds are comparable and develop at the same rate.

In elective cases with Rocuronium and Suxamethonium as RSI inducing with Thiopentone **Sparr H.J.** et al., **(1996)**[40] assessed the intubating conditions. They concluded that Rocuronium is a suitable alternative to Suxamethonium for rapid tracheal intubation even under unsupplemented Thiopentone anaesthesia, at least in elective, otherwise healthy patients. Its use for rapid sequence induction under emergency conditions, however, needs further investigation.

Tang J., Joshi G.P. and White P.F. (1996)[43] studied tracheal intubating conditions and neuromuscular effects of Suxamethonium, Rocuronium and mivacurium. They concluded that Rocuronium appears to be an acceptable alternative to Suxamethonium for tracheal intubation. However, longer duration of action of Rocuronium increases the need for reversal drugs.

Rocuronium pretreatment at 3 and 1.5 minutes before Suxamethonium administration on fasciculations by **Motamed C, Choquette R., and Donati F (1997)**[31] to assess the effect of Rocuronium. They concluded that the incidence and severity of Suxamethonium fasciculations can be reduced by giving 0.05 mg/kg Rocuronium either 1.5 minute or 3 minutes before Suxamethonium. The effects of 2 mg/kg Suxamethonium with Rocuronium pretreatment, and 1 mg/kg Suxamethonium, without pretreatment are similar with respect to intubating conditions, onset of paralysis and duration of blockade.

Rapid sequence induction of anaesthesia using Rocuronium 0.6 or 1.0 mg/kg or Suxamethonium 1.0 mg/kg as the neuromuscular blocking drugs by **McCourt K.C. et al., (1998)**[27] for tracheal intubating conditions showed the results that the intubating conditions to be significantly superior with the 1.0 mg/kg dose of Rocuronium. It is concluded that Rocuronium 1.0 mg/kg can

be used as an alternative to Suxamethonium l.0mg/kg as part of a rapid sequence induction provided there is no anticipated difficulty in intubation. The clinical duration of this dose of Rocuronium is, however, 50-60 minutes.

Stoddart P.A. and Mather SJ. (1998)[41] in a blinded randomized study, intubating conditions were compared at one minute following intravenous induction with propofol and either Suxamethonium 1.0 mg/kg or Rocuronium 0.6 mg/kg. There was no difference in the intubating conditions at one minute with 25 excellent/5 good in the Suxamethonium group and 27 excellent/3 good in the Rocuronium group. They concluded that Rocuronium 0.6 mg/kg gives optimal intubating conditions at one minute in children.

De Rossi L.et al., (1999)[11] compared the onset time of two different doses of Rocuronium (0.6 and 0.9 mg/kg) and Suxamethonium (1.5 mg/kg) preceded by 0.06 mg/kg Rocuronium at the masseter and the adductor pollicis muscle. Following Rocuronium and Suxamethonium, onset time is faster at the masseter than at the adductor pollicis muscle.

Using a new method of monitoring neuromuscular block at the laryngeal muscles by surface laryngeal electromyography by **Hemmerling T.M. et al., (2000)**[17] to compare the Suxamethonium with two doses of Rocuronium . They found that, with comparable degrees of neuromuscular

block, the onset time of Suxamethonium at the adductor pollicis was significantly shorter than for Rocuronium 0,6 mg/kg and 0.9 mg/kg. Clinical duration at the adductor pollicis was significantly longer for both Rocuronium groups than for Suxamethonium. The surface laryngeal electrode proved non-invasive, easy to use and reliable in measuring onset of the neuromuscular block at the larynx.

Cheng CA, Anu CS and Gin T (2002)[7] conducted a study to detrermine whether a smaller dose of Rocuronium than previously reported could provide similar intubating conditions to Suxamethonium during rapid-sequence induction of anaesthesia in children. They concluded that Rocuronium 0.9 mg/kg provides similar intubating conditions to Suxamethonium 1.5 mg/kg during modified rapid sequence induction. Rocuronium 0.6 mg/kg was inadequate in children.

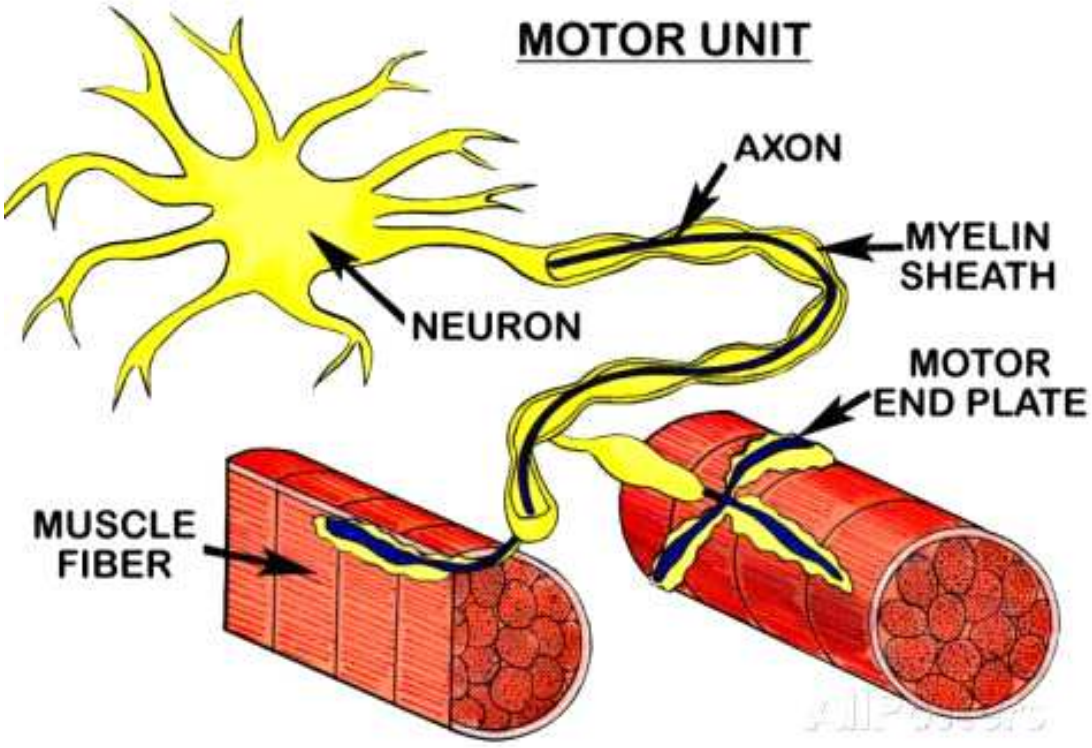
During rapid-sequence induction intubation the intubating conditions were studied by **Perry J, Lee J and Wells G (2003)**[34] Rocuronium and Suxamethonium . They concluded that Suxamethonium created superior intubation conditions to Rocuronium when comparing excellent intubation conditions. Using the less stringent outcome, clinically acceptable intubation conditions, the two agents were not statistically different.

ANATOMY

ANATOMY OF NEUROMUSCULAR JUNCTION

MOTOR UNITS:

Each motor neurons innervates many muscle fibres and the neuron together with the muscle fibre is motor unit. The reaction of a motor unit is all or none response.



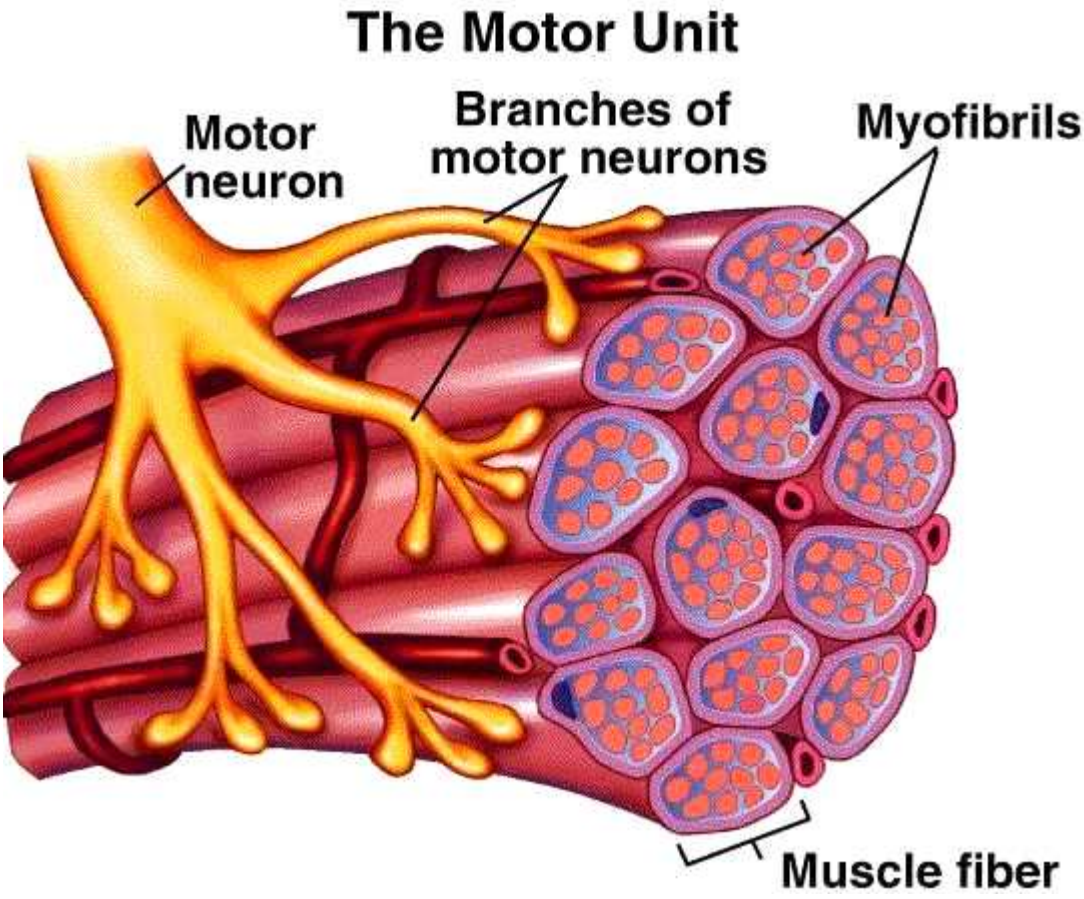


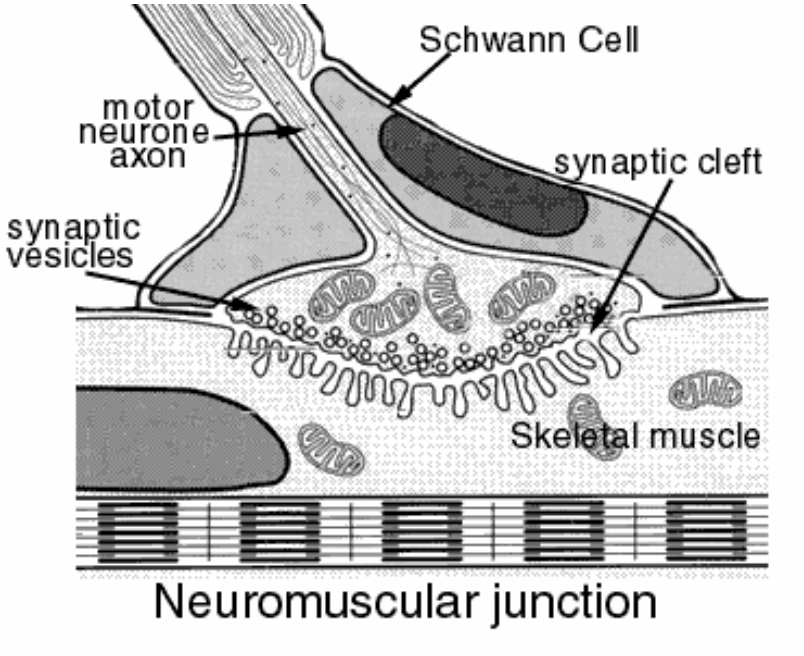
Fig 1: Diagram of motor unit containing focally innervated muscle fibres.

NEUROMUSCULAR JUNCTION:

When the neuron reaches the muscle fibres it loses its sheath and divides into many branches. It ends in a small swelling embedded in muscle fibre to form neuromuscular junction. The nerve endings contains vesicles with neurotransmitters Acetylcholine. There is a gap of 20 - 50 nm between nerve terminal and muscle fibre called the synaptic cleft or junctional cleft. This cleft is filled with collagen structure named basement membrane. To this membrane is attached the Acetylcholinesterase.

Secondary clefts are clefts formed due to folding of the muscle membrane at the junction. The acetyl choline receptors are formed at the shoulders of these clefts. There are about 10^6 to 10^7 nicotine receptors.

Each receptors is a pentamer of 4 different protein subunits. Two α subunits of 40,000 daltons molecular weight and single β, δ and ε subunits of varying daltons. The whole mol. weight of receptor is around 2,50,000 daltons.



