A COMPARATIVE EVALUATION OF ROCURONIUM AND SUXAMETHONIUM FOLLOWING RAPID SEQUENCE INTUBATION IN EMERGENCY SURGERIES

Dissertation

Submitted in partial fulfillment of university regulations for the award of

M.D. DEGREE EXAMINATION

BRANCH X – ANAESTHESIOLOGY

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

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SEPTEMBER 2006

CERTIFICATE

This is to certify that the Dissertation "A COMPARATIVE EVALUATION OF ROCURONIUM AND SUXAMETHONIUM FOR RAPID SEQUENCE INTUBATION IN EMERGENCY SURGERIES" presented herein by Dr. G. VIJAY ANAND is an original work done in the Department of Anaesthesiology, Madras Medical College and Government General Hospital, Chennai for the award of Degree of M.D. (Branch X) Anesthesiology under my guidance and supervision during the academic period of 2003-2006.

Prof. Dr. Kalavathy Ponniraivan, MD.,
DEAN
Madras Medical College & Hospital,
Chennai – 600003.

CERTIFICATE

This is to certify that the Dissertation "**A COMPARATIVE EVALUATION OF ROCURONIUM AND SUXAMETHONIUM FOR RAPID SEQUENCE INTUBATION IN EMERGENCY SURGERIES**" presented herein by **Dr. G. VIJAY ANAND** is an original work done in the Department of Anaesthesiology, Madras Medical College and Government General Hospital, Chennai for the award of Degree of M.D. (Branch X) Anesthesiology under my guidance and supervision during the academic period of 2003-2006.

Prof. Dr. G. Sivarajan, MD., DA.,
Professor & HOD,
Dept. of Anesthesiology,
Madras Medical College & Hospital,
Chennai – 600003.

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CONTENTS

INTRODUCTION

Endotracheal intubation is an integral part of administration of anaesthesia during surgical procedures. Suxamethonium, a depolarizing muscle relaxant with its rapid onset and short duration of action is still the relaxant of choice to facilitate tracheal intubation. In addition to fasciculations, Suxamethonium has got many side effects such as bradycardia and other dysrhythmias, rise in serum potassium, post operative myalgia, rise in intraocular, intragastric and intracranial pressure, prolonged recovery in patients with pseudo-cholinesterase deficiency and triggering of malignant hyperthermia. Because most of the side effects of Suxamethonium reflect its depolarizing mechanism of action, search for ideal neuromuscular blocking agent focused on non-depolarizing type of relaxants which has rapid onset time and offers good to excellent intubating conditions, as rapidly as Suxamethonium and which lacks the above mentioned adverse effects.

- Pancuronium (0.15 – 0.2 mg/kg) will provide intubating conditions in 90 seconds. Tachycardia and prolonged muscle relaxation become a problem.
- Vecuronium (0.2 mg/kg) provides adequate intubating conditions only after 90 seconds.
- Atracurium (0.5 mg/kg) will allow safe intubation in 3 minutes. A larger bolus (1.5 mg/kg) will allow intubation in 60 – 90 seconds, but may cause hypotension, tachycardia, and histamine release.
- Cis-atracurium (0.1 – 0.15 mg/kg) is not recommended for rapid sequence endotracheal intubation. A dose of 0.4 mg/kg (8 x ED 95) will allow intubation in 90 seconds without histamine release, but the duration of action may exceed 60 minutes.
- Rapacuronium (1.5 mg/kg) has a more rapid onset of action than Rocuronium or Mivacurium with good to excellent tracheal intubating conditions within 1 minute in 85% of

the adult patients, and duration of action of approximately 10 – 20 minutes. Its clinical efficacy rivals that of Succinylcholine, but with slightly slower onset and longer duration. It would clearly be the best choice of non-depolarizing muscle relaxant for rapid sequence intubation because of its rapid onset of action, minimal cardiovascular side effects even at large doses, and short duration of action. However, it is no longer available, having been withdrawn by the manufacturer in March 2001.

- An alternative is to pre-treat the patient with a small dose of the non-depolarizing muscle relaxant several minutes before induction, which may shorten the onset of action and lessen the dose required of subsequently administered relaxant. This has been referred to as a 'priming' dose. Its use is controversial in that it may lead to diplopia, muscle weakness, respiratory distress, and aspiration while offering no definite advantage over the use of larger initial doses of non-depolarizing muscle relaxants.
- Rocuronium (0.6 – 1.2 mg/kg), has a rapid onset and an intermediate course of action, providing excellent intubating conditions at 60 – 70 seconds. Several studies have shown that the onset of action of Rocuronium is significantly faster when compared to equipotent doses of other non-depolarizing agents discussed above. Hence, Rocuronium was chosen for rapid sequence intubation in the present study.

AIMS OF THE STUDY

1. To compare the intubating conditions of Rocuronium with Suxamethonium at 60 seconds, in emergency surgeries following rapid sequence intubation.

2. To compare the hemodynamic response to intubation

RAPID SEQUENCE INTUBATION

Securing and maintaining a patent airway reserves the highest priority when caring for critically ill or injured patients. When airway intervention is required it should be performed in an expedient and organized fashion by an experienced individual with the goal of providing a definitive airway safely, minimizing any possible complications. Rapid sequence intubation or RSI has just this goal in mind and to be performed successfully, takes experience, a thorough understanding of its indications, contraindications and limitations, and a working knowledge of the physiology and pharmacology of agents used.

Rapid sequence intubation (RSI) is defined as the rapid (nearly simultaneous) administration of both a neuro-muscular blocking agent and a potent sedative agent to facilitate intubation while decreasing the risks of aspiration, combativeness and potential damage to the patient. Rapid sequence intubation is developed to secure the airway of a critically ill or injured patient rapidly and safely. It applies to virtually all attempts for endotracheal intubation in the emergency departments except for arrest situations [42, 43, 44]. RSI is particularly preferred for emergency use because of the simultaneous onset of sedation, paralysis and minimizing the risk of aspiration [26]. After being launched in the late seventies, the procedure has been dynamically changing in time with introduction of many newer and advantageous agents. [5, 7, 35]

Rapid sequence intubation protocol is still in development in order to minimize the risk of aspiration of gastric contents in case of "*full stomach*" while preventing secondary brain injury via rendering unconsciousness and paralysis and to achieve higher rates of successful endotracheal intubation. Muscle relaxants are given as part of a rapid-sequence induction to facilitate tracheal intubation. Among all the muscle relaxants available, Succinylcholine is the only one with a rapid (approximately equal to 1 min) onset

and a fast recovery. Therefore it is still the most frequently used muscle relaxant for rapid-sequence induction despite its well-known side effects. The short duration of action of Succinylcholine is, however, no substitute for aggressive airway management in the case of an unexpectedly difficult intubation in order to prevent life-threatening hypoxia.

A preoperative assessment of the airway is mandatory in any patient and may indicate the need for using intubation techniques without a muscle relaxant. Laryngoscopy and intubation are performed after administering rapid and short-acting sedative, hypnotic and amnestic agents in conjunction with neuromuscular blocking agents [18]. Short-acting agents like Succinylcholine are generally preferred for fear of protracted intubation failure [32, 41]. For decades, Succinylcholine used to be the sole agent demonstrated to consistently provide paralysis in less than one minute. [3, 40, 51] It is still the sole depolarizing neuromuscular blocking agent used in the procedure. It is particularly useful in the critically ill or injured with a full stomach for which an RSI technique is needed [14]. Patients intubated in emergency conditions generally have full stomach and rapid intubation is critical to prevent aspiration of gastric contents. Succinylcholine provides a means for rapid intubation in these high-risk patients. Rocuronium is diverse from other non-depolarizing agents being the first one with a short onset time devoid of adverse effects. The object of this is study is comparing the use of Succinyl choline and Rocuronium in rapid sequence intubation protocol in adults.

The induction agent is immediately followed by administering the paralytic agent, and ventilation is not assisted once the patient is paralyzed. Pre-oxygenation is done prior to administering any agents and cricoid pressure is applied until airway establishment has been confirmed.

The sequence is as follows: 6 ‘P’s

1. **P**repare equipment (intubation kit, ambu bag, suction, RSI meds, combi-tube, cricothyrotomy kit, CO_2 detection devices.)
2. **P**reoxygenate patient with 100% oxygen for atleast 2 minutes. If trauma or spinal injury is suspected, 2nd care giver will hold manual stabilization.
3. **P**retreatment/ Premedication : LOAD

   Lignocaine – 1.5mg/kg

   Opioid – fentanyl 1-2 µ/ kg

   Atropine – 10-20 µ/ kg

   Defasciculation – 10% of paralyzing dose

4. **P**aralysis with induction. Administer Etomidate (0.2-0.6mg/kg){alternative midazolam (2-5mg)}. Administer Succinylcholine (1mg/kg).
5. **P**rotection of the airway. Apply cricoid pressure (Sellick’s maneuver) [46] by a 3rd caregiver.
6. **P**lacement with proof. Intubate the patient and verify tube placement.
7. Release cricoid pressure and secure tube placement. Reassess tube placement often especially when moving patient.
8. Document procedure, time, and results on the Anesthesia case record.

MODIFICATIONS OF RSI:

1. MODIFIED RSI
    - ✓ Gentle ventilation allowable
2. ACCELERATED RSI
    - ✓ Shortening preoxygenation-30secs-by 8 vital capacity breaths
    - ✓ shortening pretreatment - 2mts from 3mts
3. IMMEDIATE RSI
    - ✓ Eliminate pretreatment
    - ✓ Pre-oxygenate with 8 vital capacity breaths

a) Indications:

Any patient at risk of aspiration, which includes the following

- patients with full stomach (any emergent case or trauma patient)
- pregnant patients
- patients with known reflux, hiatal hernia, or delayed gastric emptying

b) Contraindications:

- Spontaneous breathing with adequate ventilation and oxygenation.

- Operator's concern that both intubation and mask ventilation may not be successful due to: major laryngeal trauma; upper airway obstruction; distorted facial or airway anatomy.
- Operator unfamiliarity with the medications used.

The true contraindication to rapid sequence intubation is any patient whom you may not be able to intubate or perform a cricothyroidotomy. Contrary to belief, the presence or suspicion of cervical spine injury is not a contraindication to rapid sequence intubation.

Disadvantages:

1. Prevents the hyoid bone from moving forward with the tongue during laryngoscopy.
2. It may cause lingual nerve damage by stretching the nerve as it crosses the hyoglossus, and lead to hyper aesthesia of the tongue.
3. Misplaced pressure can drive the thyroid up under the wings of the hyoid cartilage, reducing the visualization available for insertion of the tracheal tube.

ANATOMY AND PHYSIOLOGY OF

NEURO MUSCULAR JUNCTION

HISTORY:

1555 - Tracheal insufflation in animals was described by Andreas Vesalius of Padua.

1878 – William MacEwen of Glasgow passed a tube from mouth into the trachea, using his fingers as a guide in the conscious patient.

1901 – Franz Kuhn of Kassel extended the technique by using a flexible metal tube introduced on a curved guide through the mouth, palpating the epiglottis with the fingers of his left hand.

1907 – Barthelemy and Dufour of Nancy, blew chloroform vapour and air from a Vernon Harcourt inhaler and a rubber guided into the trachea by touch – the first use of insufflation endotracheal anesthesia.

1928 – Magill published his results of blind nasal intubation with a wide-bore rubber tube. The first blind nasal intubation was performed by Stanley Rowbotham.

Before the days of muscle relaxants, blind nasal intubation was popular. The use of muscle relaxants to facilitate intubation was pioneered by Bourne.

1850 - Claude Bernard showed that curare acts by paralyzing the myoneural junction. This led to his discovery of the concept of motor end-plate.

1934 – Sir Henry Dale described the physiological actions of acetyl choline and its association with neuromuscular transmission.

1942 – Harold R. Griffith and Enid Johnson used curare to give relaxation during surgery on 23rd January in Montreal, Canada, a famous day in the history of anesthesia.

1949 – Daniel Bovet et al introduced Suxamethonium.

1951 – Suxamethonium was first used in anesthesia by Otto Von Dardel in Stockholm and Otto Meyerhofer in Vienna.

1956 – W.D.M. Paton made the distinction between the depolarizing and non-depolarizing relaxants.

ANATOMY & PHYSIOLOGY:

Neuromuscular Junction (NMJ) is a synapse at which an electrical impulse traveling down a nerve is converted into muscle action potential and contraction by chemical transmitters. A motor neuron, along with all the muscle fibres supplied by it forms a motor unit, which follows all or none law of contraction.