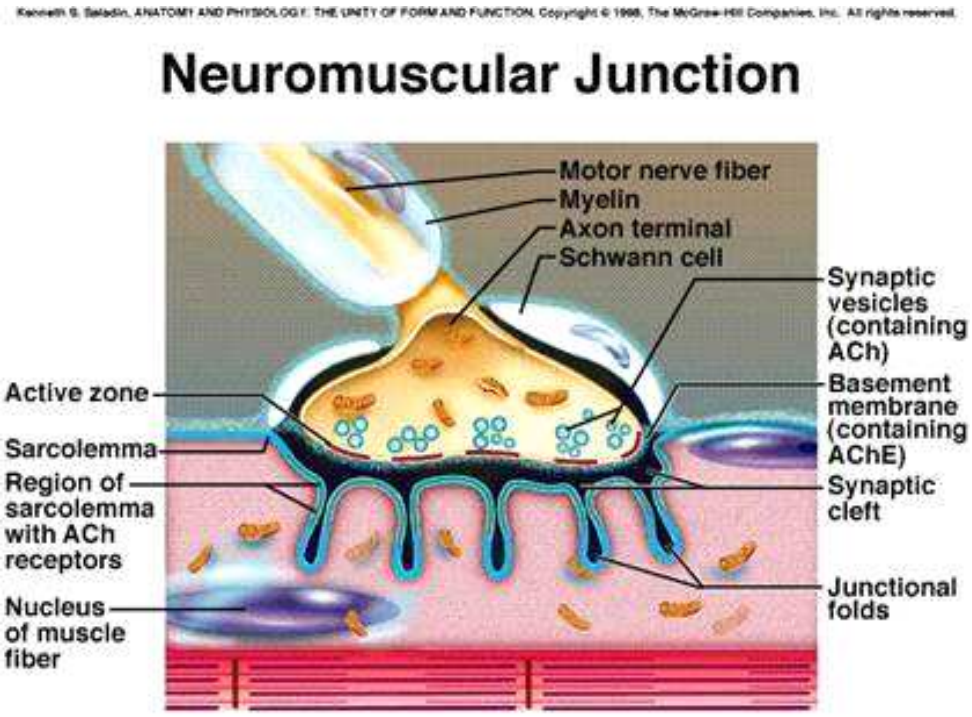


Fig 2: NMJ enlarged from motor end plate. The axon terminal contains mitochondria, microtubules and Acetylcholine containing vesicles.

POSTSYNAPTIC CHOLINERGIC RECEPTORS:

Also called as extra junctional receptors is of 2 types:

1.Those of foetal muscle and denervated muscle:

Instead of ε subunits the receptors has γ subunit, with lifetime of 17 - 24 hrs.

2.Those of innervated muscle:

More concentrated in NMJ with lifetime of days to weeks.

The 2 types of these receptors react differently to agonists and antagonist.

THE MUSCLE:

The contractile elements of a muscle cell is myofilament. The thick myosin and the thin actin filament attached to troponin and tropomyosin.

These filaments interdigitate and slide over to contract the muscle. Myofilament are grouped together to form myofibrils. Sarcoplasmic reticulum surrounding the myofibrils acts as a reservoir for calcium. The invaginations of sarcolemma, transverse tubules (T- tubules) comes in proximity to sarcoplasmic reticulum . These tubules convey the electrical impulses from the surface of the muscople to the sarclasmic reticulum,

thereby releasing the calcium and contraction of myofilament.

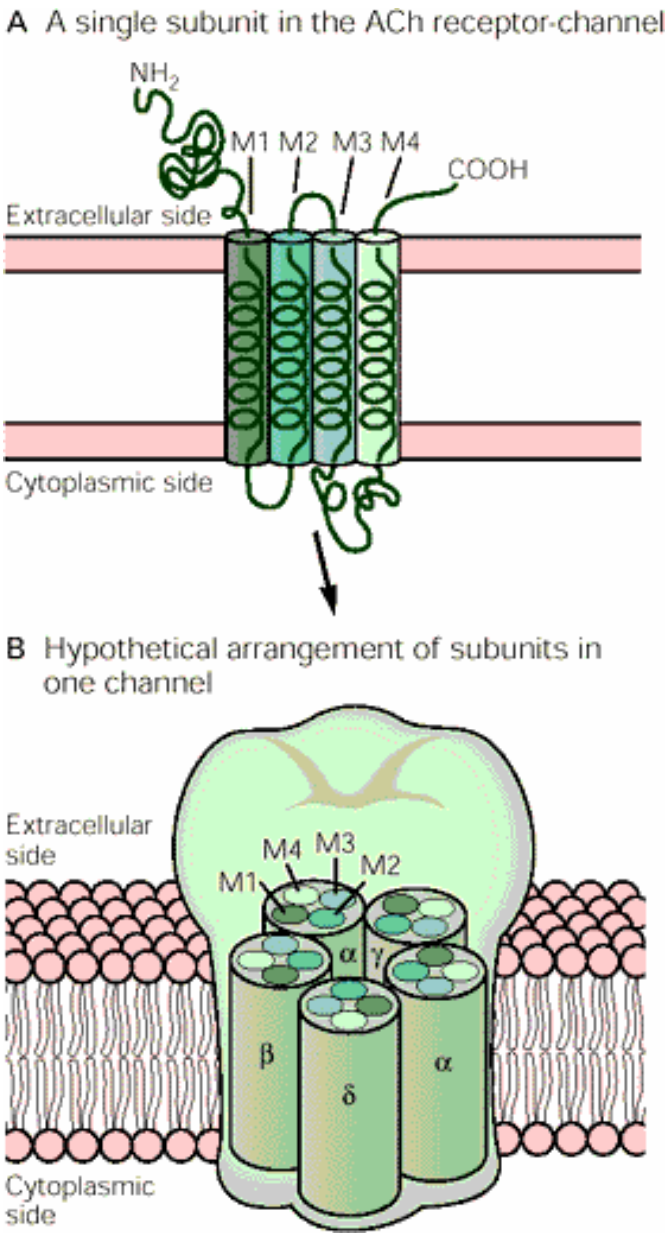


Fig 3: A schematic model showimg thr nicotinic Ach receptor localised in the lipid bilayer.

Five homologous subunits (α,α,β,γ,δ of the Ach receptor may combine to form transmembrane aqueous pore. Both α subunits contain Ach binding sites. Most of the receptor is localised in the extracellular space. Each subunit

has four membrane spanning domains which are evident from the cross section of subunits.

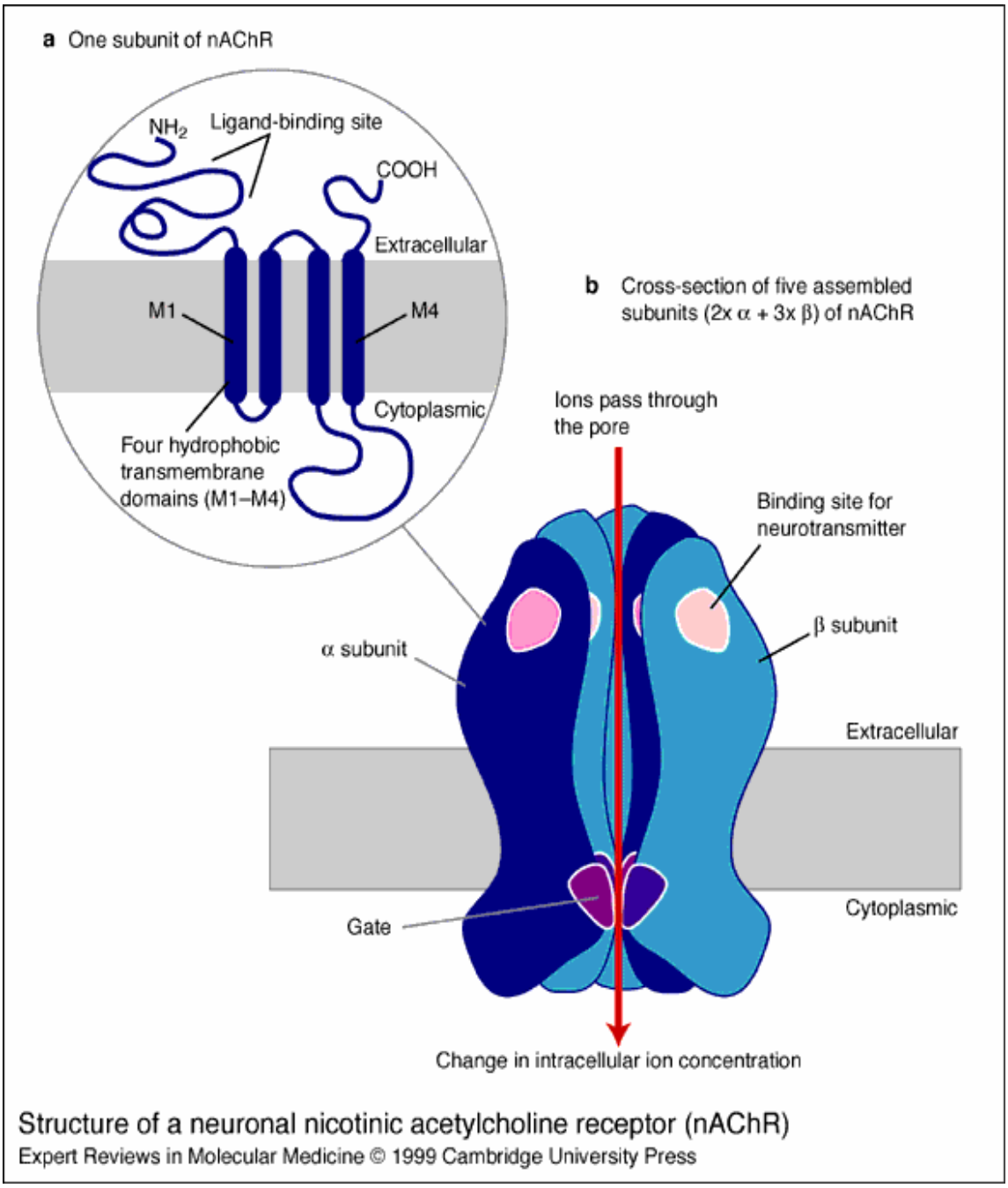
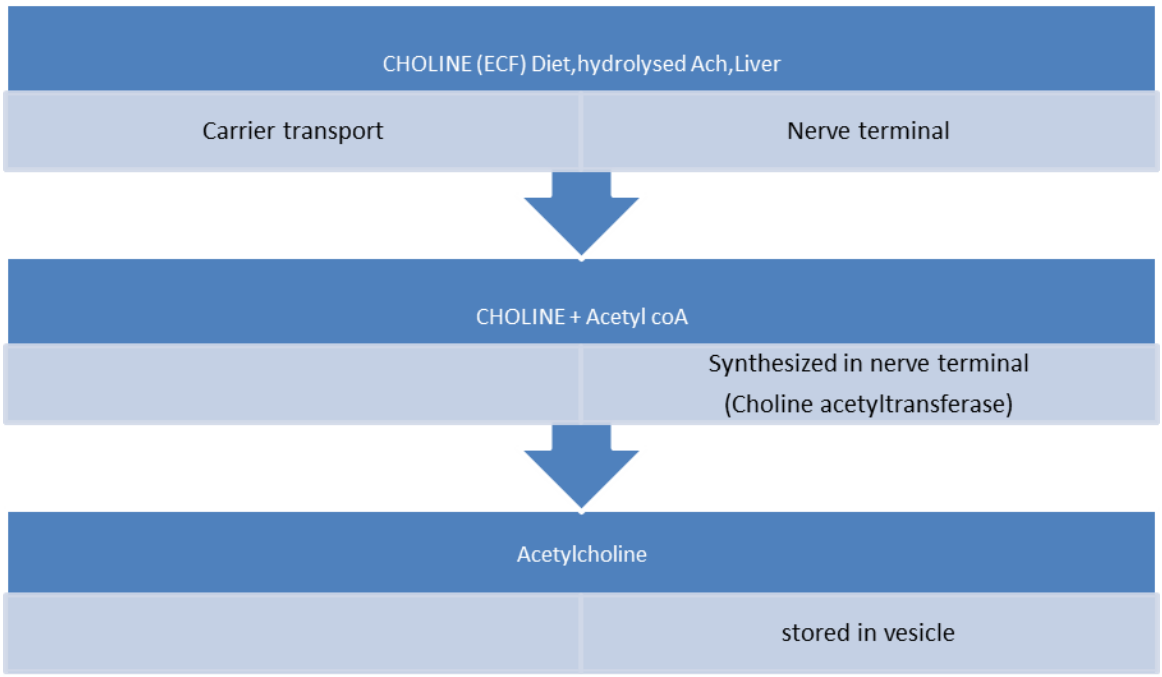


Fig 4: One of the α subunits is shown separately. The polypeptide chains of each subunit are postulated to cross the lipid bilayer as α helices.

THE MOTOR NERVE TERMINAL

Acetycholine synthesis and storage:



The two pools of Acetylcholine within the nerve terminal are :

1. Releasable pool (80%) (within the vesicle)

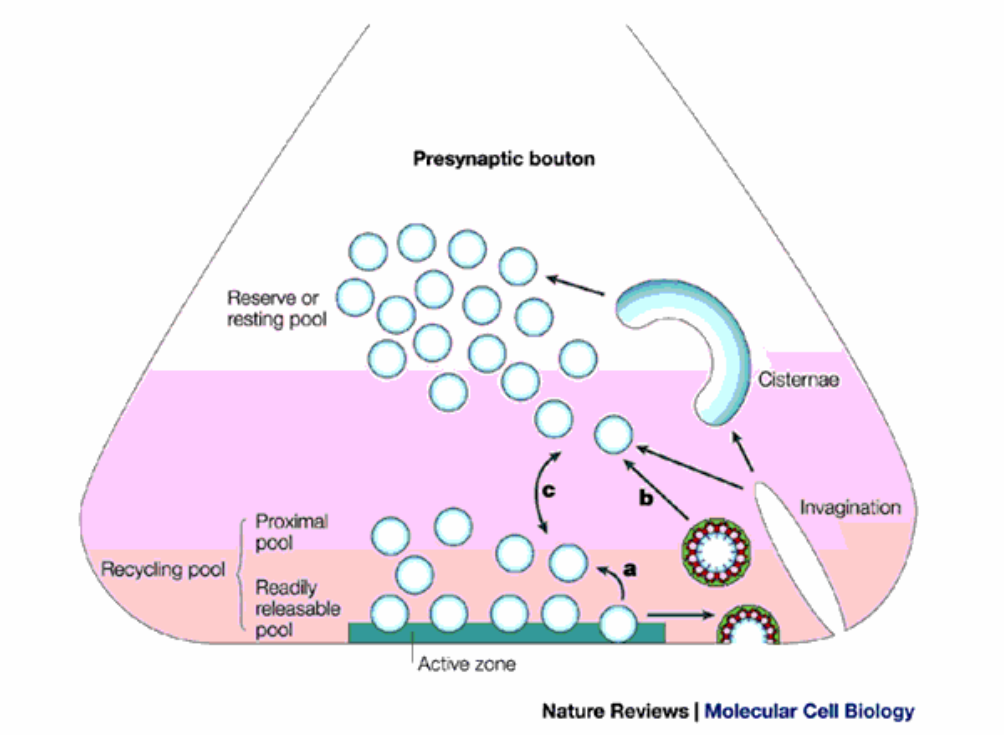
    a. Immediately available

    b.Reserve pool

2.Stationary or non releasable pool

vesicles tend to concentrate near the "Active zones" opposie crests of post synaptic membranes also called as "release sites".