PARTS OF NEUROMUSCULAR JUNCTION:

To understand the physiological events occurring during neuromuscular transmission it is essential to understand the anatomy of NMJ, which can be divided into,

1) Presynaptic nerve terminal
2) Synaptic cleft

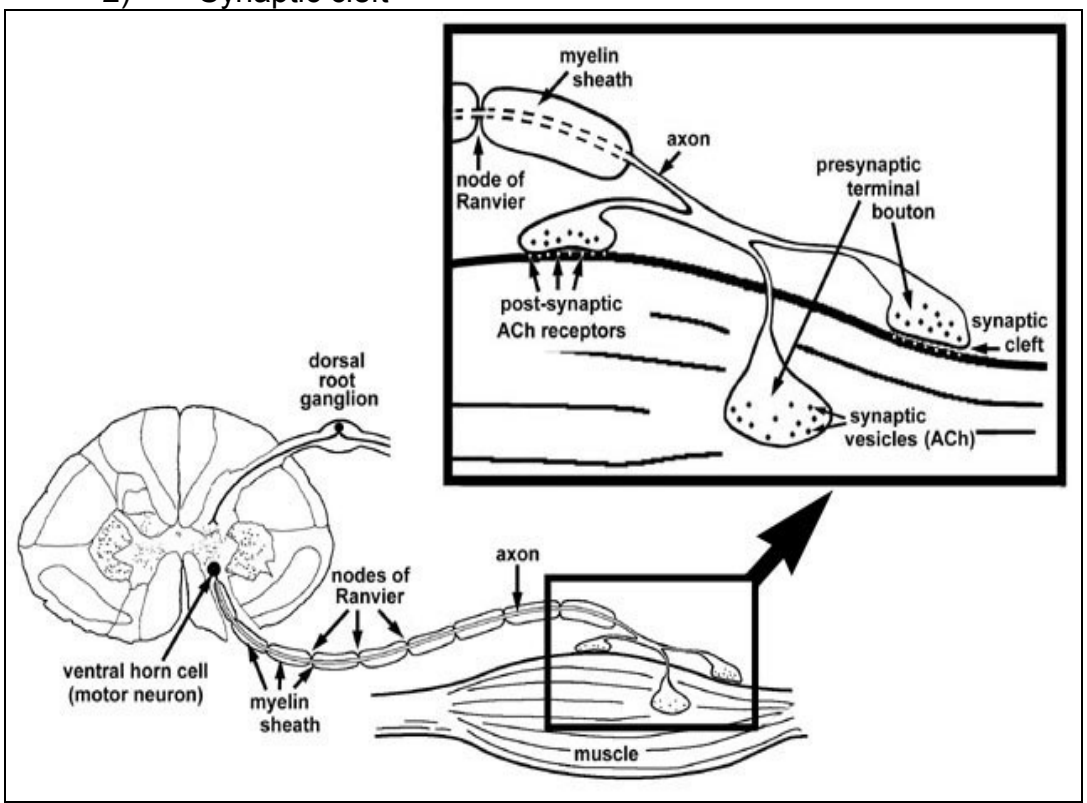
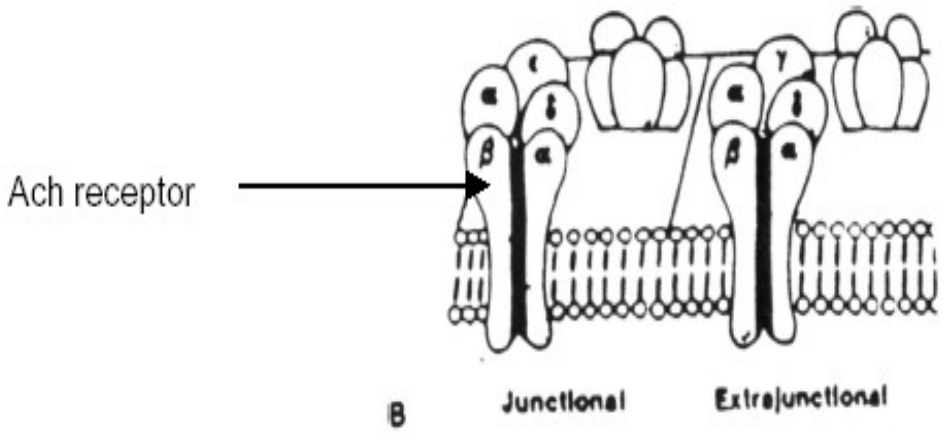


Fig. 2



PRESYNAPTIC NERVE TERMINAL:

Presynaptic nerve terminal contains all the apparatus necessary for the synthesis of acetylcholine, which exists in two forms:

1. 20% in the soluble (storage) form in the presynaptic axoplasm and
2. 80% in vesicles (releasable), which can be further, divided into a readily available pool and

a reserve pool.

The vesicles are 40-50nm in diameter each containing 1000-10000 molecules of Ach. The walls of the vesicles contain synapsins that help in anchoring the vesicle to the cytoskeletal framework of the axoplasm.

At the membrane facing the synaptic cleft, there is an electron dense patch, the active zone, around which the readily available pools of Ach vesicles are arranged. Electron microscopy shows small pores between the vesicles at the active zone. These are the calcium channels. The terminal also contains sodium and potassium channels.

The nerve endings on fast muscles are longer and more complicated than those on slow muscles. The reason for this is unclear. These differences in the nerve endings on the muscle surfaces may play a role in the differences in the response to muscle relaxants of fast and slow muscles.

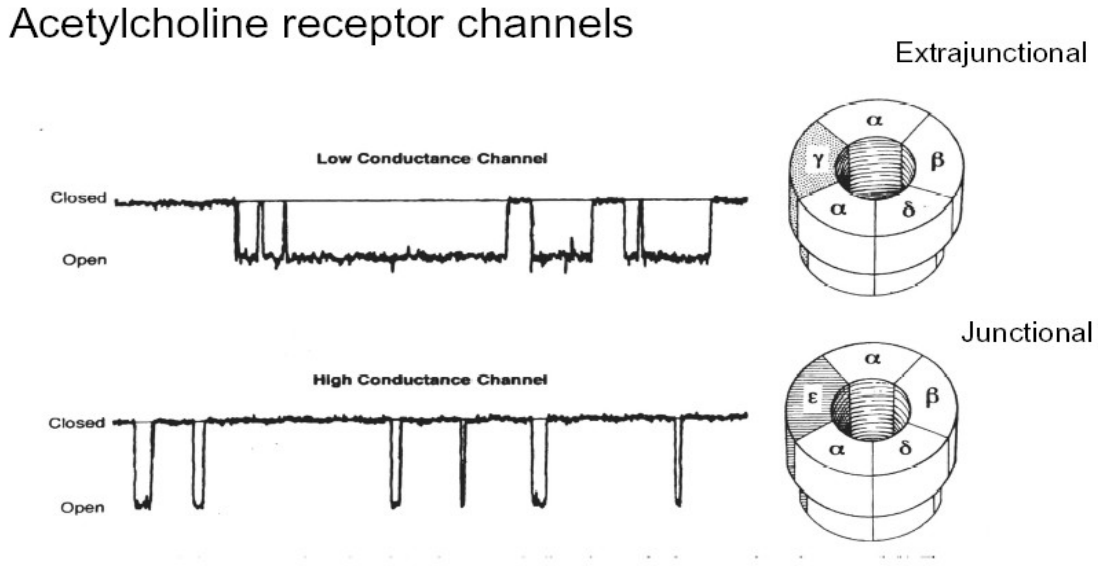
SYNAPTIC CLEFT:

It is 20nm wide space between the nerve terminal and the muscle end plate. The nerve and muscles are held in tight alignment by protein filaments, which span the cleft between nerve and end plate. The muscle surface is heavily corrugated with deep invaginations of the junctional cleft, the primary clefts and the secondary clefts, between the folds in muscle membrane. The shoulders of the folds are densely populated with acetylcholine receptors about 5 million of them in each junction. These receptors are spares in the depths between the folds. Instead these deep areas contain sodium channels. These sodium channels have two component gates, voltage and time dependent gates.

POST SYNAPTIC MEMBRANE – ACETYL CHOLINE RECEPTORS:

The Ach receptors at the NMJ are nicotinic and can be divided into pre synaptic and postsynaptic. The latter are further divided into junctional and extrajunctional.

The Ach receptor is a pentameric transmembrane spanning protein (class IV). The 5 protein subunits are arranged in the form of a rosette with a central ion channel. The molecular weight of the receptor is 250000-270000. The mature junctional receptor contains 2 α and 1 β, δ, ε sub-units. The immature extra junctional receptor contains 2 α and 1 β, δ, γ sub-units, which proliferate in abnormal conditions. The extra cellular surface of the alpha subunits contains high affinity Ach binding sites. Margin of safety: where in up to 70-80% of the receptors can be occupied before surgical relaxation develops.



CONTRACTILE APPARATUS*:*

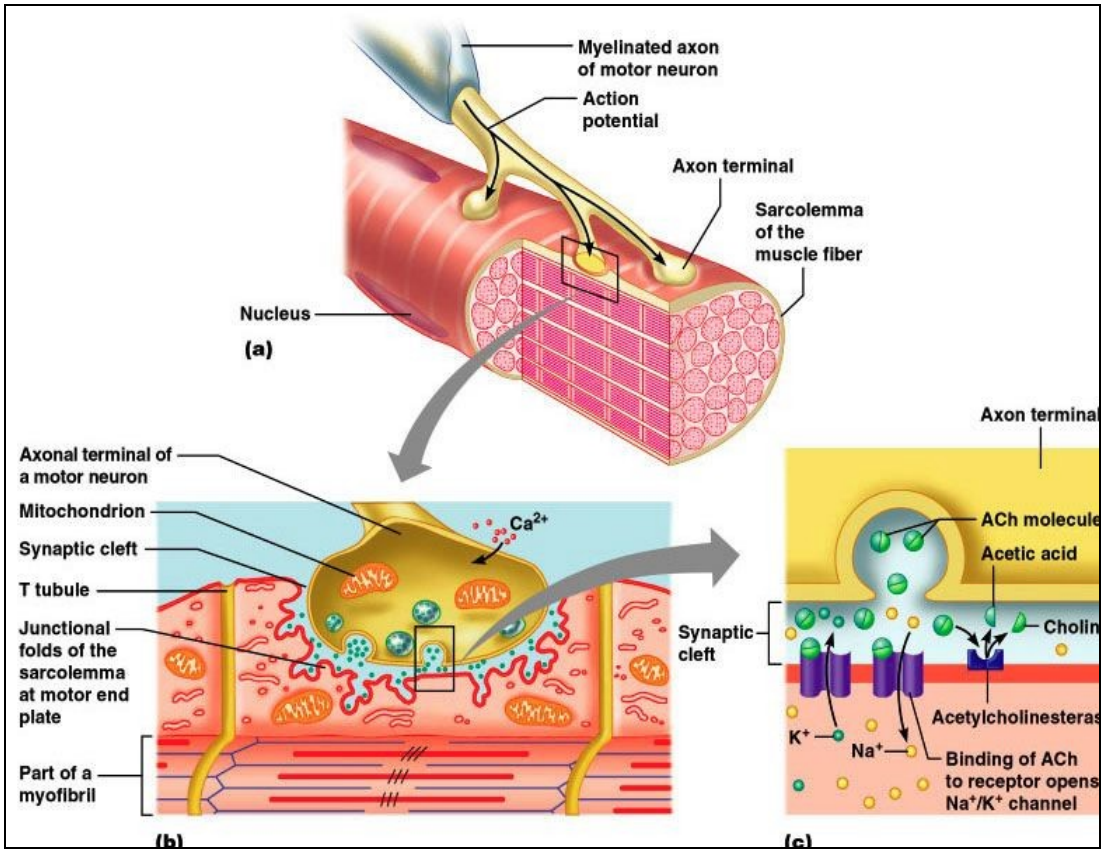
The contractile apparatus of the muscle is formed by the myofilament comprising the thin actin filaments and thick myosin filaments, along with tropomyosin, troponin I, T and C. Tropomyosin is attached to the myosin binding site of actin.

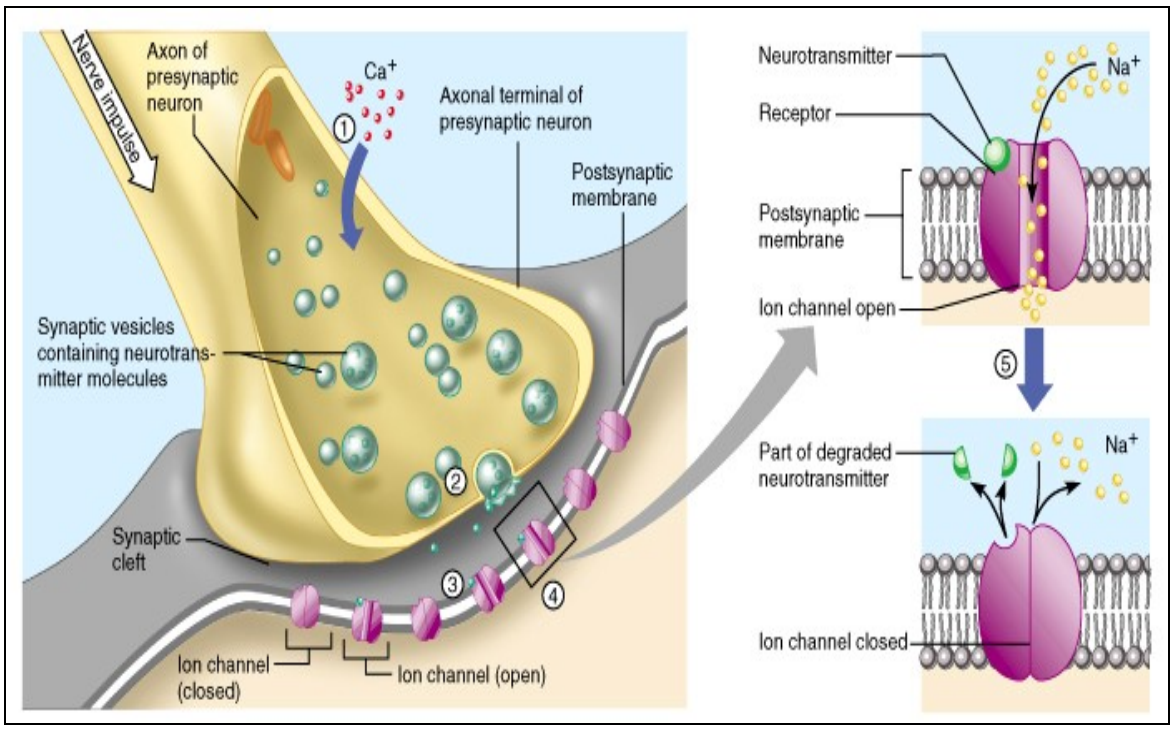
The myofilaments combine to form myofibrils. The muscle plasma membrane, the sarcolemma invaginates to form T-tubules which lie in close association with sarcoplasmic reticulum which is a collection of sacs and tubules acting as a reservoir for calcium.

MECHANISM OF ACETYL CHOLINE RELEASE:

An action potential traveling down the nerve causes the sodium channels in the presynaptic nerve terminal to open, leading to sodium influx. The change in voltage produced by such an influx activates the calcium channels, which open up leading to calcium entry. Calcium mediated activation of calcium-calmodulin dependent protein kinases lead to phosphorylation of synapsins in the vesicle wall, causing the vesicles to break away from the cytoskeletal framework. The vesicles then attach to the active zones with release of Ach molecules. Each nerve impulse causes the release of around 100-400 quanta of Ach. Activation of around 20-25% receptors is essential for impulse transmission.

MECHANISM OF NEUROMUSCULAR TRANSMISSION





BINDING OF ACETYL CHOLINE TO RECEPTOR:

The Ach molecule released into the synaptic cleft binds to the alpha subunit. Binding of Ach to both the alpha subunits activates the receptor, leading to configurational changes in the receptor structure and opening up of ion channels. This leads to depolarization of the muscle end plate which when of a sufficient magnitude causes a wave of depolarization to spread across the muscle sarcolemma by means of activation of the voltage dependent gates of the sodium channels in the peri junctional zones. This depolarization wave moving down the T tubule causes release of calcium from sarcoplasmic reticulum. Calcium so released binds to troponin C causing tropomyosin to move and expose the myosin binding sites of actin leading to the formation of cross linkage of actin and myosin heads. They slide over each other leading to shortening of the myofilaments and muscle contraction.

DISSOCIATION OF ACETYL CHOLINE FROM RECEPTOR:

The Ach molecule remains attached to its receptor for a very short period of less than 1 millisecond, after which it dissociates from the receptor and is hydrolyzed by the enzyme acetyl cholinesterase. It hydrolyses Ach into acetate and choline, the choline being taken up by the presynaptic nerve terminal and used for further Ach synthesis.

MECHANISM OF NON-DEPOLARIZING BLOCKADE:

Non-depolarizing muscle relaxants are drugs having an affinity for the alpha subunits of the acetylcholine receptors mainly at the post-junctional nicotinic receptors and also at the pre-junctional sites of nerve ending. Binding of these relaxants to the α subunits of Ach receptors can not open the ion channel and it also prevents further binding of Ach molecule. So an action potential is not developed and there is no contraction of muscle fiber. This competitive blockade of Ach receptor is termed as non-depolarizing blockade. Atleast 75% of receptors must be occupied before neuromuscular transmission is impaired and if more than 90% of the receptors are occupied, transmission fails.

CHARACTERISTIC FEATURES*:*

1) Slow onset to maximal effect and slow recovery compared to Succinylcholine.
2) The central muscles like the diaphragm, larynx, masseter, orbicularis oculi tend to be affected earlier and recover from the block sooner than those of the peripheral muscles (adductor pollicis) probably as a result of preferential perfusion.
3) Presence of fade and post tetatnic potentiation.
4) Despite flaccid paralysis, the muscles are still able to respond to direct stimulation.
5) Anticholinesterase drugs reverse the muscle block pharmacologically.
6) Low potency drugs like rocuronium and Rapacuronium have rapid onset of action while potent relaxants like Doxacurium and pancuronium have relatively slower onset of

action and a longer duration of action.

MECHANISM OF DEPOLARIZING NEUROMUSCULAR BLOCKADE

Depolarizing agents like Suxamethonium, have a biphasic action causing an initial depolarization of the endplate due to their acetylcholine like actions, followed by relaxation.

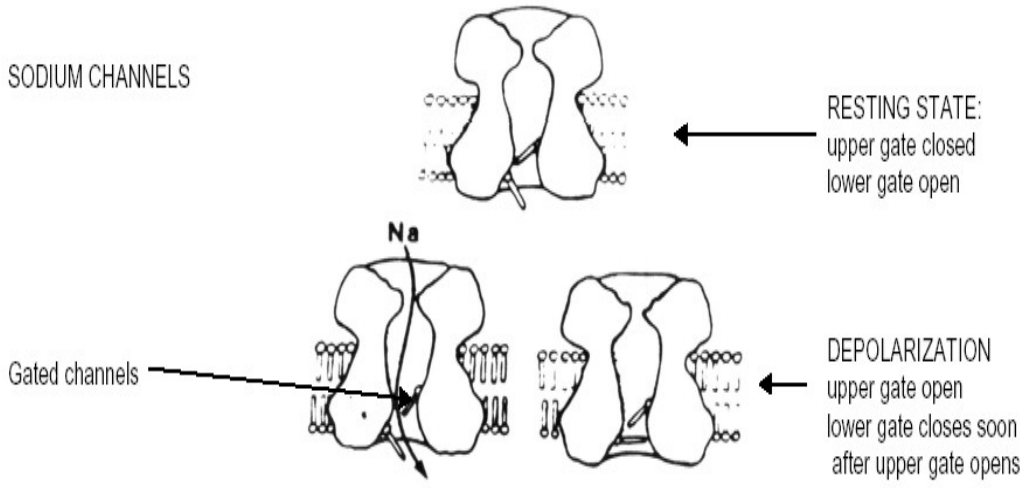
The sodium channel is a cylindrical transmembrane protein that has 3 functional conformational states, with 2 functional gates, an upper voltage dependent gate and a lower time dependent gate. Sodium ion passes only when both these gates are open.

I. At rest: Upper gate – closed
Lower gate - open

II. Depolarization: Upper gate – open
Lower gate - open

III. Shortly after : Upper gate – open
Lower gate - closes

IV. Repolarization: Upper gate – closed
Lower gate – open



Continuous end-plate depolarization causes muscle relaxation because opening of the lower gate in the peri-junctional sodium channels is time limited. After the initial excitation and opening, these sodium channels close and cannot re-open until end-plate repolarizes. The end-plate cannot repolarize as long as the depolarizing muscle relaxant continues to bind to Ach receptors, because the upper gate can close only when the receptor sites are not occupied. Consequently the lower gate can open only when the upper gate closes, being able to return to the resting or repolarized state. This is phase I block.

After a period of time, prolonged end-plate depolarization can cause ionic and conformational changes in the Ach receptor that result in a phase II block.

Thus, in a depolarizing blockade, the muscle membrane is divided into 3 zones

1. the end plate – which is depolarized by Succinylcholine
2. the peri junctional membrane – in which the sodium channels are frozen in an inactivated state
3. rest of the muscle membrane – in which the sodium channels are in the resting excitable state

This phenomenon is also called accommodation, where the synapse is unexcitable via the nerve but direct electrical stimulation of the muscle will cause muscle contraction. Accommodation does not occur in the extra-ocular muscles.

PHARMACOLOGY

ROCURONIUM (org 9426)

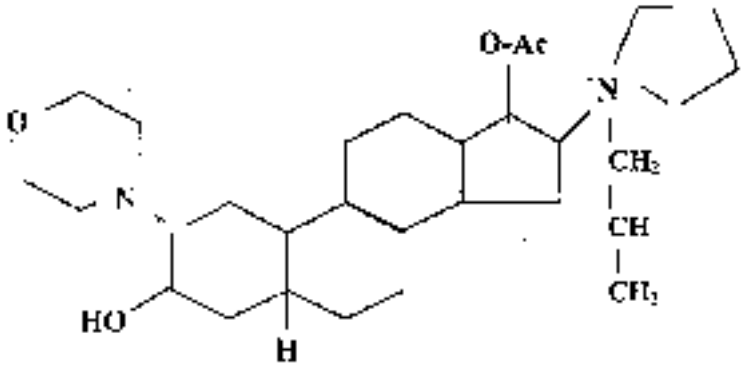
STRUCTURE:

Rocuronium is a monoquarternary aminosteroid, chemically, 2-morpholino, 3-desacetyl, 16-N-allyl pyrrolidino derivative of vecuronium, differing from it at 3 positions on steroid nucleus.

Introduced into clinical practice in 1994.

MOLECULAR STRUCTURE:

Fig. 5



PRESENTATION:

As a clear colorless solution containing 10 mg/ml of Rocuronium bromide. It is

available in 5ml & 10ml Vials.

ROUTES OF ADMINISTRATION:

Intravenous/ Intramuscular.

Doses (IV):-

ED95	:	0.3 mg / kg
Intubation at 60 – 90 sec	:	0.6 – 0.9 mg / kg
Relaxation (N2O / O2)	:	03 – 04 mg / kg
Relaxation (Vapor)	:	0.2 – 0.3 mg / kg
Maintenance	:	0.1 – 0.15 mg / kg
Infusion	:	8 – 12 µ / kg / min.

Doses (IM): into the deltoid

Infants	:	1mg/kg
Children	:	1.8 mg/kg

Rocuronium is not recommended for use in neonates.

Mechanism of action/Effect:

Rocuronium is a non-depolarizing neuromuscular blocking agent with a rapid onset of action, depending on dose, and with an intermediate duration of action. Rocuronium produces neuromuscular blockade by competing with acetylcholine for cholinergic receptors at the motor end plate. It is 7-8 times less potent than vecuronium. Thus a greater number of drug molecules are able to reach junctional receptors within a fewer circulation times, enabling faster development of neuromuscular blockade. Low potency leads to a weaker binding to receptors and prevents buffered diffusion, a process that occurs with potent drugs, which

causes repetitive binding and unbinding to receptors. Diffusion of less potent drugs away from the receptors very likely occurs much more readily, thereby helping to limit the duration of blocking effect. This is most likely reason why the duration of action of Rocuronium remains intermediate.

Onset of action:

ED_{90} – it is the dose required to produce 90% depression of the twitch response of the thumb to stimulation of the ulnar nerve.
With doses of 0.6 mg Rocuronium per kg of body weight administered over 5 seconds; effective intubating conditions are achieved within 60 to 90 seconds. Onset of action of Rocuronium may be delayed in patients with conditions, such as cardiovascular disease and advanced age, associated with slowed circulation. The onset of action is faster in infants and children than in adults.

When IM route is chosen in infants & children, tracheal intubation can be performed in 2.5 – 3 mins with a duration of 2 hours.

Time to peak effect:

The time to peak effect is dependent on dosage, the age of the patient, and the anesthetic administered concurrently. The median times to maximum block are given below.

Adults 18 to 64 years of age under opioid–nitrous oxide–oxygen anesthesia:

0.45 mg/kg: 3 (range, 1.3–8.2) minutes.

0.6 mg/kg: 1.8 (range, 0.6–13) minutes.

0.9 mg/kg: 1.4 (range, 0.8–6.2) minutes.

1.2 mg/kg: 1 (range, 0.6–4.7) minute

Duration of action:

The **CLINICAL DURATION** (*the duration until spontaneous recovery to 25% of control*

twitch height) of action with 0.6 mg/kg is 30 – 40 mins.

The **TOTAL DURATION** (*time until spontaneous recovery to 90% of control twitch height*) is 50 mins.

The mean time of spontaneous recovery of twitch response from 25 – 75% (**RECOVERY INDEX**) after a bolus dose of 0.6 mg/kg is 14 mins.

As the dose is increased, the recovery slows. The duration of action is also limited by avid liver uptake and elimination into the bile, due to an increase in the lipophilic nature of the molecule with respect to vecuronium.

Duration of clinical effect (*the time until spontaneous return of the twitch response to 25% of control value as determined using a peripheral nerve stimulator*) is dependent on dosage. Median time to spontaneous recovery from 25 to 75% of the control value is 13 minutes in adults.