THE SEPARATE POOLS OF ACETYLCHOLINE STORED WITHIN A NERVE TERMINAL



ACETYLCHOLINE RELEASE:

Acetylcholine released from the terminal occurs both spontaneously and by depolarisation of nerve terminal.

SPONTANEOUS RELEASE:

MEPPs is due to random release of quantum or packets of Acetylcholine, as the MEPPs are so small, many are required to generate Action potential.

DEPOLARISATION OF NERVE TERMINAL :

Depolarisation of nerve terminal leads to the release of hundreds of quantum of Acetylcholine concentrated near the Release sites depending upon the type of the muscle.

Following the depolarisation process, extracellular calcium passes through the voltage gated calcium channel . Inside the nerve terminal calcium binds to the proteins (Calmodulin and Calcitonin related peptide) and activates the enzyme necessary for Acetylcholine release.

The vesicular membrane consists of synaptophysin, a glycoprotein. Synaptotagmin in the vesicle acts as Calcium sensor. After attachment of calcium to synaptotagmin phosphorylation of membrane protein synapsin occurs so it moves to the release sites where synaptobrevin vesicle associated membrane protein (VAMP) attaches to the release sites leading to release of Acetylcholine into the synaptic cleft.

SYNAPTIC CLEFT:

The release of Acetylcholine into the cleft reacts with the post synaptic nicotinic receptors avoiding the Acetylcholinesterases enzyme , responsible for its hydrolysis. However eventually following its release all molecules are hydrolysed to inactive choline and acetate.

Acetylcholinesterase is a protein attached to the basement membrane. For each molecule of Acetylcholine released there are 10 active enzyme sites available. Several molecules of Acetylcholine can be hydrolysed by single molecule of enzyme . The arrangement allows for each molecule to act once with the receptor after which it is rapidly hydrolysed . Hence in normal physiological conditions there is no accumulation of Acetylcholine from one nerve stimulation to other.

THE END PLATE:

The resting membrane potential across the post synaptic membrane is 90mV with inside of cell being negative (-90mV). There is excess of positively charged ions outside the cell. When 2 Acetylcholine molecules binds to the α subunits of Acetylcholine receptors conformational change occurs leading to flow of cations according to concentration and electrical gradients. There is net inward flow of sodium leading to fall in membrane potential . At a certain threshold of EPP (-50mV) it opens specific sodium channels allowing sodium to enter leading to generation of Action potential.

Action potential draws current from the surrounding muscle fibre membrane and opens the voltage gated sodium channel in muscle fibre membrane triggering action potential in muscle fibre. Through the T tubules

it reaches the sarcoplasmic reticulum from which calcium is released and muscle contraction occurs.

MARGIN OF SAFETY:

The number of Acetylcholine receptors exceeds the number required to trigger a action potential under normal conditions . Hence around 70 - 80% of these Acetylcholine receptors are required to be blocked to prevent action potential being generated. During recovery from neuromuscular blockade margin of safety is important as even a normal inspiratory force, vital capacity and sustained head lift for 5 secs still have 70 - 80% of these Acetylcholine receptors blocked by the antagonists.[44]

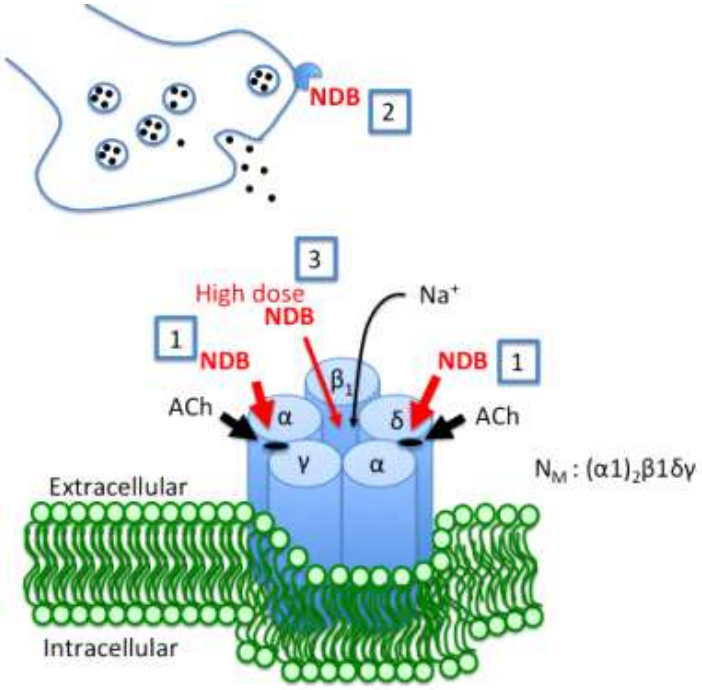
PHYSIOLOGY OF NEUROMUSCULAR BLOCK

NON DEPOLARISING NEUROMUSCULAR BLOCK:

Competitive antagonist:

Non Depolarising Neuromuscular Blockers are competitive antagonist of Acetylcholine receptors. It competes with Acetylcholine to binds with these receptors and prevent the action potential generation. The higher the concentration of this drug to the Acetylcholine, more of the receptor sites are occupied and neuromuscular block occurs. Similarly recovery from the block

occurs by decreasing the concentration of the drug or increasing the Acetylcholine levels by inhibiting the enzyme that hydrolyses it. However in this compeition between drug and Acetylcholine the bias is in favour of the drug. The blocker has to bind to one of the α subunit to block the channel whereas Acetylcholine has to bind to 2 α subunits to open the channel.



Drawing Adapted from: *Karlin A: Nature Reviews Neuroscience 3, 102-114 (February 2002)*
Pentameric data from: *Millar NS: Assembly and subunit diversity of nicotinic acetylcholine receptors. Biochem Soc Trans 31:869, 2003.*

In the figure above numbered 1 , at low concentrations the non depolarising NMB competes with Acetylcholine (ACh) for binding to postsynaptic nicotinic receptor sites in the skeletal muscle NMJ.

In number 2 the nondepolarizing NMB also interfere with presynaptic release of ACh from motor nerve endings by mechanism poorly understood. Both the Na channels and pre-synaptic nicotinic autoreceptors blockade have been implicated. The presynaptic nicotinic receptors have a different subunits compared to the muscle-type nicotinic receptors.

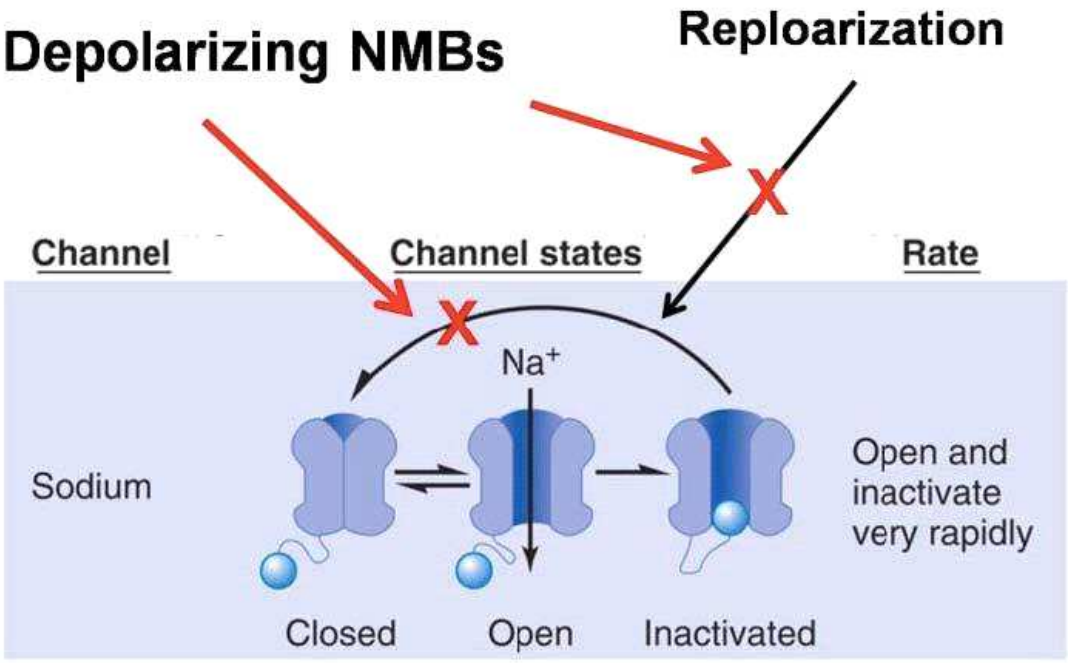
In number 3 when non depolarising NMB are given at higher concentrations they produce a more intense motor blockade by blocking the pore of the nicotinic receptor-channel complex

DEPOLARISING NEUROMUSCULAR BLOCK:

PHASE I BLOCK:

Suxamethonium, depolarising neuromuscular blocker acts by depolarising the neuromuscular end plate. Suxamethonium is hydrolysed by the plasma cholinesterase (pseudocholinesterase) and not by the cholinesterase in the cleft. So it has to diffuse from the cleft into the plasma for its clearance which is slower than Acetylcholine.

There is continuous depolarisation of the end plate resulting in inactivation of voltage gated sodium channels preventing depolarisation of muscle membrane. This lasts untill Suxamethonium is diffused from the cleft and the end plate is repolarised.



In the above figure it is seen when there is continuous depolarisation of the end plate, the voltage gated sodium channels remains open and inactive preventing depolarisation of muscle membrane. This lasts untill Suxamethonium is diffused from the cleft and the end plate is repolarised.

PHASE II BLOCK:

When Suxamethonium remains at NMJ for a prolonged time - due to infusion in a normal pseudocholinesterase activity patient , or because of relative overdose in abnormal pseudocholinesterase activity patient, it causes a phase ii block. The original depolarising block changes to non depolarising block as the membrane potential gradually recovers to normal but block is persistent.

This is described as Phase I to Phase II block. It is also called dual block, mixed block, desensitisation block. The term desensitisation block should not be used synonymously with Phase II block.

THEORIES OF PHASE II BLOCK:

- Some researchers are convinced that the block is caused by desensitisation of receptors.
- Some blelieved it to be by conformational changes in receptor protein.
- Some believe the reason to be abnormal electrolyte balance over the end plate by prolonged depolarisation.
- Some observed it to be channel blockade

Management of a patient with Phase II block depends on the activity of

cholinesterases. In normal patients the block is antagonised by cholinesterase inhibitor within few minutes after discontinuing the Suxamethonium. In abnormal genotypics the reversal may become unpredictable leading to partial reversal or potentiation of the block.

This is due to changes of quality and quantity of the pseudocholinesterases. Hence in abnormal genotypics Suxamethonium is very slowly or not hydrolysed at all in plasma, persisting in plasma. Hence Phase I block dominates initially followed by Phase II block, which should not be tried for reversal; but rather patient should be anaesthetised and ventilated untill full recovery from block.

FFP and blood have been used to treat prolonged apnea.

DESENSITISATION BLOCK:

Thesleff studied that neuromuscular block caused by Acetylcholine, Suxamethonium and decamethonium applied to end plates for prolonged periods is due to decrease in receptor sensitivity rather than persistent depolarisation. The initial depolarisation occured returned to normal level and the receptor had turned refractory to drug effects.

Evidence says that desensitisation is a physiological phenomenon occuring even when no agonists or antagonists are applied.

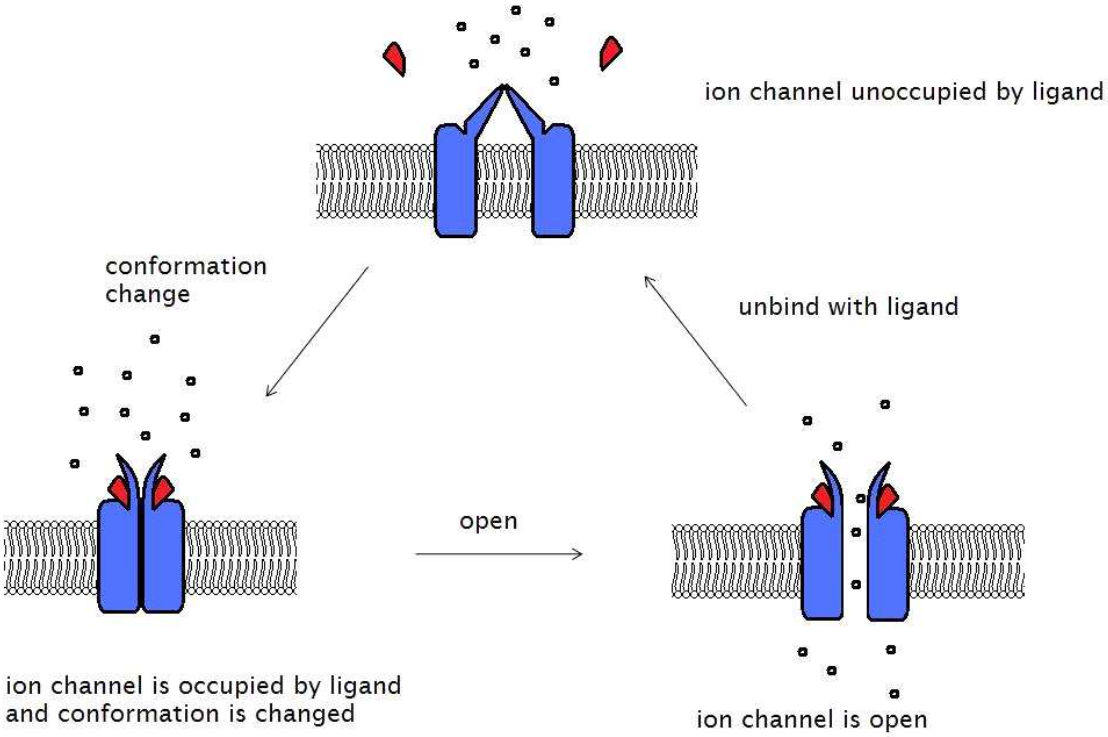


Fig 5: Different normal stages of the Acetylcholine receptors.

Normally receptors exists in 3 different states

- Resting state (closed ion channel)
- Active (open ion channel)
- Desensitised (closed ion channel)

Several factors promote desensitisation of receptors

- High concentration of both agonists and antagonists speed up the process of desensitisation.
- Drug like local anaesthetics ,volatile anaesthetics, iv anaesthetics , calcium channel blockers hasten the desensitisation.

Mechanism by which this occurs is unknown but believed due to phosphorylation of one or more amino acids of receptor proteins.

CHANNEL BLOCK:

Many drugs produce block without depolarisation of end plate or competing with Acetylcholine to receptors, by acting at different sites of the receptors and preventing the passage of ions.[12]

3 different mechanisms proposed are

- Open channel block
- Closed channel block
- Alteration in lipid environment of receptors

In open channel block - drugs act in receptors only in open state and blocks the channel. Increased potentiation of receptors with use of anticholinesterase drug can prolong the blockade. Local anaesthetic, barbiturates, antibiotics and both depolarising and non depolarising muscle relaxants are examples of drugs causing this block. Most believe only a small fraction of this receptors are normally blocked in open position. when doses of high concentration are used the possibility of open channel block can occur hence difficulty in reversing these blocks can be a problem.

In closed channel block, the drug binds to the receptors when channels are in closed position. Drug like tricyclic antidepressants and quinidine causes this type of block.

Some lipid soluble drugs like inhalational agents and alcohol dissolve through membrane lipids changing the channel properties.[21]

FACTORS THAT AFFECT NEUROMUSCULAR TRANSMISSION AND BLOCK:

Temperature:

Temperature may influence events taking place in motor nerve, synaptic cleft, end plate, muscle. Due to a marked margin of safety in NMJ it is of little significance. Temperature is important in muscle contraction thus it is essential to maintain near normal core and peripheral body temperature.

If there is a drop in core temperature there is a prolonged effect of all the blocking agent.

Electrolyte imbalance:

Changes in the plasma potassium levels can alter the neuromuscular transmission and also the action of muscle relaxants.

According to Nernst equation. Em (mV)=61 log (k+)o/(k)i

Em=Potential difference across the membrane

(k+)o - potassium concentration outside the cell

(k)i - potassium concentration inside the cell

An acute decrease of k+ outside the cell with no change in the inside of cells will make the cell more resistant for depolarisation to Acetylcholine, thus a low dose of depolarising agents are enough for blocking the channel.[47]

Acid base changes:

Changes in Ph may influence

- Membrane conduction
- Contraction of muscles
- Ratio of potassium both outside and inside of the cell
- Affinity of muscle relaxant to receptors[47]

DRUG INTERACTIONS OF THE NMJ

Drugs causing increased sensitivity to muscle relaxants,

- Antibiotics- polymyxin B, Aminoglycosides, polypeptides, tetracyclines, clindamycin, lincomycin by decreasing the evoked release of Acetylcholine and decreased sensitivity of nicotinic receptor.[47]
- Anticholinesterases- OPC, cyclophosphamide, ecothiophate eye drops by inhibiting the plasma cholinesterase.[47]
- Inhalational agents- by dissolving in lipids of membrane influencing the channel protein and decreasing the Acetylcholine release. [47]
- Intravenous agents- No interaction with muscle relaxants seen.[47]
- β blockers- potentiation of muscle relaxants seen but mechanism unknown. [47]
- Calcium channel blockers- by acting in both pre and post junctional receptors they potentiate the action of muscle relaxants occasionally reversal of blockade is difficult. [47]
- Local anaesthetics - these are fast channel blockers potentiating muscle relaxants action. [47]

- Magnesium sulphate - It decreases the Acetylcholine release and decreases the sensitivity of post junctional membrane and excitability of muscle cells. [47]

Drugs causing decreased sensitivity to muscle relaxants

- Antiepileptics (phenytoin, carbamazepine)
- Azathioprine (immunosuppressants)
- Corticosteroids and
- Methylxanthines (Aminophylline ,theophylline)

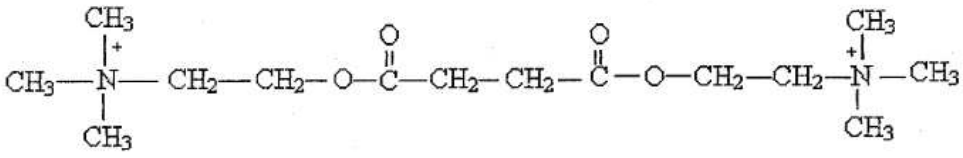
Mechanism of action unknown but methylxanthines inhibit the enzyme phosphodiesterase thereby increasing cAMP levels and possibly Acetylcholine. [47]

PHARMACOLOGY OF SUXAMETHONIUM

PHARMACOLOGY OF SUXAMETHONIUM

Suxamethonium introduced by Thesleff and Foldes et al in 1952, revolutionized anaesthetic practice by providing intense neuromuscular blockade of very rapid onset and ultra short duration, thereby greatly easing the maneuver of tracheal intubation. Suxamethonium is the only depolarizing neuromuscular blocking drug in clinical use., which is characterized by a rapid onset and short duration of action. A dose of 0.5 to 1 mg/kg IV Suxamethonium has a rapid onset (30-60 seconds) and short duration of action (3 to minutes). These characteristics make Suxamethonium the ideal drug for tracheal intubation.

Chemistry:



Structure of Suxamethonium

Two molecules of Acetylcholine linked back to back through the acetate methyl groups forms Suxamethonium.

Fig 6: Suxamethonium 50mg/ml (10ml vial)

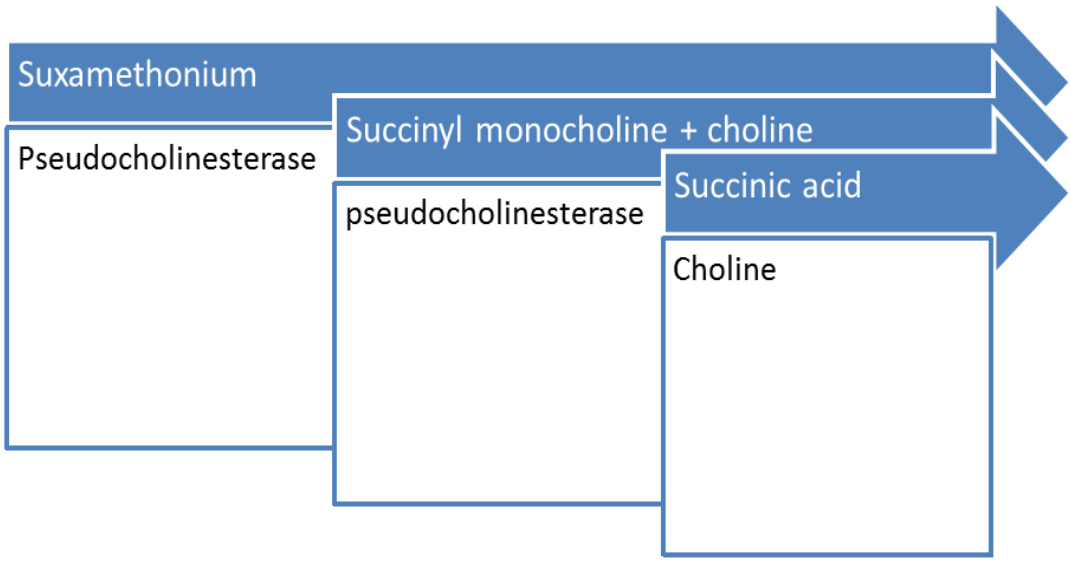
Structure of Suxamethonium

The drug is supplied in two forms, viz., the chloride and the bromide salts. The chloride is a white crystalline solid with a melting point of 160°C. It is freely soluble in water and the solution is sufficiently stable to permit the supply of drug as a 5% solution for clinical use. It is necessary to refrigerate the drug as significant degree of spontaneous hydrolysis occurs in warm surroundings.

Pharmacokinetics:

Suxamethonium is rapidly hydrolyzed in the body by pseudocholinesterase (plasma cholinesterase). The hydrolysis of Suxamethonium is a two stage process.

Hydrolysis of Suxamethonium



Only a small fraction of the original IV dose of Suxamethonium reaches the neuromuscular junction because of the enormous capacity of pseudocholinesterase to hydrolyse Suxamethonium. Since there is little or no pseudocholinesterase at NMJ, the block of Suxamethonium is terminated by its diffusing away from the NMJ into the circulation. So pseudocholinesterase is responsible for the onset and duration of action of Suxamethonium.[37]

Pharmacodynamics :

Mechanism of action :

Suxamethonium produces flaccid paralysis of skeletal muscle by causing persistent depolarization of post-junctional membrane. Suxamethonium attaches to each of the alpha sub-units of the nicotinic cholinergic receptors and mimics the action of Acetylcholine. Compared to acetylcholme the hydrolysis of Suxamethonium is slow, resulting in sustained depolarization of receptor ion channels. Depolarizing neuromuscular blockade is also known as *Phase* I blockade.[36]

If Suxamethonium is administered in a large dose (> 2 mg/kg), repeated doses, or as continuous infusion, it may result in a type of blockade where the post junctional membranes do not respond normally to Acetylcholine even when the post-junctional membranes have become

repolarized. This type of blockade is known as *phase II* blockade.

Clinical characteristics of Phase I and Phase 2 neuromuscular Blockade during Suxamethonium infusion

Characteristic	**Phase I**	**Transition**	**Phase** 2
Tetanic stimulation	No fade	Minimal fade	Fade
Post-tetanic facilitation	None	Slight	Yes
TOF	No	Mod. fade	Marked fade
TOF ratio	>0.7	0.4-0.7	<0.4
Edrophonium bromide	Augments	Little effect	Antagonizes
Recovery	Rapid	Rapid to slow	Increasingly prolonged
Does requirements (mg/kg)	2-3	4-5	>6
Tachyphylaxis	No	Yes	Yes

Dibucaine number and pseudocholinesterase Activity:

A Suxamethonium blockade is prolonged in patients with abnormal genetic variant of pseudocholinesterase. The variant was found by Kalow and Genest. Dibucaine inhibits normal pseudocholinesterase greatly than the abnormal variant which led to the development of Dibucaine number. Under standardized test conditions, dibucaine, a local anaesthetic inhibits the

normal enzyme about 80 percent and the abnormal enzyme about 20 percent.

Although the dibucaine number gives genetic makeup of an individual with respect to pseudocholinesterase, it does not measure the quantity of enzyme in the plasma, nor the quality of the enzyme in hydrolyzing a substrate such as Suxamethonium . Both the factors are accounted for in measurements of pseudocholinesterate activity.

Cardiovascular effects :

The drug stimulates the cholinergic receptors ; nicotinic receptors on both sympathetic and parasympathetic ganglia and muscarinic receptors in SA node of the heart. In low doses, both negative inotropic and chronotropic effect may occur. These can be decreased by prior administration of atropine. With large doses of Suxamethonium, these effects may become positive. One prominent clinical manifestation is the development of cardiac arrhythmias, manifested as sinus bradycardia, junctional rhythms, and ventricular arrhythmias, ranging from unifocal premature ventricular contraction to ventricular fibrillation in certain circumstances such as burns.

Sinus Bradycardia:

The mechanism involved in sinus bradycardia is stimulation of cardiac muscarinic receptors in the SA node, individuals with high sympathetic tone, such as children who have not received atropine. Sinus bradycardia noted in adults appear more commonly if second dose is given 5 minutes after the first. The bradycardia is prevented by thiopental, atropine, ganglion-blocking drugs, and nondepolarizing muscle relaxants. This effect is due to increased muscarinic stimulation, and ganglionic stimulation. The high incidence of bradycardia after a second dose of succinylcholine suggests that the hydrolysis products of Suxamethonium may sensitize the heart to a subsequent dose.

Nodal (Junctional) Rhythms:

Junctional rhythms are bradycardia slower than the sinus rate measured before the administration of Suxamethonium and intubation of the trachea. The mechanism involves greater stimulation of muscarinic receptors in the sinus node, suppreses the sinus mechanism and allowing the emergence of the atrioventricular node as the pacemaker. The incidence is greater after second dose of Suxamethonium but is prevented by prior administration of d-tubocuraine (dTc).