During rapid sequence induction of anaesthesia under propofol or fentanyl/thiopental anaesthesia, adequate intubation conditions are achieved within 60 secs. In 93% and 96% of the patients respectively, following a dose of 1mg/kg rocuronium bromide. Of these 70% are rated excellent.

Following a dose of 0.6 mg/kg, adequate intubation conditions are achieved within 60 secs. in 81% and 75% of the patients during a rapid sequence induction technique with propofol or fentanyl/Thiopentone respectively.

The clinical duration is shorter in children than in adults.

With doses higher than 1 mg/kg, the intubating conditions will not improve appreciably. However the duration of action will be prolonged.

Adults 18 to 64 years of age—

0.45 mg/kg—22 (12–31) minutes.

0.6 mg/kg—31 (15–85) minutes.

0.9 mg/kg—58 (27–111) minutes

1.2 mg/kg—67 (38–160) minutes

Maintenance dose:

0.075-0.15 mg/kg given when the twitch height has recovered to 25% of control twitch height, or when 2 or 3 responses to TOF is present. No cumulation of effect with repetitive maintenance dosing at the recommended level has been observed.

Continuous infusion:

A loading dose of 0.6 mg/kg is administered, and the infusion is started at 0.3 – 0.6 mg/kg/hr, when the neuromuscular function starts to recover. The infusion rate should be adjusted to maintain twitch response at 10% of control twitch height or to maintain 1 or 2 responses to TOF.

Distribution:

Rocuronium has a biphasic distribution. The rapid distribution half-life is 1 to 2 minutes and the slower distribution half-life is 14 to 18 minutes. Approximately 80% of the initial Rocuronium dose is redistributed. As administration of Rocuronium continues, tissue compartments fill. Within 4 to 8 hours, less Rocuronium is redistributed away from the site of action, and the dosage requirement to maintain neuromuscular blockade via continuous infusion falls to about 20% of the initial infusion rate.

Vd – 203 (193 – 214) ml/kg

Cl – 3.7 l (3.5 – 3.9) ml/kg/min; $t^{1/2}$ – 73 (66 – 80) mins.

Protein binding:

Low (30%)

Biotransformation:

Deacetylated in the liver to 17-desacetyl-rocuronium (ORG 9943) and 16-N-desallyl-rocuronium (ORG 20860), these are usually not detectable in plasma and therefore are not expected to contribute significantly to the pharmacodynamic effects of Rocuronium.

Elimination:

Rocuronium is primarily eliminated by the liver, with a small fraction (10%) eliminated by the kidneys. It is taken up into the liver by a carrier mediated active transport system. Rocuronium is excreted in urine and bile. Excretion in urine approaches 40% within 12 – 24 hrs.

Hepatic disease:

In hepatic disease (most commonly cirrhosis), the volume of distribution of Rocuronium is increased, and its clearance is decreased. The duration of action is prolonged and its onset may be prolonged. Consequently dosing in patients with hepatic disease should be conservative and guided by careful monitoring of neuromuscular function.

Adult and geriatric patients with normal hepatic function:

1.4 ± 0.04 hours during opioid–nitrous oxide–oxygen anesthesia and 2.4 ± 0.08 hours during Isoflurane anesthesia.

Adult and geriatric patients with hepatic function impairment:

4.3 ± 2.6 hours during Isoflurane anesthesia

Renal failure:

In patients with renal failure, the plasma clearance of rocuronium may be decreased, and its volume of distribution is increased. The duration of action of single and repeated dose is not significantly affected. In the elderly, the clearance is decreased and volume of distribution is increased, with consequent prolongation in duration of action.

Cardiovascular effects:

The cardiovascular effects of muscle relaxants may be produced by

1. muscarinic receptor block
2. ganglionic block
3. increased nor-adrenaline release
4. blockade of nor-adrenaline uptake
5. histamine liberation

Initial animal studies with Rocuronium suggested the occurrence of muscarinic receptor and ganglion blocking effects only with doses that are much higher than those required for neuromuscular block.[36]

Further studies in dogs confirmed that cardiovascular effects were minimal with doses of up to $3xED_{95}$, although the heart rate tended to increase with doses greater than $5xED_{95}$.[9]

Routine measurements of heart rate and arterial pressure during neuromuscular studies showed that rocuronium had minimal effects on these variables with doses of 2-3 ED_{95} [11, 51]

The autonomic margin of safety for vagal block (3.0-5.0) is about 10 times less than that of vecuronium. In equipotent doses ($2xED_{95}$), the administration of rocuronium was associated with a small increase in heart rate of 7% (not statistically significant). However, there was increase in cardiac index of about 11% (statistically significant). There was little change in mean arterial pressure.

Rocuronium causes increases in heart rate of over 30% of baseline in some patients. While the etiology of the tachycardia is believed to be multifactorial, pain on injection or vagal blockade may contribute to tachycardia. Rocuronium is more likely than vecuronium but less

likely than pancuronium to cause tachycardia.

Histamine liberation:

Rocuronium may cause histamine release. In a study of histamine release, 1 of 88 (1.1%) patients receiving rocuronium had clinically significant concentrations of histamine. In pre-marketing clinical trials, Rocuronium administration was accompanied by clinical signs of histamine release (e.g., flushing, rash, or bronchospasm) in 9 of 1137 (0.8%) patients. No clinical evidence of histamine release was observed in the 45 patients enrolled in one study designed to provoke histamine release by the rapid injection of Rocuronium. No significant histamine release with doses of Rocuronium up to $3xED_{95}$.

Cumulation:

Lack of cumulation has also been demonstrated by the absence of significant change in the dosage of Rocuronium required to maintain stable relaxation with infusions lasting for over 2h.

Reversibility and post –operative curarization:

When adequate spontaneous recovery (an average of $>T_1$ of 25%) has occurred, the neuromuscular block induced with Rocuronium can be easily antagonized by edrophonium or neostigmine.

Anaphylactic/anaphylactoid reactions:

No such anaphylactic/anaphylactoid responses have so far been reported following administration of Rocuronium.

IOP & ICP:

Rocuronium appears to be safe, in terms of minimal changes in IOP, for use in rapid sequence induction for anesthesia in perforated eye injuries, particularly if rocuronium is administered before the induction agent, as in the case of vecuronium. Neither vecuronium nor rocuronium have any significant effect on ICP.

Other actions/effects:

Rocuronium shows no significant interaction with commonly used antibiotics as given for prophylaxis immediately prior to surgery.

The duration of action of Rocuronium may be prolonged in patients with marked hepatic disease. The clearance of Rocuronium may be reduced in patients with renal failure. However there was no significant increase in the duration of action of Rocuronium in these patients nor was there any significant difference in the elimination half-life.

Side/Adverse Effects:

Pain on injection – especially when the patient has not completely lost consciousness and when particularly propofol is used as an inducing agent, in rapid sequence induction. hiccups, nausea, vomiting, hypertension, hypotension, arrhythmia, bronchospasm, pruritus, rhonchi, skin rash, swelling at injection site, tachycardia, wheezing.

Parenteral Dosage Forms:

For rapid sequence intubation—

Intravenous, 0.6–1.2 mg per kg of body weight.

This dose results in blockade sufficient for intubation in one (range, 0.4–6) minute, allows intubation to be completed within two minutes, and achieves maximum blockade within three minutes.

A lower dose of 0.45 mg per kg of body weight may be used with a small prolongation

of time to blockade sufficient for intubation (1.3 minutes) and of time to achievement of maximum blockade (within 4 minutes). With a dose of 0.45 mg per kg of body weight, intubation can still be accomplished in most patients within two minutes.

Doses of 0.9 and 1.2 mg per kg of body weight have been administered during surgery under opioid–nitrous oxide–oxygen anesthesia without adverse cardiovascular effects.
The use of a priming dose (i.e., administration of ten percent of the dose of Rocuronium, followed three minutes later by the remaining ninety percent of the intubating dose) significantly shortened the onset time in one study. However, the peripheral intravenous injection of priming doses into patients who are conscious can be expected to be associated with burning pain on injection. Patients may experience sensations of weakness and difficulty in breathing after receiving a priming dose.

Maintenance:

Intravenous—

Doses of 0.1, 0.15, and 0.2 mg per kg of body weight given when twitch response returns to twenty-five percent of the control value provide a median of twelve (range, 2–31), seventeen (range, 6–50), and twenty-four (range, 7–69) minutes, respectively, of clinical relaxation under opioid–nitrous oxide–oxygen anesthesia. Additional maintenance doses should be guided by recovery of neuromuscular function following the initial dose and should not be administered until recovery of neuromuscular function is evident.

Intravenous infusion —

0.01 to 0.012 mg per kg of body weight per minute after evidence of recovery from the intubating dose. Additional doses may be needed until steady state has been achieved. The rate of the maintenance infusion must be individualized for each patient and should be guided

by the patient's twitch response to peripheral stimulation. In clinical trials, satisfactory blockade was obtained with maintenance infusion rates of 0.004 to 0.016 mg per kg of body weight per minute.

SUCCINYL CHOLINE

History:

1906 – Reid hunt described its pharmacological actions

1949 – Bovet et al described its neuromuscular blocking actions

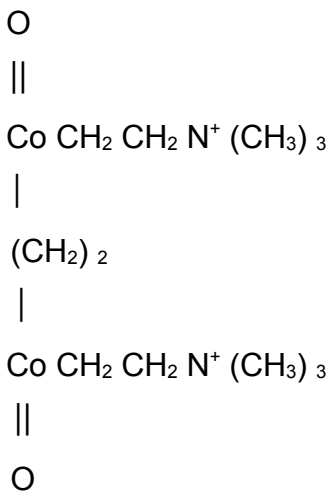
1951 – Thesleff first used the drug in man at Stockholm

The first report on the administration of SCh for performing ETI in multiple cases in the ED was published by Thompson et al in 1982.

Chemistry:

Succinyl choline is a synthetic muscle relaxant, a quaternary amine ester, consisting of two molecules of acetylcholine joined together through their acetyl groups.

Molecular Structure:



Presentation:

As a solution, it is available in 10ml vials containing 50mg/ml and in vials containing 100mg powder form.

Storage: 4^0C. Spontaneous hydrolysis occurs in warm/alkaline conditions.

Routes of administration:

Intravenous/ Intramuscular

Dose

ED_{95}	-	0.51 – 0.63 mg/kg
Intubation dose	-	Adults: 1-1.5 mg/kg IV bolus
		Children: 2-2.5 mg/kg
Onset of action	-	30 to 60 sec.
Duration of action	-	4 to 10 min.

Mechanism of action:

It is the only depolarizing muscle relaxant in use today. It has a rapid onset (30 – 60 secs) and short duration (<10 mins) of action. Rapidity is due to its low lipid solubility and the relative overdose that is usually administered. The drug binds to presynaptic, postsynaptic and extrajunctional receptors, where it exhibits an Ach like activity. Succinyl choline attaches to each of the alpha subunits of the nicotinic cholinergic receptor and mimics the action of Acetyl Choline thus depolarizing the post junctional membrane. Here, the hydrolysis is slow resulting in sustained depolarization (opening) of the receptor ion channels.

Neuromuscular blockade develops because a depolarized post junctional membrane

cannot respond to subsequent release of Acetyl Choline (Depolarizing Blockade). It is otherwise called as

Phase I Blockade**,** which is characterized by

- Absence of fade with TOF or tetanic stimulation.
- Absence of post titanic facilitation
- Increased blockade with anticholinesterase drug such as Neostigmine and Edrophonium

The presynaptic receptors are involved in the production of fasciculations.

Phase II Blockade : (non-depolarizing/dual)

- Single large dose of succinyl choline (> 2mg /kg IV)
- Repeated small doses of succinyl choline
- Prolonged continuous infusion

may result in post junctional membranes that do not respond normally to Acetyl choline even when the post junctional membranes have become repolarized. Mechanism for this blockade is unknown. Phase II block is a complex and ever-changing phenomenon. Desensitization is one of the many factors that contribute to the process. Phase II blockade has non-depolarizing characteristics such as

- fade with TOF or titanic stimulation
- post tetanic facilitation
- antagonism of blockade with anticholinesterase agents

The development has 4 phases

Phase A – depolarizing block which may last 30 – 50 mins.