Ventricular Arrhythmias:

Drugs like tricyclic antidepressants, digitalis, exogenous catecholamines, monoamine oxidase inhibitors, and anesthetic drugs such as halothane and cyclopropane lowers the ventricular threshold for ectopic activity or increase the arrhythmogenic effect of catecholamines. Ventricular escape beats occur as a result of severe sinus and atrioventricular nodal slowing secondary to Suxamethonium administration. The incidence of ventricular arrhythmias is further increased by the release of potassium from skeletal muscle as a consequence of the depolarizing action of the drug.

Suxamethonium and hyperkalemia:

Studies have shown that in patients with certain disease and conditions, an exaggerated release of potassium occurs in response to Suxamethonium. Such conditions include bums, nerve damage or neuromuscular disease, closed head injury, intraabdominal infection and renal failure.[37]

Rhabdomyolysis and hyperkalemia may occur when Suxamethonium is administered to children with undiagnosed myopathy.[42] For these reasons some anaesthesiologists avoid the use of Suxamethonium in paediatric patients and prefer nondepolarizing neuromuscular blocking drugs. Proliferation of extrajunctional cholinergic receptors providing more sites for

potassium to leak outward from cells during depolarization is the presumed explanation for hyperkalemia that follows the administration of Suxamethonium to patients with denervation injury.[37]

In burns patients, the hyperkalaemic response that follows Suamethonium administration is markedly exaggerated. The mechanism of this exaggerated response to Suxamethonium seems to be similar to that in vicitims of denervation inujuries.[45]

Patient with chronic renal failure often have elevated baseline plasma potassium. More studies have shown that renal failure patients are not susceptible to an increased response to Suxamethonium than those with normal renal function.

Suxamethonium and intraocular pressure :

The increase in intraocular pressure is known to be caused by contraction of tonic myofibrils or transient dilatation of choroidal blood vessels. The intravenous administration of Suxamethonium is typically followed by an increase in intraocular pressure (by 5-10 mm Hg). The onset is within 1 minute after injection, peaks around 2-4 minutes and subsides in 6 minutes. The patients undergoing ophthalmic procedures are likely to be at risk from increased introcular pressure.[37]

Suxamethonium and intragastric pressure:

Suxamethonium produces inconsistent increase in intragastric pressure. When intragastric pressure increases *it* seems to be related to the intensity of skeletal muscle fasciculation induced by Suxamethonium. Pretreatment with either a nondepolarizing muscle relaxant or lignocaine decrease both the fasciculation and the increased gastric pressure effectively. A far less increase in intragastric pressure is observed in infants and children. This may be related to the minimal or absent fasciculations from Suxamethonium in these age groups. [37]

Suxamethonium and intracranial pressure:

Increase in intracranial pressure after administration of Suxamethonium to patients with intra cranial tumours or head trauma have not been a consistent observation. Patients in whom such an increase in intracranial pressure is not acceptable, a nondepolarizing muscle relaxant should be substituted for Suxamethonium, if at all possible. [37]

Suxamethonium and myalgia:

Postoperative skeletal muscle myalgia can occur after administration of Suxamethonium. It is said that the muscle pain is due to the damage produced in the skeletal muscle by unsynchronized contraction of muscle fibres just before paralysis occurs. Pretreatment with a minimal dose of a

nondepolarizing muscle relaxant prevents Suxamethonium induced muscle fasciculation and reduces the incidence and severity of post operative muscle pain. [37]

Masseter Spasm :

Suxamethonium causes masseter spasm, especially in children. In all likelihood, this is an increased contractile response at the NMJ.[37]

PHARMACOLOGY OF ROCURONIUM

PHARMACOLOGY OF ROCURONIUM

Rocuronium is classified under non depolarising muscle relaxants

CHEMISTRY: NON-DEPOLARIZING BLOCKERS

- Non-depolarizing blocking drugs are classified according to their chemical structure into benzylisoquinolines and ammonio steroids.

Benzylisoquinolines	Ammonio steroids
Tubocurarine	Pancuronium
Atracurium	Pipecuronium
Cisatracurium	Rocuronium
Doxacurium	Vecuronium
Mivacurium	

8

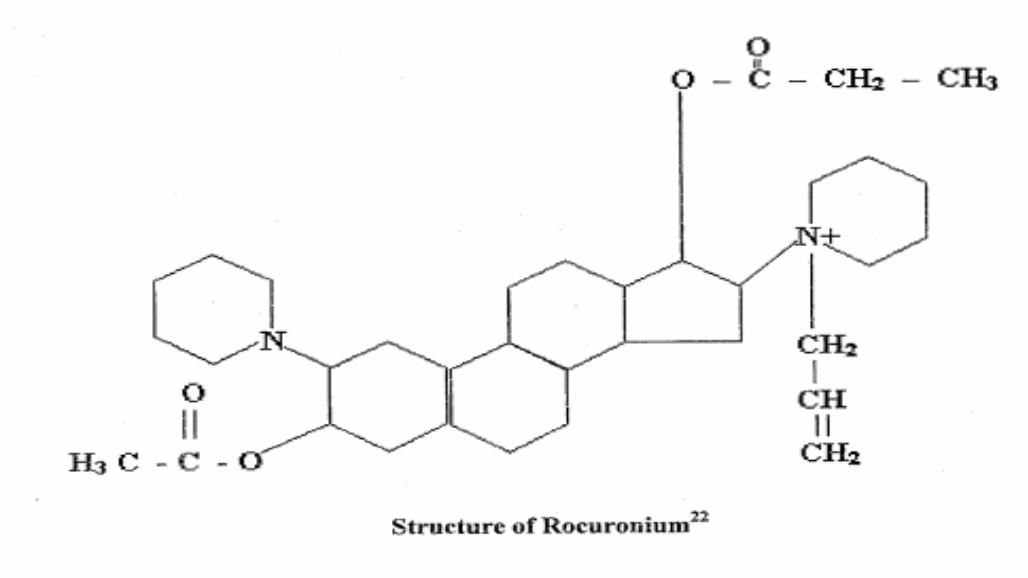
NON-DEPOLARIZING BLOCKERS

DURATION OF ACTION

SHORT-ACTING	INTERMEDIATE-ACTING	LONG-ACTING
Mivacurium	Atracurium	Tubocurarine
	Cisatracurium	Metocurine
	Rocuronium	Pancuronium
	Vecuronium	Doxacurium
		Pipecuronium

15

STRUCTURE



Structure of Rocuronium[22]

Fig 7: Rocuronium vial 100mg/10ml (10ml vial).

Structure of Rocuronium

Rocuronium is a newer amino steroid based neuromuscular blocking agent with short onset of action and intermediate duration of action. Recuronium is a 2-morpholino, 3-desacetyl, 16-N-allyl pyrolidino derivative of vecuronium. It differs from vecuronium at third position on the steroid nucleus and the absence of the Acetylcholine like fragment. The methyl group attached to the quaternary nitrogen of vecuronium is replaced by an allyl group and the absence of Acetylcholine like fragment in the A-ring may be partly responsible for the decrease in potency seen with Rocuronium. Rocuronium possess tertiary nitrogen at the ring A end of the molecule. It is the replacing of acetate group by a hydroxy group attached to the A-ring, made it possible to present Rocuronium as a stable solution.

PHARMACOKINETICS

Rocuronium is taken up by a carrier mediated active transport system into the liver. Rocuronium is excreted unchanged in the bile. Desacetylation of Rocuronium does not occur and the putative metabolities 17-desacetylRocuronium have not been detected in significant quantities. Renal excretion of Rocuronium may be > 30% in 24 hours. In patients with renal failure, Rocuronium may produce longer duration of action.[10] In patients with liver disease there is increase in the volume of distribution and may result in prolonged duration of action.

PHARMACODYNAMICS

Mechanism of Action:

Rocuronium being an aminosteroid based neuromuscular blocking agents, has a post junctional effect and high degree of selectivity for receptors at the neuromuscular junctions. Muscle paralysis is produced by competitive antagonism of nicotinic cholinergic receptor of skeletal muscle. Its potency is about 10 - 15% of vecuronium in man.[32] Rocuronium antagonizes Acetylcholine receptor, therefore, it is likely that it competes with Acetylcholine at its binding site. The tetanic fade phenomenon is observed with Rocuronium indicating activity not only at post synaptic but also at pre synaptic nicotinic receptors. Activity is terminated by gradual dissociation from the receptor shifting the agonist/antagonist equilibrium in favour of Acetylcholine.

Dosage, Onset and Duration of action :

Rocuronium has a rapid onset of neuromuscular block, presumably due to the relatively low potency of Rocuronium. The intubating dose of Rocuronium is 0.6 mg/kg.

Dosage and Clinical duration of Rocuronium

	Dosage (mg/kg)	**Clinical duration (minutes)**
ED_{95}	0.3-0.4	
Intubation at t=60-90 seconds	0.6-1.0	35-75
Relaxation (N_20/ 0_2)	0.3-0.4	30-40
Relaxation (vapour)	0.2-0.3	30-40
Maintenance	0.1-0.15	15-25
Infusion	8-12 **u/kg-^{1}/min^{-1}**	

Onset of action of Rocuronium is shorter when compared with other nondepolarizing muscle relaxants.[6] When the dose of Rocuronium is increased, onset of action decreases further.

Onset and Duration of action of Rocuronium

	Rocuroniu m 0.6 **mg/kg**	**Rocuroniu m 0.9 mg/kg**	**Rocuronium 1.2 mg/kg**
Onset			
Mean	89	75	55
SD	33	28	14
Range	48-156	48-144	36-84
Duration **(minutes)**			
Mean	37	53	73
SD	15	21	32
Range	23-75	25-88	38450

When the dose of Rocuronium is increased the onset of action is definitely decreased but the duration of action is increased.

Rocuronium can be used for continuous infusion. The infusion rate will depend on the anaesthetic technique and age of the patient. It can be used at a rate of 0.3 to 0.6 mg/kg/hr (5-10 ug/kg/min).[38]

Recovery:

For an intubating dose of Rocuronium 0.6 mg/kg, the time required for the recovery of twitch height from 25% to 75% is approximately 14 minutes.

Recovery index of three doses of Rocuronium

	Rocuronium 0.6 mg/kg	**Rocuronium 0.9 mg/kg**	**Rocuronium 1.2 mg/kg**
Recovery Index			
Mean	**14**	**22**	24
SD	**8**	**14**	**11**
Range	6-27	8-29	11-43

Rocuronium and cardiovascular effects

Rocuronium is typically devoid of cardiovascular effects. Circulatory effects or the release of histamine do not occur after the rapid IV administration of even large doses of Rocuronium. The structural feature responsible for this difference is the absence of Acetylcholine-like character of A-ring substitution, which decreases the action on cardiac muscaranic receptors.

Rocuronium, however, may produce a slight vagolytic action. This feature of Rocuronium may be useful in patients undergoing surgical procedures that may be associated with vagal stimulation.

Rocuronium and cardio pulmonary bypass :

Under hypothermic (post-bypass conditions) the Rocuronium requirements are reduced[39]. Factors, which may play a role in the changed concentration response relationship and changed biodisposition during hypothermia are:

- An increased sensitivity of NMJ related to a decreased acetylcholine mobilization.
- A diminished muscle contractility due to changed mechanical properties and / or electrolyte shifts (Mg^{2+} and Ca^{2+}) resulting from the application of cardio pulmonary bypass.
- Increased unbound relaxant fraction due to haemodilution, despite a decreased total Rocuronium concentration.

Rocuronium and age:

The potency of Rocuronium is significantly greater in infants than in children or adults.[28] Infants have 20-30% smaller ED50 and ED95 values than children or adults, while differences between children and adults were minimal. This pattern of age dependency is similar to that with other non-depolarizing muscle relaxants, which show that dose, requirement is smallest in infants. If this difference in potency is translated into clinical practice it means that if children or adults are given a dose of 600 ug/kg, an equipotent does in infants would be 450 ug/kg. If no adjustment in dose is made, there would be a much longer duration of effect in infants than children or adults.

Rocuronium and caesarean section :

Rocuronium had no untoward effects on the neonates, evaluated by 1 and 5 minutes scores, when Rocuronium 0.6 mg/kg" was used in 40 elective caesarean section patients full term, without fetal distress.[2]

Rocuronium and hepatic cirrhosis:

The clearance of Rocuronium may be reduced in the presence of hepatic cirrhosis and thus it is advisable to reduce the dose of drug used in these patients.[20]

Rocuronium and renal failure:

There is no significant difference in the onset and duration of action of Rocuronium between patients with and without renal failure. Patients with renal failure showed a significantly lower clearance and an increased mean residence time.[9]

Rocuronium Bromide in the ICU:

Muscle relaxation with Rocuronium should be maintained by continuous infusion, whenever its use is indicated in the ICU. An average of 45mg Rocuronium per hour provide, optimal conditions for ventilation and nursing maneuvers. Monitoring of neuromuscular function is strongly advised because of the substantial inter-individual differences in the dose required by ICU patients. With continuous monitoring of neuromuscular function, no residual paralysis or muscle weakness is observed.[22]

METHODOLOGY

METHODOLOGY

This study was conducted in Institute of Anaesthesiology and Critical care at Madras medical college, Chennai during the period 2014 – 15. Ethical committee clearance was obtained from the institution for this study purpose

INCLUSION CRITERIA:

- Age : 18 – 60 years
- Weight : BMI < 30 Kg/m2
- ASA : I & II
- Surgery : Elective
- Mallampatti scores : I & II
- Who have given valid informed consent.

EXCLUSION CRITERIA:

- Not satisfying inclusion criteria.
- Patients posted for emergency surgery
- Patients with difficult airway
- Lack of written informed consent

- Pregnant female
- Neuromuscular disorders
- Obese individual
- Allergy to Suxamethonium or Rocuronium

Materials:

- Mac Intosh laryngoscope
- Single use PVC endotracheal tubes with size 7.0 & 8.0mm ID
- Drugs – Suxamethonium and Rocuronium
- Monitors – ECG,NIBP,SPO2.

Methods:

The study involved 100 patients who were randomly divided into main groups of 50 patients each with the first group being the Suxamethonium and the second group being the Rocuronium assessed for intubating conditions after administration of corresponding drug.

All patients were subjected to a detailed pre-anaesthetic evaluation and the presence of significant systemic diseases and difficult airways were ruled out. Informed consent was taken and the procedure was explained to them. All patients were given 0.5mg of Alprazolam and 150mg of Ranitidine orally on the previous night of surgery. On the morning of surgery an intravenous line was secured with appropriate size.

Patient monitors:

Monitors included non - invasive blood pressure monitor, ECG, pulseoximeter.

Induction:

All patients were preOxygenated with 100% Oxygen for 3 – 5 minutes. Pre induction heart rate and blood pressure was measured. Patients were induced with Thiopentone 5 mg/kg iv. Patients were ventilated with 100% Oxygen for 60 seconds. Intubating conditions were assessed after administration of neuromuscular blocker in 60 seconds. The intubating conditions were assessed according to the scoring system by Kreig et al (1980) modified by Cooper et al (1992). Parameters taken into consideration were jaw relaxation, vocal cords movement and gross response to intubation.

Intubating conditions scoring system

Score	JAW RELAXATION	VOCAL CORDS MOVEMENT	RESPONSE TO INTUBATION
0	Poor(impossible)	Closed	Severe coughing or bucking
1	Minimal(difficult)	Closing	Mild coughing
2	Moderate(fair)	Moving	Slight diaphragmatic movement
3	Good(easy)	Open	None

The scores were added up and grouped as

8 – 9 = Excellent 6 – 7 = Good

3 – 5 = Fair 0 – 2 = Poor

After intubation the cuff of the endotracheal tube was inflated and the tube was connected to the circuit and controlled ventilation was started with Nitrous oxide, Oxygen and volatile anaesthetic. The intubating conditions assessed in 60 seconds was noted and the results were analysed and tabulated. The Fisher Exact test and t-test were used in statistical analysis of data. At the end of surgery the block was reversed with 0.05 mg/kg of neostigmine and 0.04mg/kg of glycopyrrolate. The patients were extubated after thorough oral suctioning. Any untoward effects were recorded.

RESULTS

RESULTS

This study was conducted during the period 2014 – 15 and involved 100 patients undergoing elective surgery under GA. They were randomly divided into two main groups with Group 1 receiving Suxamethonium and Group 2 receiving Rocuronium and the intubating conditions were assessed in 60 seconds according to the system proposed by Cooper et al and were classified as excellent, good, fair and poor.

Table 1: group distribution with t- test below

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Age (In Years)	GROUP - I Suxamethonium (1.5 mg/kg)	50	30.34	12.245	1.732
	GROUP - II Rocuronium (1.0mg/kg)	50	33.08	12.127	1.715

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age (In Years	Equal variances assumed	.283	.596	-1.124	98	.264	-2.740	2.437	-7.577	2.097
	Equal variances not assumed			-1.124	97.991	.264	-2.740	2.437	-7.577	2.097

Table 2: Age distribution in each group

Age (In Years) * Group Crosstabulation

			Group		
			GROUP - I Suxamethonium (1.5 mg/kg)	GROUP - II Rocuronium (1.0mg/kg)	Total
Age (In Years)	< 30 Years	Count	31	23	54
		% within Group	62.0%	46.0%	54.0%
	31 - 40 Years	Count	10	13	23
		% within Group	20.0%	26.0%	23.0%
	41 - 50 Years	Count	4	10	14
		% within Group	8.0%	20.0%	14.0%
	51 - 60 Years	Count	5	4	9
		% within Group	10.0%	8.0%	9.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Table 3 : Weight distribution in each group with t- test below

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Body Wt Kg	GROUP - I Suxamethonium (1.5 mg/kg)	50	54.14	9.493	1.343
	GROUP - II Rocuronium (1.0mg/kg)	50	61.98	9.027	1.277

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Body Wt Kg	Equal variances assumed	.071	.791	-4.232	98	.000	-7.840	1.853	-11.516	-4.164
	Equal variances not assumed			-4.232	97.753	.000	-7.840	1.853	-11.517	-4.163

Table 4 : Sex distribution in each group with t- test below

Sex * Group Crosstabulation

			Group		
			GROUP - I Suxamethonium (1.5 mg/kg)	GROUP - II Rocuronium (1.0mg/kg)	Total
Sex	Male	Count	28	28	56
		% within Group	56.0%	56.0%	56.0%
	Female	Count	22	22	44
		% within Group	44.0%	44.0%	44.0%
Total		Count	50	50	100
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.000[b]	1	1.000		
Continuity Correction [a]	.000	1	1.000		
Likelihood Ratio	.000	1	1.000		
Fisher's Exact Test				1.000	.580
Linear-by-Linear Association	.000	1	1.000		
N of Valid Cases	100				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 22.00.

Table 5 : Intubating conditions distribution in each group with t-test below

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Cooper Scoring System	GROUP - I Suxamethonium (1.5 mg/kg)	50	8.36	.749	.106
	GROUP - II Rocuronium (1.0mg/kg)	50	7.54	.994	.141
Jaw Relaxation	GROUP - I Suxamethonium (1.5 mg/kg)	50	2.70	.463	.065
	GROUP - II Rocuronium (1.0mg/kg)	50	2.52	.544	.077
Vocal Cords	GROUP - I Suxamethonium (1.5 mg/kg)	50	2.68	.471	.067
	GROUP - II Rocuronium (1.0mg/kg)	50	2.34	.557	.079
Response to Intubation	GROUP - I Suxamethonium (1.5 mg/kg)	50	2.98	.141	.020
	GROUP - II Rocuronium (1.0mg/kg)	50	2.70	.463	.065

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Cooper Scoring Syst	Equal variance assumed	1.971	.163	4.658	98	.000	.820	.176	.471	1.169
	Equal variance not assumed			4.658	91.100	.000	.820	.176	.470	1.170
Jaw Relaxation	Equal variance assumed	8.712	.004	1.783	98	.078	.180	.101	-.020	.380
	Equal variance not assumed			1.783	95.574	.078	.180	.101	-.020	.380
Vocal Cords	Equal variance assumed	2.667	.106	3.294	98	.001	.340	.103	.135	.545
	Equal variance not assumed			3.294	95.363	.001	.340	.103	.135	.545
Response to Intubati	Equal variance assumed	137.533	.000	4.090	98	.000	.280	.068	.144	.416
	Equal variance not assumed			4.090	58.068	.000	.280	.068	.143	.417

In both the groups with respect to age, body weight and sex distribution it is statistically not significant

The intubating conditions assessed at 60 seconds following the administration of corresponding neuromuscular blockers were observed to be excellent in 42 patients(84%) in group I (Suxamethonium) while they were excellent in 26 patients(52%) in group II (Rocuronium) .The intubating conditions were good in 8 patients(16%) in group I (Suxamethonium) while they were good in 21 patients (42%) in group II (Rocuronium). The intubating conditions was observed to be fair in 3 patients (6%) in group II (Rocuronium). In all the patients (100%) in Group I (Suxamethonium) it was observed that the intubating conditions was better with dense neuromuscular blockade whereas it was observed in 47 patients (94%) in group II (Rocuronium) the intubating conditions were good to excellent and was acceptable. The result was significant with a p value of < 0.01.

According to the cooper scoring system the scores of vocal cord movement in group I (Suxamethonium) was 2.68(mean) ±0.471 and in group II (Rocuronium) was 2.34±0.557 , the scores of response to intubation in group I (Suxamethonium) was 2.98±0.141 and in group II (Rocuronium) was2.70±0.463 with better intubating conditions in group I receiving Suxamethonium than Rocuronium.The results was significant with p value of

<0.05. whereas the scores of jaw relaxation in group I patients(Suxamethonium) was 2.70(mean)±0.463 and group II patients (Rocuronium) was 2.52±0.544 with better jaw relaxation.The results was not significant as p value >0.05. In overall scoring the results was significant with better intubating conditions in patients receiving Suxamethonium.