Phase B – non-depolarizing block develops quite quickly

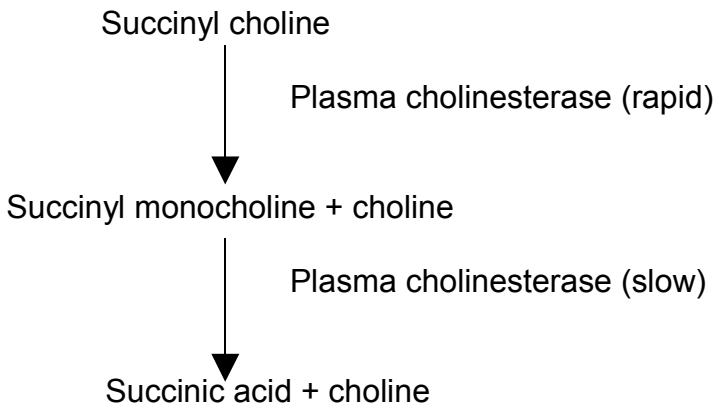
Phase C – a plateau 30 min. period of no change

Phase D – a wearing-off phase up to 2 hour long

Reversal of phase II blockade by cholinesterase inhibitors is best not attempted**.**

Metabolism:

Succinylcholine is rapidly hydrolyzed by plasma cholinesterase to choline and succinyl monocholine.



Dibucaine number and pseudocholinesterase activity*:*

Dibucaine, a local anaesthetic, inhibits the normal pseudocholinesterase activity by about 80% and the homozygous atypical enzyme by about 20%. The heterozygous enzyme is characterized by an intermediate 40 – 60% inhibition. The percentage of inhibition of cholinesterase by 10^{-5} molar solution of dibucaine is termed the dibucaine number. The percentage of inhibition of cholinesterase by 5×10^{-5} molar sodium fluoride is termed as Fluoride number. Dibucaine number indicates the genetic make up of an individual with respect to pseudocholinesterase. It does not measure the concentration of the enzyme in the plasma nor does it indicate the efficiency of the enzyme in hydrolyzing the substrate such as succinyl choline. The activity of the enzyme refers to the number of substrate molecules in mmols hydrolyzed per unit of time. Pseudocholinesterase activity is certainly markedly

influenced by the genotype, but is also dependent on the concentration of the enzyme in the plasma. Of the population 94% are normal E^u E^u genotypes (homozygous atypical) with normal enzyme activity and a dibucaine number of 75 – 85.

Three abnormal genes exist:

1. E^a (atypical) homozygotes comprise 0.03% of the population
2. E^f (fluoride resistant) homozygotes comprise 0.0003% of the population
3. E^s (silent) homozygotes comprise 0.001% of the population.

Normal serum cholinesterase level is about 80 u/ml

type of pseudo cholinesterase	genotype	frequency	dibucaine number	response to suxa
Homozygous typical	$E^u E^u$	Normal	70 – 80	Normal
Heterozygous	$E^u E^a$	1/ 480	50 – 60	Slightly prolonged
Homozygous atypical	$E^a E^a$	1/3200	20 – 30	Markedly prolonged

Abnormalities of Suxamethonium metabolism:

1. Abnormal plasma cholinesterase (inherited):

i. Atypical cholinesterase – Mendelian recessive E^a E^a homozygotes (1/3000 population) have 1 – 2 hours apnoea, during which phase 2 block develops (DN 16 – 25). Heterozygotes E^uE^a (1/25 population) have little or no disturbance (DN 50 – 65), with apnoea up to 10 mins.

ii. Fluoride resistant – homozygotes have 1 hour apnoea, with phase II block (DN 16 –

25). Heterozygotes have 10 min apnoea (DN 50 – 65).

iii. Silent gene

2. Plasma cholinesterase deficiency

Factors lowering pseudocholinesterase concentration are

i. liver disease

ii. pregnancy

iii. burns

iv. drugs – OCPs, MAO inhibitors, echothiophate, cytotoxic drugs, anticholinesterases, tetrahydroaminacrine, metoclopramide, hexafluorenium, banbuterol, Esmolol.

v. neoplastic disease

Adverse Effects:

1. ***Prolonged apnoea*** [39, 54]***:***

As discussed above, patients with abnormal pseudocholinesterase or deficient enzyme will experience markedly prolonged paralysis (range: 20 mins – 8 hrs.)

2. ***Cardiovascular effects*** [4, 6, 8, 17, 22, 25, 29, 37, 45, 49, 50].

Bradycardia: It is the most frequently encountered change in rate, especially in children due to high sympathetic tone. It is usually seen after the administration of relatively large single dose injections. The higher incidence of bradycardia after a second dose of succinyl choline suggests that the hydrolysis products of succinyl choline may sensitize the

heart to a subsequent dose.

Succinylcholine stimulates all cholinergic autonomic receptors – nicotinic receptors on both sympathetic and parasympathetic ganglia, and muscarinic receptors in the sinus node of the heart. In low doses, both negative inotropic and chronotropic responses may occur and in large doses, these effects may become positive. One prominent clinical manifestation of this generalized autonomic stimulation is the development of cardiac arrhythmias, such as nodal bradycardia and ventricular ectopics, ventricular fibrillation. Succinylcholine lowers the ventricular threshold to catecholamine induced arrhythmias. A high vagal background may predispose to asystole when a single dose of succinyl choline is administered.

3*. Fasciculations:*

Appear within a few seconds of succinyl choline administration and are most often evident in young muscular adults. They are uncommon in children and intensity is less in the elderly. Muscle fasciculations can increase serum potassium level by 0.5-1.0 meq/L and produce arrhythmias The mechanism is most likely a depolarization of nerve terminals through succinyl choline's action at the presynaptic receptors. This produces anti-dromic firing in the nerve, with the propagation of the action potential to all branches supplying a motor unit. The extension of fasciculations in the body is dependent on the arterial blood distribution. Muscles close to the aorta and receiving the drug first are early affected.

4. ***Muscle pains***:

There is an increased incidence of post-operative myalgia, 24 – 48 hrs after succinyl choline, more frequently following minor surgery, especially in women and in ambulatory. Pregnancy and extremes of age seem to be protected. Pain is secondary to damage

produced in muscle by the unsynchronized contractions of adjacent muscle fibres just before the onset of paralysis. The finding of myoglobinemia and increased serum Creatine kinase following Sch administration substantiates this. The efficacy of non-depolarizing pre-treatment is controversial.

5. **Hyperkalemia** [20, 51]

Potassium is released from muscles following suxamethonium injection, causing a rise of serum potassium of 0.2 – 0.4 mmols/L. A life threatening elevation of potassium is possible in patients with

a) Massive trauma, closed head injury
b) Muscular dystrophy, neuropathies, denervation, stroke
c) Third degree Burns
d) UMN/ LMN Lesions
e) Tetanus
f) Spinal cord injuries
g) Congenital cerebral palsy
h) Wasting secondary to chronic arterial insufficiency
i) Prolonged total body immobilization
j) Severe intra-abdominal injury

In denervation, the extra-junctional receptors allow succinyl choline to effect widespread depolarization and extensive potassium release.

6. Malignant Hyperpyrexia [24, 53]:

Suxamethonium is a potent triggering agent in patients susceptible to malignant hyperthermia, together with potent inhalation agents.

7. Masseter muscle spasm [21]:

Paradoxical contraction of jaw muscle following Succinyl choline may be a premonitory sign of malignant hyperpyrexia***.***

8. Increased Intra Gastric Pressure [19, 42]:

Increases to >20 mmHg due to severe muscle fasciculations. However, it causes a greater rise in lower esophageal sphincter tone, and hence it does not appear to increase the risk of aspiration unless the LES is incompetent, such as in pregnancy, hiatus hernia and obesity.

9. Increased Intra Ocular Pressure [38]:

Suxamethonium 1 mg/kg raises the pressure by 7mm Hg partly as a result of tonic contraction of the extra-ocular muscles. The increase in IOP is manifested within 1 minute after injection, peaks at 2-4 mins, and subsides by 6 mins. The phenomenon of accommodation does not occur in extra ocular muscles. The extra ocular muscles also contain a special type of receptor that do not become desensitized in the continued presence of acetyl choline or other agonists.

10. Increased intracranial pressure [33]:

A mean increase of 5 mm Hg over the baseline is observed. This may have serious consequences with intra-cranial compliance is limited.

REVIEW OF LITERATURE

1) **Ajeet Singh, Bhatia Pradeep Kumar, Tulsiani Kishan Lal** [2] (2004)

   In a prospective randomized double blind study, tracheal intubating conditions, using 0.6 mg/kg Rocuronium (Group A) and 1.5 mg/kg Suxamethonium (Group B) were compared in 40 patients. The time to achieve maximum blockade and the clinical duration of action were also compared by twitch stimulation using biometer accelograph. All patients were premedicated with inj. pentazocine, inj. diazepam and inj. atropine and induced with inj. thiopentone. Intubating conditions were assessed and graded at 60 seconds after injection of relaxant. While the onset time and duration of action were found to be more with rocuronium but the results showed no significant difference in the intubating conditions achieved in both the groups.

2) ***Andrews Jl., et al*** (1999) Compared Rocuronium and Succinylcholine for rapid sequence induction of anaesthesia along with propofol and anesthesia was induced using propofol 2.5mg/kg followed immediately by either rocuronium 0.6mg/kg or 1mg/kg or succinylcholine 1mg/kg. Intubating conditions were assessed at one minute and intubation was performed. They concluded rocuronium 1mg/kg given along with propofol in a rapid sequence induction of anaesthesia is clinically equivalent to Succinylcholine 1mg/kg.

3) In the study by ***Awarez-Gomez et al***, [3] (1994) the intubating conditions of standard doses of vecuronium and Rocuronium were compared at 60 secs or 90 secs. At 60 sec after administration of Rocuronium, excellent conditions were present in all patients.

4) ***K.Barclay., et al*** (1997) assessed whether low doses of Rocuronium improved conditions for tracheal intubation during induction of anaesthesia with Propofol 2.5mg/kg and alfentanil 10ug/kg. They have studied three groups. One group received saline, second

group Rocuronium 0.1 mg/kg and the third group received 0.3mg/kg Rocuronium and they assessed the intubating conditions as judged by jaw opening and laryngoscopy, position of the vocal cords and degree of straining after tracheal intubation. They concluded that injection of Rocuronium 0.3mg/kg with Propofol and alfentanil provided a high proportion of optimal intubating conditions.

5) ***Cooper et al*** [11] found the onset time for Rocuronium 0.6 $mgkg^{-1}$ as 90 sec by 0.1 Hz stimulation and 58 sec using TOF stimulation.

6) ***Cooper R, Mirakhur RK, Clarke*** [34] (1992) compared intubating conditions after administration of Rocuronium and Suxamethonium and concluded that Rocuronium 0.6mg/kg produces clinically acceptable intubating conditions at 60 seconds after induction with Thiopentone 5mg/kg.

7) ***J.D. Crul*** [12] ***& Colleagues*** (1995) observed clinically acceptable intubating conditions at 45 seconds with Rocuronium 0.6mg/kg

8) ***De Mey J.C., et al***[13] *(1994*) evaluated onset and intubating conditions of Rocuronium bromide 0.5, 0.75 or 0.9mg/kg in adult patients anaesthetized with Propofol 2mg/kg and alfentanil 0.5 to 1 μg/kg. They concluded that a dose of Rocuronium equal to or larger than 0.6 mg/kg provides acceptable intubations at 60 seconds after administration.

9) ***Dubois et al,*** [15] ***Huizinga et al***.(1995): In these studies no difference was observed in the frequency distribution of clinically acceptable intubating conditions at 60 secs and 90 secs after the administration of Suxamethonium or Rocuronium.

10) ***Kirkegaard – Nielsen H., et al***.(1999) [23] studied rapid tracheal intubation with Rocuronium using a probability based approach. 80 adult patients anaesthetized with Fentanyl 2μg/kg and Propofol 2mg/kg randomly received Rocuronium 0.0, 0.4, 0.8, or 1.2 mg/kg (n=20/dose). Laryngoscopy was initiated at 40 seconds aiming for intubation at 60 seconds. Doses giving 90 and 95% probability of successful intubation were calculated

and found to be 0.83 and 1.04mg/kg respectively. Estimated times until first tactile train of four response after ED_{50} and ED_{95} doses were 32 and 46 minutes respectively. They concluded that after induction with Fentanyl and Propofol, Rocuronium 1.04 mg/kg gives 95% probability of successful intubation at 60 seconds.

11) ***Lam AM., et al*** (2000) [27] compared the onset and offset time and intubating condition after 1min obtained with Rocuronium bromide 0.6mg/kg and Succinylcholine 1mg/kg after induction with Propofol and Fentanyl. They concluded that Rocuronium 0.6mg/kg, when used with Propofol and Fentanyl for induction provides intubating conditions similar to Succinylcholine 1mg/kg at 1 minute.

12) ***Land and Stovner*** [28] (1962) were probably the first to introduce a rating scale as a tool for the assessment of intubating conditions in which the three main criteria: ***Jaw relaxation, vocal cords*** (position and motility) and ***reaction to intubation*** were rated by descriptive scores such as excellent, satisfactory or fair but this allows a large room for subjective interpretation of data. These three main criteria [66] remained the basis of numerous subsequent modification of their rating scale by others. One of the most frequently used modifications, still in use today, was introduced by ***Krieg et al*** [26] in 1980 in which a numeric value is assigned to signify quality of intubating conditions. ***Cooper's modification*** of this rating scale was used in the present study.