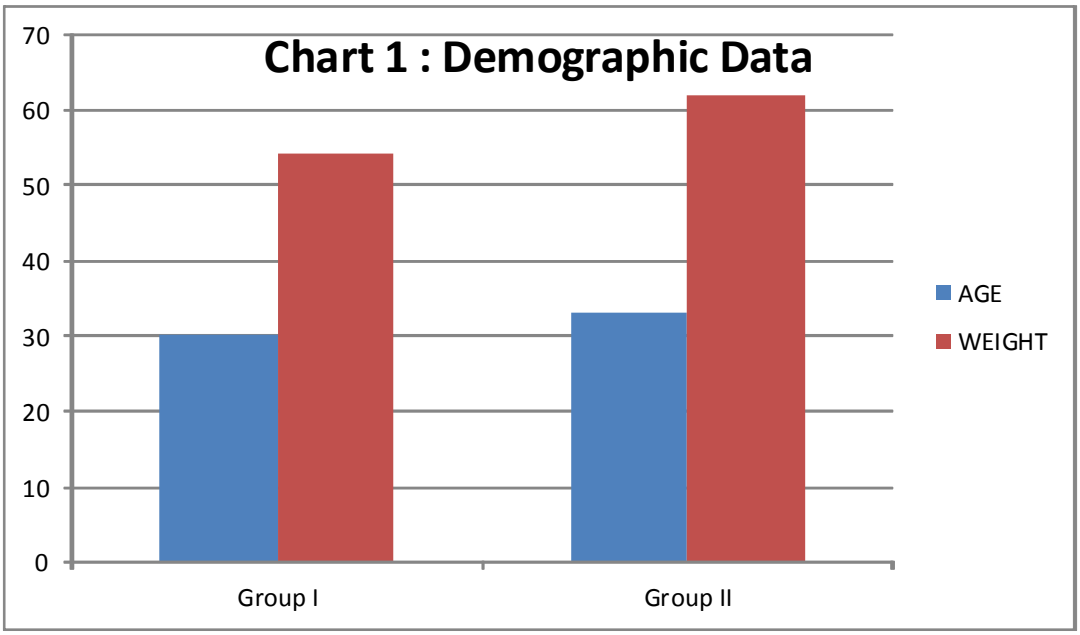


Chart 1 : Demographic Data
70
60
50
40
30
20
10
0
Group I
Group II
AGE
WEIGHT

Chart 2 :Sex distribution in each group

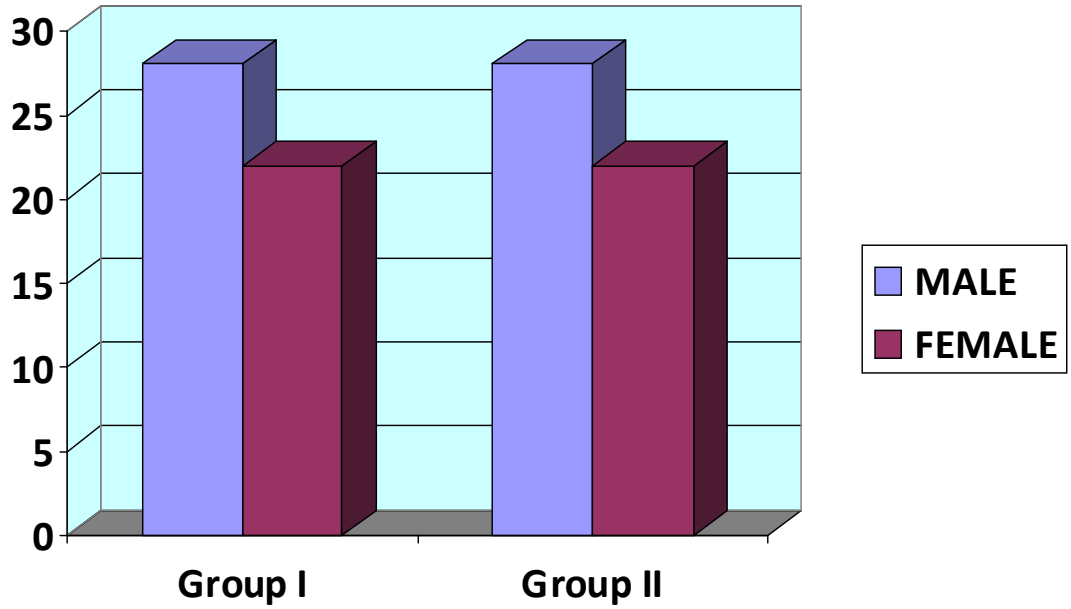


Chart 3: Intubating conditions in each group

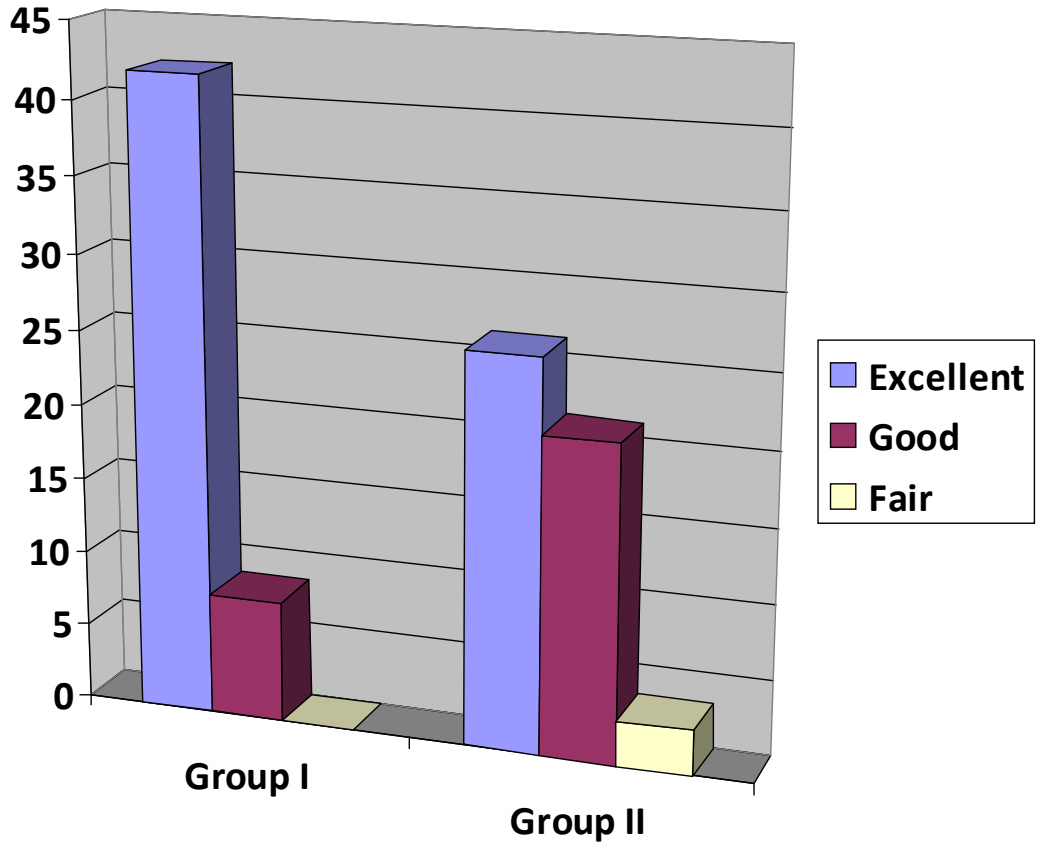


Chart 4 : distribution of scoring parameters in the groups

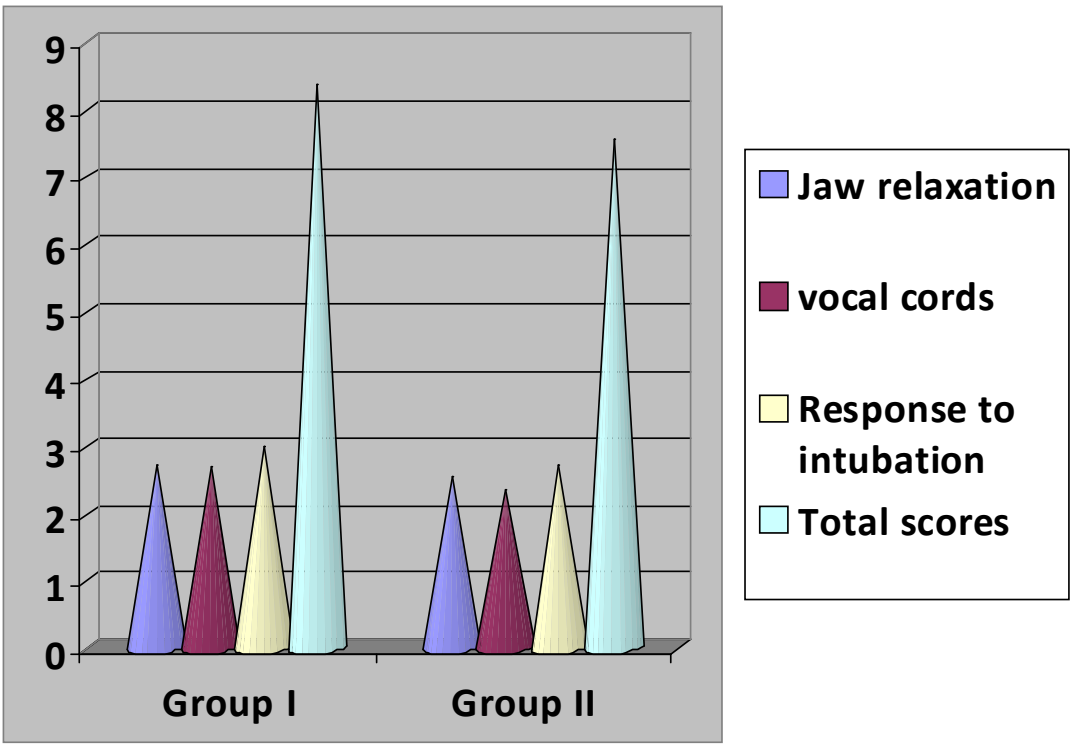


Table 7: HEART RATE VARIATION

Time of monitoring	I	II
Resting	83.4 ±9.9	84.2±12.9
After induction	95.4±12.6	97.6±14.4
After intubation at 1 minute	100±10.2	103.4±12.4
At 2 minutes	98±10.1	100.2±11.6
At 5 minutes	92.6±11.4	94.6±12.2

Table 8: MEAN ARTERIAL PRESSURE

Time of monitoring	I	II
Resting	91.8±7.0	93.3±6.7
After induction	92.6±8.4	93.6±5.9
After intubation at 1 minute	98.4±7.2	106.4±8.2
At 2 minutes	95.4±8.5	98.2±6.3
At 5 minutes	94.6±10.2	96.4±9.2

The above tables shows mean heart rate and mean arterial pressure variation in two groups. It shows that both are increased in two groups after induction was maximum at 1 minute afterwards it gradually returns to normal.

DISCUSSION

DISCUSSION

In patients undergoing elective surgeries under GA the airway of anaesthetised patient needs to be secured at the earliest for which we need a muscle relaxant of rapid onset, which also prevents the aspiration of gastric contents in patients who have full stomach, delayed gastric emptying time, impaired function of lower oesophageal sphincter. Suxmethonium was the often used drug till now for rapid onset of intubating conditions. Still the side effects it may produce may range from post operative myalgia to life threatening complications like dysrhythmias, hyperkalemia ,malignant hyperthermia.

Rocuronium is a non depolarising muscle relaxant that first came into use in 1990s . It showed acceptable faster onset of action compared to other non depolarising muscle relaxant. There are studies showing different dosage regimens of Rocuronium producing acceptable intubating conditions. Certain studies shows that it can be used as an alternative to Suxamethonium in rapid sequence induction.[27, 34]

Previous studies showed that intubating conditions at 60 seconds were generally good with a dose of 0.6 mg/kg of Rocuronium.[10,35,46] Use of higher doses of Rocuronium by workers have been observed to increase the onset of intubating conditions during rapid sequence induction with increased duration

of action.[40,27,34]

In our study the intubating conditions following administration of 1 mg/kg of Rocuronium was compared with Suxamethonium 1.5 mg/kg in 60 seconds in different patients undergoing elective surgeries.

The intubating conditions assessed at 60 seconds following the administration of corresponding neuromuscular blockers were observed to be excellent in 42 patients(84%) in group I (Suxamethonium) while they were excellent in 26 patients(52%) in group II (Rocuronium) .The intubating conditions were good in 8 patients(16%) in group I (Suxamethonium) while they were good in 21 patients (42%) in group II (Rocuronium). The intubating conditions was observed to be fair in 3 patients (6%) in group II (Rocuronium).

In our study the hemodynamic response were also recorded . the results shown in table 7 & 8 was comparable and statistically not significant in both the groups.

Our findings were comparable with to the study conducted by Cooper et al, (1992).[8] Rocuronium used at the dose of 0.6mg/kg produced excellent intubating conditions in 60% of patients compared to 95% in patients received Suxamethonium. In our study it was found when Rocuronium used at the dose of 1mg/kg it produced excellent intubating condition in 52% of

patients compared to 84% in patients received Suxamethonium.

Acceptable intubating conditions in Cooper 's study were 95% in Rocuronium group compared to 100% in Suxamethonium in 60 seconds, in our study the intubating conditions were acceptable in around 94% of the patients compared to 100% patients received Suxamethonium

Our findings were also similar to findings of Huzinga et al (1992)[18] who reported the intubating conditions were acceptable in 100% of patients but the dosage Rocuronium used was 0.6 mg/kg at 60 seconds after administration

Puhringer et al (1995)[35] reported 100% acceptable intubating conditions with both Suxamethonium and Rocuronium in 100% of the patients.

Larsen et al (2005) reported comparable acceptable intubating conitions in both Suxamethonium(1.5mg/kg) and Rocuronium(1mg/kg) for rapid sequence intubation in trauma emergency cases.

It is seen that Rocuronium can be used to provide acceptable intubating conditions near equivalent to Suxamethonium making it an alternative. Rocuronium has the disadvantage of having intermediate duration of action, with its standard intubating dosage regimens. Hence it is not recommended for patients with anticipated difficult intubation. A failed intubation in

patients given Rocuronium can prove dangerous because of its intermediate duration of action. Suxamethonium with its rapid termination of action is a safer agent with anticipated difficult intubation.

CONCLUSION

CONCLUSION

Suxamethonium provides ideal intubating conditions very rapidly than Rocuronium, but Rocuronium also provides intubating conditions that are acceptable for earlier establishment of airway with minimal injury at 60 seconds at a dose of 1mg/kg near equivalent to Suxamethonium. As Suxamethonium has numerous side effects, Rocuronium can be chosen as an alternative to it even in rapid sequence intubation in emergency cases, provided the airway is properly assessed and no anticipated difficult intubation is present.

SUMMARY

SUMMARY

This prospective controlled study was conducted with Suxamethonium and Rocuronium in 100 patients undergoing elective surgeries under GA.

Each of the drug was given to a group of 50 patients and the intubating conditions was assessed in 60 seconds. The results obtained showed that acceptable (good to excellent) intubating conditions were present in 94% of the patients in 60 seconds after administration. While all (100%) patients had acceptable intubating conditions in 60 seconds after administration of Suxamethonium.

The results showed that Rocuronium had equivalent amount of jaw relaxation in patients compared with Suxamethonium, while the vocal cords movement and response to intubation was better with Suxamethonium when compared with Rocuronium.

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BIBLIOGRAPHY

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ANNEXURES

PROFORMA

DATE: ROLL NO: AIRWAY DEVICE:

NAME:

AGE: SEX: IP NO:

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

Ht: CVS: HB:

Wt: RS:

AIRWAY:MMC - IID - DENTITION -

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

H/O any drug allergy

MEASURES OF STUDY OUTCOME:

INTRAOPERATIVE HAEMODYNAMICS:

HR SBP DBP MAP SPO2

PRE OP:

INDUCTION:

MR WITH SUXAMETHONIUM/ROCURONIUM

GRADING OF INTUBATING CONDITION

Score	**JAW RELAXATION**	**VOCAL CORDS MOVEMENT**	**RESPONSE TO INTUBATION**
0	Poor(impossible)	Closed	Severe coughing or bucking
1	Minimal(difficult)	Closing	Mild coughing
2	Moderate(fair)	Moving	Slight diaphragmatic movement
3	Good(easy)	Open	None

EXTUBATION

SIDE EFFECTS

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. S. RAJAMANIKANDAN,
Postgraduate M.D. Anaesthesiology,
Madras Medical College,
Chennai – 600 003.

Dear Dr. S. Rajamanikandan,

The Institutional Ethics Committee has considered your request and approved your study titled **"A Prospective, randomized controlled study to compare the intubating conditions achieved with suxamethonium and rocuronium bromide." No.54082014.**

The following members of Ethics Committee were present in the meeting held on 05.08.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr.C.Rajendran, M.D.,	: Chairperson
2.	Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3.	Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4.	Prof.R.Nandhini, M.D., Inst.of Pharmacology, MMC	: Member
5.	Dr.G.Muralidharan, Director Incharge, Inst.of Surgery	: Member
6.	Prof.K.Ramadevi, Director i/c, Inst.of Biochemistry, MMC	: Member
7.	Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
8.	Prof.Tito, M.D., Director i/c, Inst.of Internal Medicine, MMC	: Member
9.	Thiru S.Rameshkumar, Administrative Officer	: Lay Person
10.	Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
11.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

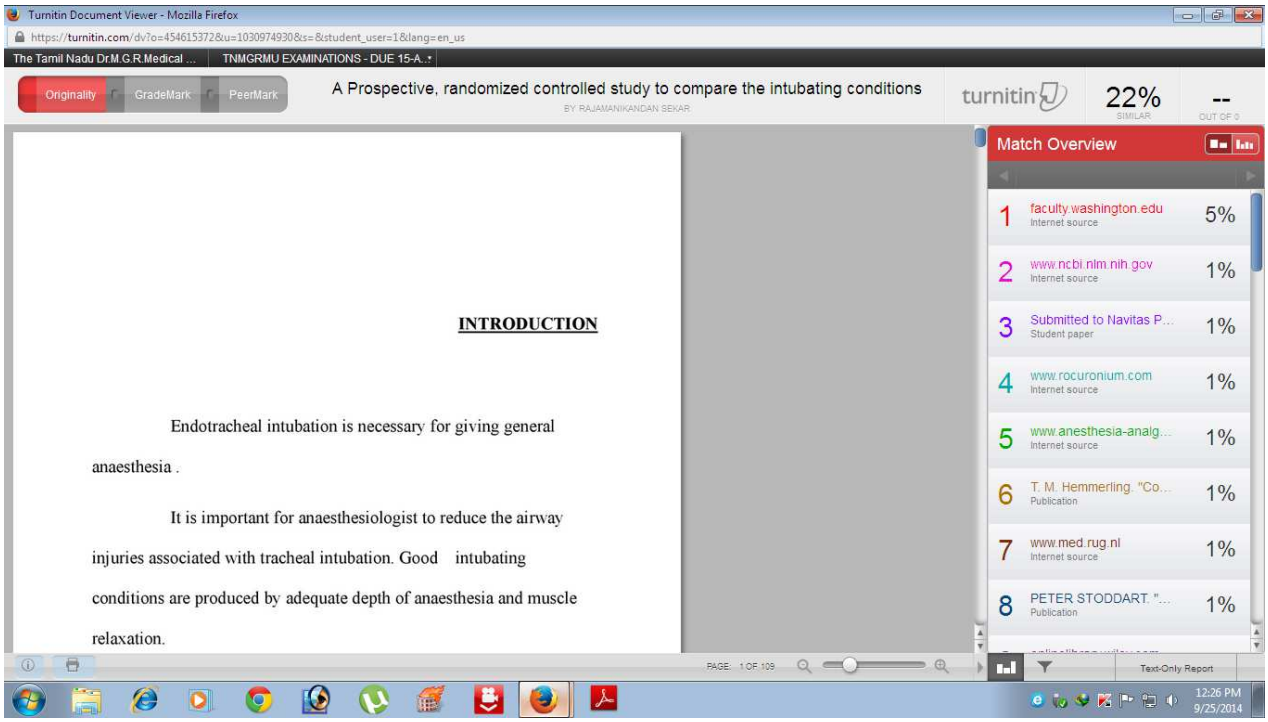
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