13) ***Magorian et al*** [30] (1993) compared the duration of action of Rocuronium in doses of 0.6 mgkg-1, 0.9 mgkg-1 and 1.2. mgkg-1 with that of Suxamethonium in the dose of 1 mgkg-1. They were found to be 2220 sec, 3180 secs, 4380 sec and 540 secs respectively. In our study duration of action of Rocuronium 0.6 mgmkg-1 and Suxamethonium 1.5 mgmkg-1 are 1704 secs and 318 sec respectively.

14) ***Mazurek A J ; Hann S***. compared Rocuronium versus Succinylcholine for Rapid Sequence induction and concluded larger doses of Rocuronium may be an alternative to

Suxamethonium.

15) In a trial by ***Mc Court et al*** [32],(1998) tracheal intubating conditions during rapid induction of anaesthesia using 0.6 $mgkg^{-1}$ Rocuronium or 1 $mgkg^{-1}$ Suxamethonium, were studied and conditions were scored at 60 secs. Intubating conditions were found to be equally acceptable in both groups.

16) ***Mirakhur R.K. et al*** (1994) [34] compared onset and intubating conditions of Rocuronium bromide 0.6mg/kg and Suxamethonium 1mg/kg in adult patients anaesthetized with Thiopentone, N_2O in oxygen and small doses of Fentanyl. Intubating conditions after Rocuronium 0.6mg/kg were found to be clinically acceptable.(good or excellent)in 95% of patients at 60 seconds and in all patients at 90 seconds and in all patients at both times after Suxamethonium. There was no significant difference in acceptable intubating conditions between Suxamethonium and Rocuronium.

17) ***Peter M.C. Wright., et al*** (1994) [57] studied the onset and duration of Rocuronium and Succinylcholine at the adductor pollicis and laryngeal adductor muscles in anaesthetized adults. They found that the onset of effect with Succinylcholine was significantly more rapid at the laryngeal adductors (34+/-12 sec) than at the adductor pollicis (56+/-15 sec.) Onset times were similar at the two muscle groups with Rocuronium 0.8 and 1.2mg (96+/-29 and 74+/- 36 sec. with 0.8 mg/kg and 54+/-30 and 65+/- sec with 1.2mg/kg at the laryngeal adductors and the adductor pollicis, respectively.) Rocuronium 0.4mg/kg had a more rapid effect at the laryngeal adductors than the adductor pollicis (92+/-29 sec. and 155+/- sec. respectively). They concluded that the laryngeal adductors are more resistant to the action of Rocuronium than is the adductor pollicis. Onset of effect of Rocuronium in doses greater than 0.8mg/kg is similar to that of Succinylcholine at the adductor pollicis but is significantly delayed compared with that of Succinylcholine at the laryngeal adductors.

18) ***Previs TH, Zahn P., et al*** (1994) Studied the ED95 dose of Rocuronium bromide and the tracheal intubating conditions and time course of actions. They concluded the ED_{95} dose of Rocuronium bromide was 0.3mg/kg and duration of action was 20 minutes.

19) ***Puhringer et al*** [41] (1992) and ***Dubois et al*** [15] (1995) found the onset times as 72 sec and 48 sec and 130 secs and 74 secs respectively for Rocuronium 600 µ/kg and Suxamethonium 1mg/kg respectively.

20) ***Sparr*** [48] ***and Crul et al***,[12] (1996) investigated Rocuronium's potential in emergency intubating conditions using it strictly according to the scenario for rapid sequence induction in unpremedicated but still elective cases. In those studies, the frequency distribution of 'excellent', 'good' or clinically acceptable intubating conditions, 60 secs after 600 mcg/kg or 900 mcg/kg Rocuronium were compared with those observed after 1 mgkg-1 Suxamethonium. The results indicate that intubating conditions were more favorable at 60 sec after administration of Rocuronium in the dose of 900 mgmkg-1 compared to dose of 600 mgmkg-1 in unpremedicated patients. In premedicated patients, who received 600 mgmkg-1 Rocuronium after induction with I.V. anaesthetic, intubating conditions were comparable with those obtained with a dose of 900 mgmkg-1 Rocuronium.

21) ***Watanabe K, Chen K., et al*** (1991) described the pre and postsynaptic effects of org 9426 (Rocuronium) during the onset and recovery from neuromuscular blockade. They found that the relaxant to have moderate potency with rapid onset time, intermediate duration of action and rapid recovery.

22) ***Wierda et al*** [56] (1995) compared the onset time of Rocuronium 250 µg/kg and found it to be 220 sec and 190 secs respectively.

MATERIALS AND METHODS

Study design:

This study was a randomized prospective comparative study.

Study setting and population:

After obtaining institutional ethical committee clearance, the study was carried out on 40 patients in the emergency OT, Department of Anesthesiology, Madras Medical College, Chennai, from January to June 2005.

The patients were randomly selected from either sex, between 18 to 60 years of age, and weighing between 50-70 kgs. Emergency cases posted under G.A. and assessed between ASA status I – III, without significant disturbance in hemodynamic status or metabolic/electrolyte/ acid-base disturbance were chosen. These cases included

1. neurosurgical emergencies for craniotomy & evacuation such as
   extra-dural / sub-dural haematoma and depressed fracture of the skull.
2. blunt injury abdomen for laparotomy
3. hollow viscus perforation
4. acute appendicitis for appendicectomy
5. vascular/tendon injuries of the upper limb
6. compound fracture both bones of the fore-arm for external fixator application

INCLUSION CRITERIA:-

- Adults between 18 – 60 years
- ASA Physical status I , II & III
- Emergency surgeries posted under G.A.
- Closed head injuries with GCS > 13

EXCLUSION CRITERIA:-

- Children
- Pregnancy
- Obesity
- Known / suspected difficult Intubation
- H/o any neuromuscular disorder
- Renal / Hepatic disorder
- Head injuries with GCS < 13
- Hypovolemia/ Shock
- Severe metabolic/electrolyte/ acid-base disturbances
- Known allergy to drugs.
- Surgical procedures of very short duration.
- Patients receiving any medication known to interact with Neuromuscular blocking agent.

PRE OPERATIVE EVALUATION:-

In all the patients, Age, I.P.No, Body Weight, Baseline vital parameters were recorded. History regarding previous anaesthesia, surgery, any significant medical illness, medications and allergy were recorded. The fasting time was taken as the time interval between the last meal/drink and the time of trauma. Complete physical examination and Airway assessment was done.

Following laboratory investigations were done:

- Hemoglobin %
- Blood : sugar, urea, S. Creatinine
- S. Electrolytes : Na+, K+
- Chest X-Ray
- ECG in all leads

STUDY METHOD:

Informed consent was obtained from all the patients and they were divided into 2 groups, ***group I*** (n=20) patients receiving Rocuronium bromide (0.6 mg/kg) & ***group II*** (n=20) patients receiving Suxamethonium (1.5 mg/kg). To ascertain the ease of intubation, every patient was examined for Mallampati classification [31] (Young and Samson modification). Aspiration prophylaxis with inj. Metoclopramide 10 mg and inj.Ranitidine 50 mg I.V. was given to all the patients half to one hour prior induction. Patients were premedicated with inj. Glycopyrrolate (0.2 mg) and inj. Pentazocine 0.5 mg/kg, I.V. 5 min before induction.

In the operation theatre the vital parameters were recorded, venous access established, and infusion of crystalloid solution was started. Chest leads for continuous

cardiac and respiratory monitoring were attached, prior to induction and monitoring started. Oxygen saturation was measured by pulse oximeter using a finger probe.

The patients were pre-oxygenated with 100% O_2 for 3 minutes and induced with a fixed dose of inj. Thiopentone sodium 250 mg I.V. Cricoid pressure was given when Thiopentone was administered and released following successful tracheal intubation and inflation of the cuff. Where the patient had a Ryle's tube inserted prior to induction, Sellick's maneuver was carried with Ryle's tube in-situ..

In-***group I***, inj. Rocuronium bromide was given in a dose of 0.6 $mgkg^{-1}$ (2 x ED_{95}) and the patients in-***group II*** received Suxamethonium 1.5 $mgkg^{-1}$. 60 seconds after injection of muscle relaxant, the patients were

intubated orally; Simultaneously, intubating conditions were noted and scored according to a modification of the method described by

Mirakhur R.K., Cooper A.R. and Clarke R.S.J (Table 1 & 2)

TABLE –1

SCORING OF INTUBATING CONDITIONS

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

TABLE –2

GRADING OF INTUBATING CONDITIONS

Intubating Conditions	***Score***
Excellent	8-9
Good	6-7
Poor	3-5
Bad	0-2

After inflating the cuff of endotracheal tube, it was connected to circle absorber and controlled ventilation was instituted.

The following hemodynamic parameters

- Heart rate
- Mean arterial pressure

were recorded continually at

-3 mins. – pre induction values at the onset of pre-oxygenation

-60 s – administration of muscle relaxant

0 secs. – intubation

1 m, 3m & 5m – after intubation.

Patients were maintained with O_2 + N_2O, Vecuronium/Atracurium and at the end of surgery; muscle paralysis was reversed with inj. neostigmine and inj. Glycopyrrolate. At the end of study, the data collected were analyzed statistically.

OBSERVATION AND RESULTS

The study was conducted on 40 patients randomly allotted into 2 groups as given below:-

TABLE – 3

DRUG DOSAGE AND SCHEDULE

Group	***Drug and Dose***	***Sample Size***
I	Rocuronium 0.6 mg/kg	20
II	Suxamethonium 1.5 mg/kg	20

- ✓ No intubation difficulty was encountered during the study.
- ✓ No airway adjuncts were used
- ✓ None of the patients desaturated during the performance of RSI.
- ✓ The application of cricoid pressure did not worsen the view during laryngoscopy and intubation.
- ✓ Few patients had Ryle's tube inserted prior to induction, which was not removed subsequently, and Sellick's maneuver carried out with the Ryle's tube in-situ.
- ✓ All intubations were successful in both the groups during the first attempt.
- ✓ No significant adverse effect other than tachycardia & hypertension were noted.

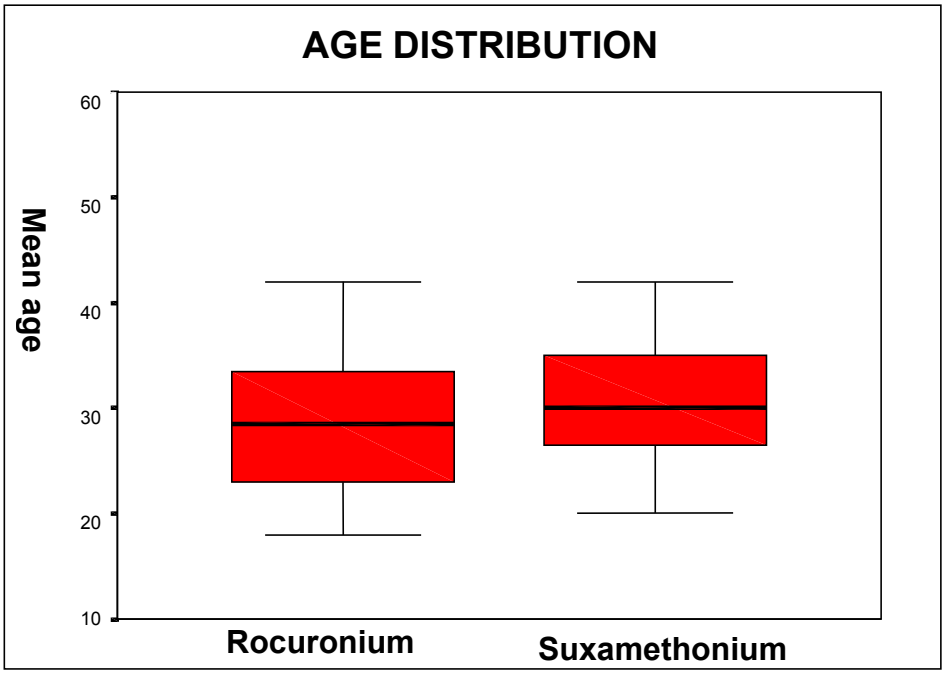
DEMOGRAPHIC PROFILE

I. AGE

TABLE –4

Group	n	Mean	Std. Deviation	Student's t-test
Rocuronium	20	29.60	8.982	t=0.63 **P=0.54**
Suxamethonium	20	31.25	7.656	

P > 0.05: Not significant



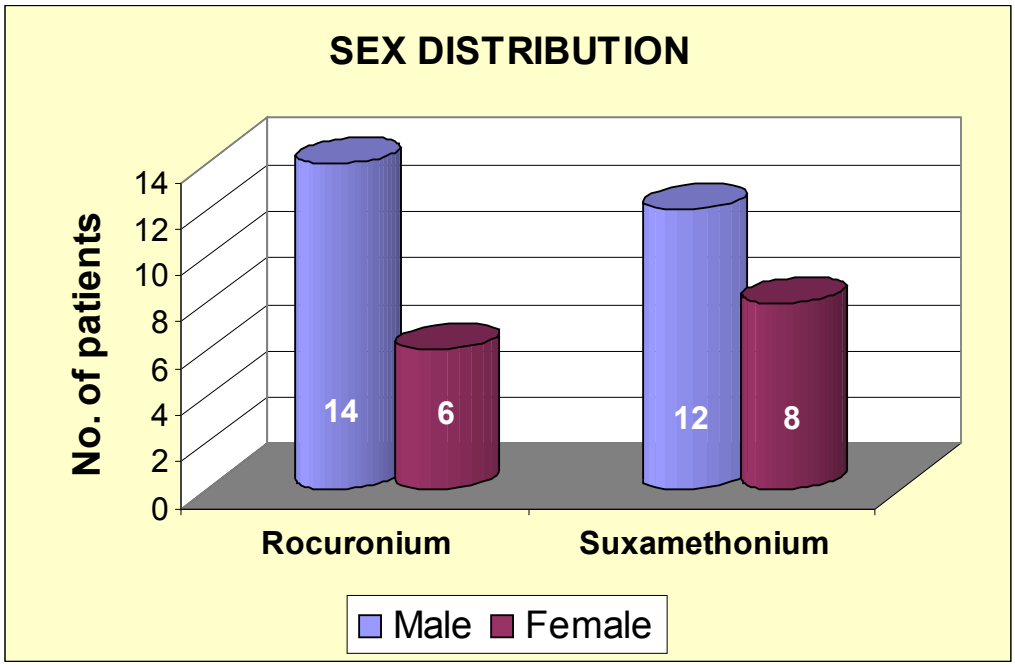
Statistical Analysis using Student's t-test showed no significant difference between the distributions of age among the study groups.

II. SEX DISTRIBUTION

TABLE – 5

		Group		Total
		Rocuronium	Suxamethonium	
Sex	Male	14	12	26
	Female	6	8	14
Total		20	20	40

$\chi 2=0.44$ P=0.51



Statistical Analysis using Chi-square test showed no significant difference between the distributions of sex among the study groups.

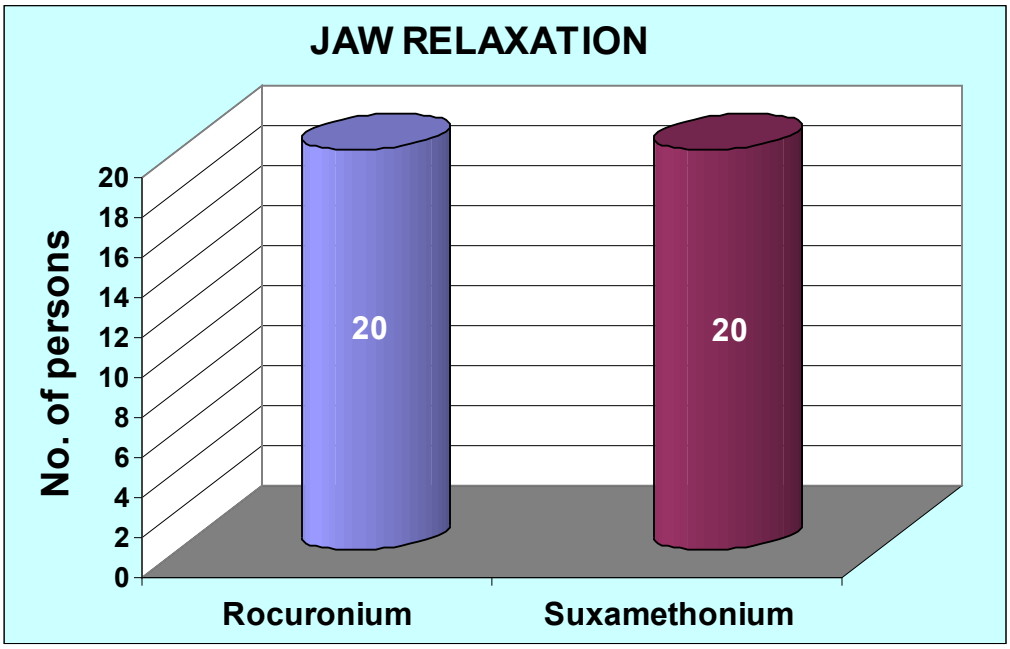
III. TRACHEAL INTUBATING CONDITIONS

The scores for Jaw Relaxation, vocal cord position and response to intubation and the total scores were compared between 2 groups.

TABLE - 6

JAW RELAXATION	group		Total
	Rocuronium	Suxamethonium	
Score 3	20	20	40
Total	20	20	40

χ2=0.00 P=1.00



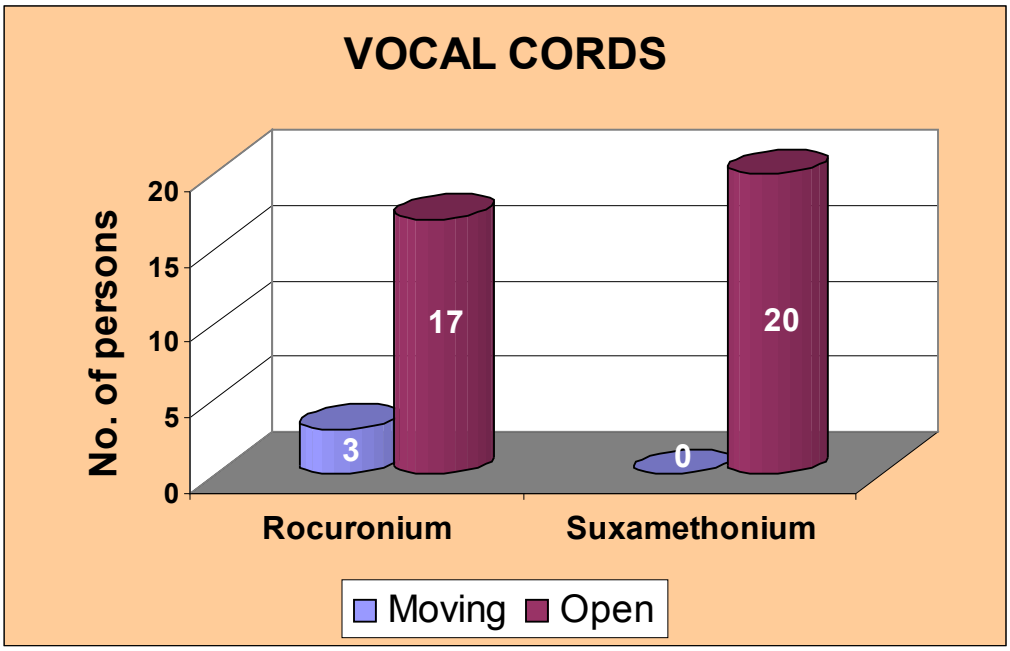
Statistical analysis by Chi-square test showed that there was no difference with respect to jaw

relaxation among the study groups. A mean score of 3, which corresponded to easy opening of the jaw, was observed in all the patients in both the study groups.

TABLE - 7

VOCAL CORDS		group		Total
		Rocuronium	Suxamethonium	
score	2	3	0	3
	3	17	20	37
Total		20	20	40

$\chi 2=3.24$ P=0.07



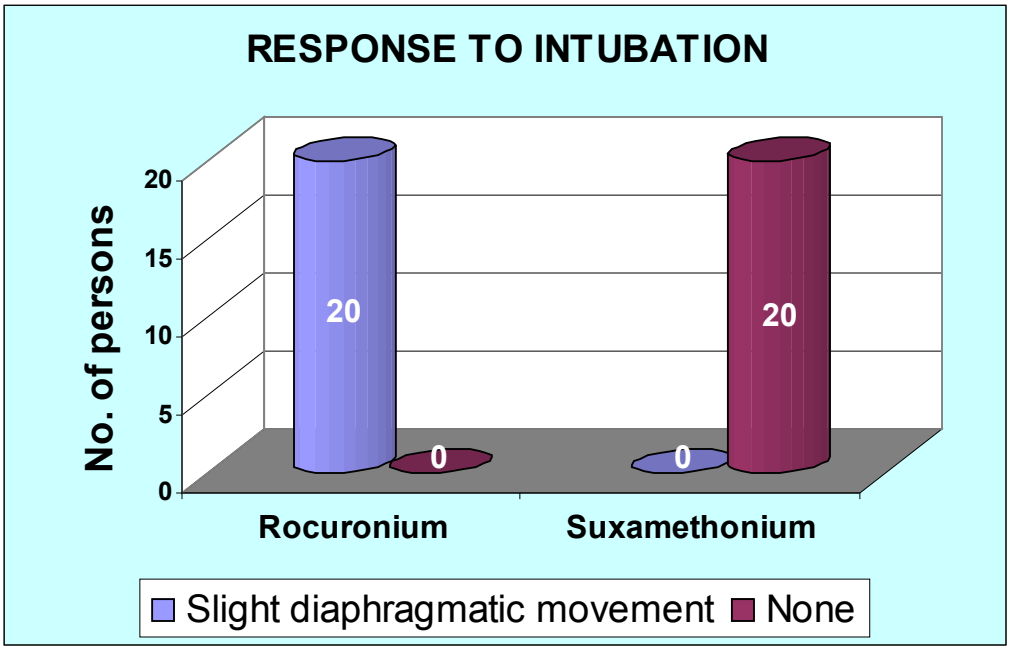
Statistical analysis by Chi-square test showed that the condition of the vocal cords during intubation with Suxamethonium was not significantly different from that of Rocuronium. A mean score of 2.85 was observed in the Rocuronium group. A mean of 3.0 was observed in

Suxamethonium group.

TABLE – 8

Response to intubation		group		Total
		Rocuronium	Suxamethonium	
score	2	20	0	20
	3	0	20	20
Total		20	20	40

$\chi 2=40$ P=0.001

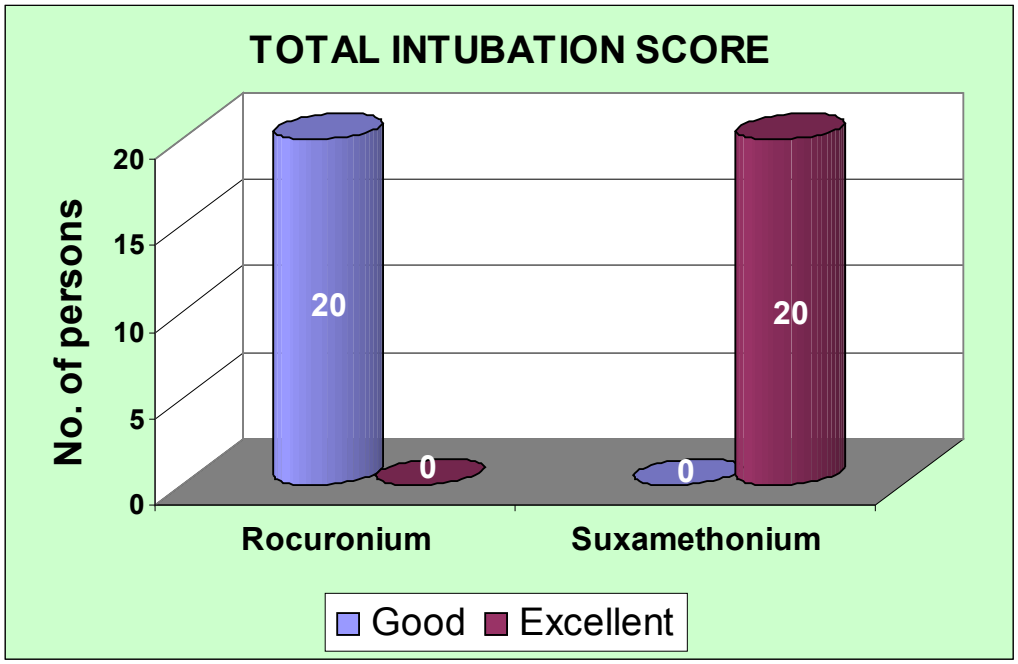


Statistical analysis by Chi-square test showed that the response to intubation was higher in the Rocuronium group and was statistically significant (P = 0.001), from that of the Suxamethonium group. Rocuronium showed a mean score of 2 ± 0.0 (slight diaphragmatic movement), and Suxamethonium showed a mean score of 3 ± 0.0 (no response).

TABLE – 9

Total score		group		Total
		Rocuronium	Suxamethonium	
score	7	3	0	3
	8	17	0	17
	9	0	20	20
Total		20	20	40

$\chi 2=40$ P=0.001



Statistical analysis by Chi-square test showed that the total intubation score with Suxamethonium was higher than Rocuronium and was statistically significant (P = 0.001). The overall intubating conditions were better with Suxamethonium with a mean total score of 9. The mean total score in Rocuronium group was 7.85.