Member Secretary, Ethics Committee

TURNITIN PLAGIARISM SCREEN SHOT



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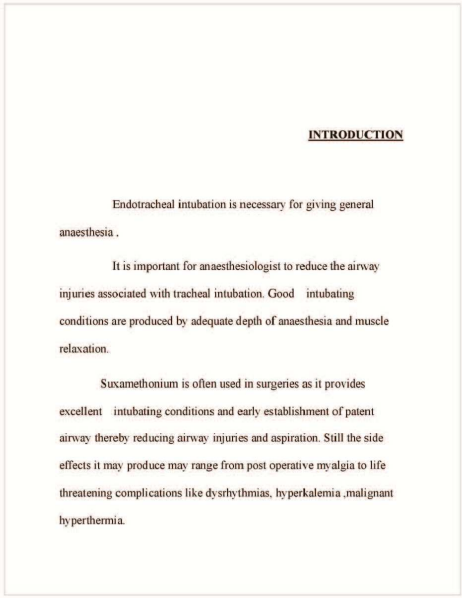

INTRODUCTION

Endotracheal intubation is necessary for giving general anaesthesia .

It is important for anaesthesiologist to reduce the airway injuries associated with tracheal intubation. Good intubating conditions are produced by adequate depth of anaesthesia and muscle relaxation.

Suxamethonium is often used in surgeries as it provides excellent intubating conditions and early establishment of patent airway thereby reducing airway injuries and aspiration. Still the side effects it may produce may range from post operative myalgia to life threatening complications like dysrhythmias, hyperkalemia ,malignant hyperthermia.

INFORMATION TO PARTICIPANTS

Investigator :

Name of the Participant:

Title: "*A Prospective, randomized controlled study to compare the intubating conditions achieved with suxamethonium and rocuronium bromide "***.**

You are invited to take part in this research study.We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria.We want to compare the onset time and intubating condition achieved with suxamethonium and rocuronium bromide.

What is the Purpose of the Research:

This study is done to compare the intubating conditions achieved with suxamethonium and rocuronium bromide.

The Study Design:

All the patients in the study will be divided into two groups.

Group 1-Muscle relaxant with suxamethonium(1.5mg/kg).

Group 2-Muscle relaxant with rocuronium bromide(1mg/kg)

Benefits

The use of muscle relaxants will facilitate in easier intubation and minimizing the risk of airway injury and maintaining haemodynamic stability.

Discomforts and Risks

The use of muscle relaxants can cause post operative myalgia, rise in serum potassium, bradycardia, rise in intra ocular and intra cranial pressure, prolonged recovery and malignant hyperthermia.

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time :

Date :

Place :

Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study title : "A Prospective, randomized controlled study to compare the intubating conditions achieved with suxamethonium and rocuronium bromide."

Study center:

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE,

RAJIV GANDHI GOVT. GENERAL HOSPITAL,

MADRAS MEDICAL COLLEGE,

CHENNAI 3.

Participant name : Age: Sex:
I.P.No:

I confirm that I have understood the purpose of procedure for the above study . I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator ,regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study .

Time:
Date: Signature / thumb impression of patient
Place: Patient name:
Signature of the investigator:
Name of the investigator:

KEY TO MASTER CHART

S.No	-	Serial number
IP.No.	-	In patient no
M	-	Male
F	-	Female

GROUP-I Suxamethonium (1.5mg/kg)

S.No.	I.P.No.	Age Yrs	Sex	Body Wt Kg	Surgery	Intubating Conditions	Cooper Scoring System (0, 1, 2, 3)			
							Score	Jaw Relaxation	Vocal Cords	Response to Intubation
1	56159	16	F	33	Right Modified Radical Mastoidectomy	Excellent	8	3	3	2
2	63793	18	F	40	Right Modified Radical Mastoidectomy	Excellent	9	3	3	3
3	27411	49	M	65	Right Modified Radical Mastoidectomy	Excellent	9	3	3	3
4	20787	25	M	60	Left Tympanomastoid Exploration	Excellent	9	3	3	3
5	20282	57	F	60	Right Tympano Mastoid Exploration	Good	7	2	2	3
6	35824	29	F	50	Left Cortical Mastoidectomy	Excellent	8	2	3	3
7	48851	22	M	60	Tonsillectomy	Excellent	9	3	3	3
8	19928	54	M	62	Left Tympanomastoid Exploration	Excellent	9	3	3	3
9	28692	19	F	47	Tonsillectomy	Excellent	8	2	3	3
10	25160	20	M	56	Tonsillectomy	Good	7	2	2	3
11	20853	17	M	40	Tonsillectomy	Excellent	9	3	3	3
12	11765	32	F	60	Right Cortical Mastoidectomy	Excellent	9	3	3	3
13	17290	17	M	46	Tonsillectomy	Excellent	8	3	2	3
14	14428	28	F	52	Right Myringoplasty	Good	7	2	2	3
15	14125	28	M	68	Right Tympano Mastoid Exploaration	Excellent	8	3	2	3
16	24200	16	M	32	Tonsillectomy	Excellent	9	3	3	3
17	44737	20	F	42	Tonsillectomy	Excellent	9	3	3	3
18	25012	23	F	40	Left Myringoplasty	Good	7	2	2	3
19	72896	20	M	54	Tonsillectomy	Good	7	2	2	3
20	72920	16	F	32	Tonsillectomy	Excellent	8	3	2	3
21	68352	28	M	60	Flap Cover Thigh	Excellent	9	3	3	3
22	63156	28	M	52	ORIF Clavicle Fracture	Excellent	8	3	2	3
23	63156	28	M	52	ORIF Clavicle Fracture	Excellent	8	3	2	3
24	80541	28	M	68	Breast Lumpectomy	Excellent	8	2	3	3

25	63152	25	F	52	Fibro Adenoma Excision	Excellent	9	3	3	3
26	59968	24	M	58	ORIF Fracture Monteggia	Excellent	9	3	3	3
27	62314	34	M	62	ORIF Fracture Olecranon	Excellent	9	3	3	3
28	86315	40	F	51	SSG Forearm	Good	7	2	2	3
29	72582	40	M	62	Superficial Parotidectomy	Excellent	8	2	3	3
30	65575	60	M	58	Hernia repair	Excellent	9	3	3	3
31	60718	55	F	49	Lymph node excision	Excellent	9	3	3	3
32	63216	38	M	68	ORIF # Clavicle	Excellent	9	3	3	3
33	70430	18	F	45	Fibro Adenoma Excision	Excellent	8	2	3	3
34	62064	48	M	56	ORIF # Clavicle	Excellent	8	3	2	3
35	68788	19	M	51	Rec. Shoulder Dislocation	Excellent	9	3	3	3
36	80640	32	M	52	ORIF Supra Condylar # Humerus	Excellent	9	3	3	3
37	54125	23	M	48	ORIF BB # Forearm	Excellent	9	3	3	3
38	55782	28	M	58	ORIF BB # Forearm	Excellent	9	3	3	3
39	58421	32	F	62	ORIF Supra Condylar # Humerus	Good	7	2	2	3
40	64041	31	F	68	Fibro Adenoma Excision	Excellent	9	3	3	3
41	63960	19	F	69	Hydatid cyst Excision	Excellent	9	3	3	3
42	65590	32	F	53	Fibro Adenoma Excision	Excellent	8	3	2	3
43	66061	57	F	62	Lymph Node Excision	Excellent	8	2	3	3
44	525740	46	F	63	Mastectomy	Excellent	9	3	3	3
45	73665	28	F	58	Phylloides Tumor Excision	Excellent	8	3	2	3
45	58581	45	M	63	ORIF # Lat. Condyle Humerus	Good	7	2	2	3
47	62314	33	M	50	ORIF # Shaft Humerus	Excellent	9	3	3	3
48	77408	26	M	49	ORIF BB # Forearm	Excellent	9	3	3	3
49	77485	18	M	60	Implant Exit	Excellent	9	3	3	3
50	60942	28	F	49	Fibro Adenoma Excision	Excellent	8	2	3	3

GROUP-II Rocuronium (1.0mg/kg)

S.No.	I.P.No.	Age Yrs	Sex	Body Wt Kg	Surgery	Intubating Conditions	Cooper Scoring System (0, 1, 2, 3)			
							Score	Jaw Relaxation	Vocal Cords	Response to Intubation
1	44400	18	M	49	Modified radical mastoidectomy	Excellent	8	3	2	3
2	16353	30	F	52	Modified radical mastoidectomy	Good	7	2	2	3
3	21822	35	M	65	FESS	Good	7	3	2	2
4	22238	16	M	45	Modified radical mastoidectomy	Excellent	8	3	2	3
5	22353	24	M	68	Modified radical mastoidectomy	Excellent	8	2	3	3
6	56483	16	F	56	Modified radical mastoidectomy	Good	7	2	2	3
7	66524	40	F	60	Left Tympano Mastoid Exploration	Excellent	8	2	3	3
8	70196	35	M	70	Left Tympano Mastoid Exploration	Good	7	2	2	3
9	89125	27	M	52	Tonsillectomy	Excellent	9	3	3	3
10	70497	37	F	54	Right Myringoplasty	Excellent	8	3	2	3
11	11201	22	M	70	Tonsillectomy	Good	7	2	3	2
12	145058	43	F	56	Right Cortical Mastoidectomy	Excellent	9	3	3	3
13	20112	20	F	51	Tonsillectomy	Excellent	9	3	3	3
14	15079	49	F	54	Tympano mastoid exploration	Excellent	8	3	2	3
15	51193	18	M	52	Tonsillectomy	Excellent	8	3	2	3
16	28332	27	M	60	R Cortical Mastoidectomy	Excellent	9	3	3	3
17	28171	22	M	80	Left Myringoplasty	Good	7	2	2	3
18	67167	18	M	56	Tonsillectomy	Good	7	2	2	3
19	68169	42	F	58	Modified radical mastoidectomy	Good	6	2	2	2
20	14692	17	F	42	Bilateral Myringoplasty	Good	7	2	2	3
21	68070	36	M	65	Right Myringoplsty	Fair	5	1	2	2
22	606526	26	M	70	Modified radical mastoidectomy	Excellent	8	3	2	3
23	88328	46	F	80	Breast Lumpectomy	Excellent	8	2	3	3
24	68357	35	M	62	ORIF Humerus #	Good	7	3	2	2
25	87971	29	M	69	Submandibular Gland Excision	Good	7	3	2	2

26	63145	30	M	49	Neuro Fibroma Exicision	Faier	5	2	1	2
27	61952	35	F	71	ORIF BB/ Forearm	Excellent	8	3	2	3
28	73426	46	M	68	ORIF # Clavicle	Excellent	8	3	3	2
29	89256	47	F	80	Granulomatous Mastitis Excision	Good	7	2	3	2
30	24718	18	F	52	Preauricular sinus excision	Good	7	2	2	3
31	83049	40	F	58	Fibro Adenoma Excision	Good	7	23	2	2
32	79828	60	M	69	ORIF Clavicle #	Good	7	2	2	3
33	76554	45	F	62	ORIF ULNA #	Excellent	8	3	2	3
34	75009	19	F	60	Pre Auricular Sinus Excision	Excellent	8	3	3	2
35	14692	18	F	66	Fibro Adenoma Excision	Excellent	9	3	3	3
36	72897	20	M	58	ORIF # Humerus	Excellent	8	3	2	3
37	56159	45	M	69	ORIF Clavicle #	Fair	5	2	1	2
38	22253	24	M	75	ORIF Galeazzi #	Excellent	8	2	3	3
39	50887	60	M	72	ORIF # Humerus	Excellent	9	3	3	3
40	42333	38	F	66	ORIF # SOF	Good	7	2	3	2
41	53774	32	M	68	Elbow Dislocation Repair	Excellent	9	3	3	3
42	48817	35	M	70	ORIF # Acetabulum	Good	7	2	2	3
43	52811	29	M	62	Lymph Node Excision	Excellent	8	2	3	3
44	53877	18	M	56	ORIF # Femur	Good	7	3	2	2
45	56812	37	M	62	ORIF # Humerus	Good	7	2	2	3
46	52787	52	F	68	Mastectomy	Excellent	9	3	3	3
47	67116	53	F	70	Mastectomy	Excellent	8	3	2	3
48	53817	32	F	59	Axillary Lipoma Excision	Good	7	3	2	2
49	39487	50	M	62	ORIF # Humerus	Good	7	2	3	3
50	49786	50	F	51	Mastectomy	Excellent	8	3	2	3