IV. HAEMODYNAMIC PROFILE

MAP
TABLE – 10

MAP	Group	n	Mean	Std. Deviation	Student's t -test
Baseline	Rocuronium	20	96.20	14.285	t=0.76
	Suxamethonium	20	93.20	10.521	P=0.45
Induction	Rocuronium	20	85.25	13.459	t=0.09
	Suxamethonium	20	84.95	6.909	P=0.93
Intubation	Rocuronium	20	106.65	14.805	t=1.07
	Suxamethonium	20	102.65	7.693	P=0.29
1m	Rocuronium	20	105.55	14.099	t=1.13
	Suxamethonium	20	101.55	7.302	P=0.27
3m	Rocuronium	20	104.10	13.626	t=1.22
	Suxamethonium	20	99.90	7.144	P=0.23
5m	Rocuronium	20	101.90	13.006	t=1.54
	Suxamethonium	20	96.75	7.268	P=0.13
10m	Rocuronium	20	99.75	12.920	t=1.33
	Suxamethonium	20	95.10	8.717	P=0.19

TABLE – 11

MAP	Group			
	Rocuronium		Suxamethonium	
	Mean	SD	Mean	SD
Baseline	96.20	14.29	93.20	10.52
Induction	85.25	13.46	84.95	6.91
Intubation	106.65	14.80	102.65	7.69
1m	105.55	14.10	101.55	7.30
3m	104.10	13.63	99.90	7.14
5m	101.90	13.01	96.75	7.27
10m	99.75	12.92	95.10	8.72

TABLE – 12

MAP	F	Sig.
Within group	194.49	.001
Between group	1.09	.301

HEART RATE

TABLE – 13

Heart rate	group	n	Mean	Std. Deviation	Student t-test
Baseline	Rocuronium	20	87.70	12.127	t=1.56
	Suxamethonium	20	82.15	10.323	P=0.13
Induction	Rocuronium	20	97.10	10.983	t=1.39
	Suxamethonium	20	92.00	12.230	P=0.17
Intubation	Rocuronium	20	103.65	26.908	t=0.02
	Suxamethonium	20	103.55	13.040	P=0.99
1m	Rocuronium	20	107.75	13.958	t=1.52
	Suxamethonium	20	101.25	13.074	P=0.14
3m	Rocuronium	20	101.45	12.804	t=1.07
	Suxamethonium	20	97.10	12.876	P=0.29
5m	Rocuronium	20	94.35	12.106	t=0.37
	Suxamethonium	20	92.95	11.673	P=0.71
10m	Rocuronium	20	91.55	10.909	t=1.15
	Suxamethonium	20	87.65	10.520	P=0.26

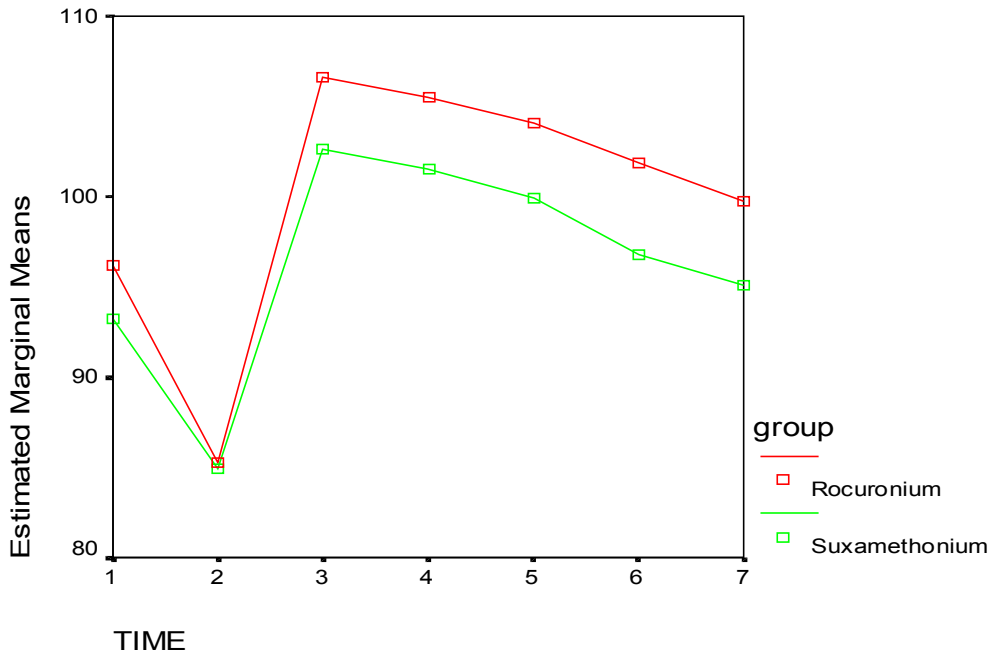
TABLE – 14

HEART RATE	Group			
	Rocuronium	Suxamethonium		
	Mean	SD	Mean	SD
Baseline	87.70	12.13	82.15	10.32
Induction	97.10	10.98	92.00	12.23
Intubation	103.65	26.91	103.55	13.04
1m	107.75	13.96	101.25	13.07
3m	101.45	12.80	97.10	12.88
5m	94.35	12.11	92.95	11.67
10m	91.55	10.91	87.65	10.52

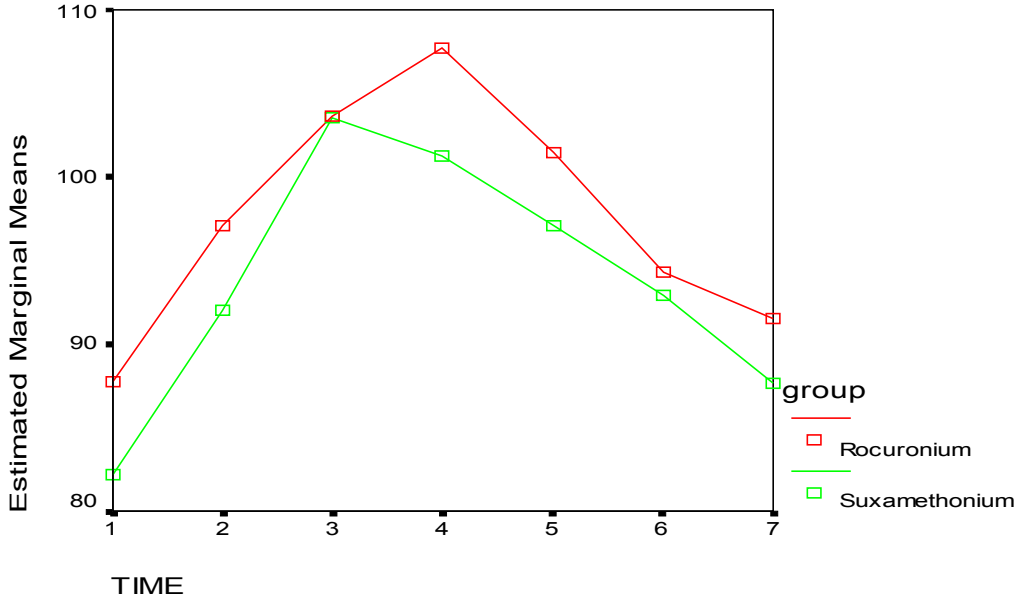
TABLE – 15

Heart rate	F	Sig.
Within group	35.82	.001
Between group	1.07	.31

MAP compared between groups



HEART RATE compared between groups



Statistical analyses between groups on MAP and HR in different time were obtained using repeated measures of **Analysis of Variance**.

The mean rise in MAP and HR was higher within the groups (P = 0.001) during intubation, and was statistically significant.

The rise in MAP & HR between the groups (P = 0.3) showed no statistical significance.

V. ADVERSE EFFECTS

TABLE – 16

adverse effect	group		Total
	Rocuronium	Suxamethonium	
HT, Tachycardia	2	0	2
Pain	1	0	1
Nil	17	20	37
Total	20	20	40

$\chi 2=3.24$ P=0.19

The adverse effects looked for were evidences of histamine release like flushing, wheal, bronchospasm, hypotension and pain on injection.

No sign of histamine release was noted in any of the patients, in this study. Two of the patients in Rocuronium group had hypertension and tachycardia, and 1 patient experienced pain during injection. No significant adverse effects were observed in Suxamethonium group.

Statistical analysis with Chi-square test showed no significant difference in the adverse effects between both the groups (P = 0.19).

- Demographic information like age and sex were given in frequencies with percentage.
- Difference between groups on age was analyzed using the Student's t-test.
- Difference between groups on sex was analyzed using the Chi-square test.
- MAP, HR, Intubation score were given as mean and SD.
- Statistical analysis between groups on MAP and HR in different time was obtained using repeated measures of Analysis of Variance.

DISCUSSION

Traditionally Suxamethonium has been the neuromuscular blocking drug of choice for rapid sequence induction and minimizing the chances of regurgitation and aspiration. Since its introduction in 1949, Succinylcholine has become the drug of choice to produce paralysis in rapid sequence intubation. The use of Suxamethonium can however be associated with many side effects like hyperkalemia, bradycardia, cardiac arrest, raised ICP and IOP. Hence, a non-depolarizing neuromuscular blocker with a rapid onset of action, preferably of a shorter duration is desirable.

Initial studies in animals showed that Rocuronium, being a low potency compound, was associated with a rapid onset of effect when compared with other compounds such as Pancuronium and Vecuronium. [7, 35] This has since been demonstrated in many clinical studies that the onset of action of Rocuronium is significantly faster when compared to equipotent doses of Atracurium and vecuronium, although slightly slower than that of Suxamethonium. That's why Rocuronium was selected for the purpose of rapid sequence induction, in the present study.

The extra anesthetic depth needed, coupled with these laryngeal movements are two drawbacks that cannot make the low dose Rocuronium [0.3 $mgkg^{-1}$ (1xED90)] as a desirable technique for rapid sequence intubation. Use of higher dose of Rocuronium to improve intubating conditions during rapid sequence intubation and to cut short the onset time below 60 seconds has been advocated by various workers [1, 12, 13, 51] but doses larger then 0.6 $mgkg^{-1}$ would be associated with a long duration of action which may be inappropriate in many situations.

In most studies, an appropriate timing of tracheal intubation has been determined by 3 ways.

1. Clinical judgment

2. Neuromuscular monitoring either by twitch suppression (maximum blockade) or TOF ratio

3. Predetermined time after the administration of

neuromuscular blocking agent e.g. 60 secs, 90 secs,

120 secs etc.

The technique using judgment alone is relatively insensitive. Onset time differs with different nerve stimulation rates used.

The development of neuromuscular block was not monitored, as it has been clearly shown in the studies of ***Peter M.C. Wright et al [57] and De Mey et al [13],*** that there is poor correlation between onset time measured at the adductor pollicis and the quality of intubating conditions. So, for more than 40 years, authors have abandoned instrumental means to evaluate laryngoscopy and intubating conditions and are using scales that assess clinical criteria only to assess the quality of tracheal intubation. The scale used in the study was used originally by ***Cooper et al [11]***. in their study and is recommended for studies with neuromuscular blockers [70].

Land and Stovner [28] were probably the first to introduce a rating scale as a tool for the assessment of intubating conditions in which the three main criteria: ***Jaw relaxation, vocal cords*** (position and motility) and ***reaction to intubation*** were rated by descriptive scores such as excellent, satisfactory or fair but this allows a large room for subjective interpretation of data. These three main criteria [66] remained the basis of numerous subsequent modification of their rating scale by others. One of the most frequently used modifications, still in use today, was introduced by ***Krieg et al [26]*** in 1980 in which a numeric value is assigned to signify quality of intubating conditions. ***Cooper's modification*** of this rating scale was used in the present study.

In the ***present study***, intubation was attempted at 60 secs after the injection of muscle

relaxant for rapid sequence induction as proposed by ***Mc Court et al [32], Cooper et al [11], De Mey et al [13], Sparr [48] and Crul et al [12].***

The patients were pre-medicated with 0.5 mg/kg Pentazocine and 0.2 mg Glycopyrrolate and Rocuronium (0.6 mg/kg) / Suxamethonium (1.5 mg/kg) given immediately after receiving the I.V. anaesthetic, as done in the study by ***Dr. Ajeet Singh et al [2]***

The *condition of the vocal cords* during intubation with Suxamethonium was not significantly different from that of Rocuronium, with a mean score of 2.85 and 3.0 respectively. The *response to intubation* was higher in the Rocuronium group and was statistically significant (P = 0.001), from that of the Suxamethonium group. Rocuronium group showed a mean score of 2 ± 0.0 (slight diaphragmatic movement), and Suxamethonium group showed a mean score of 3 ± 0.0 (no response). The total intubation score with Suxamethonium was higher than that of Rocuronium and was statistically significant (P = 0.001). The overall intubating conditions were better with Suxamethonium with a mean total score of 9. The mean total score in Rocuronium group was 7.85. Though Rocuronium fell back against Suxamethonium with respect to the total scores, the mean score reflected good intubating conditions.

The results with respect to intubating conditions in the present study go well in concurrence with the results of the study by ***Dr. Ajeet singh et al***.

Moreover, the intubating conditions achieved at 60 secs, according to the present study, were also observed in the studies of ***Mirakhur R.K. et al [34], Clarke [11] , De Mey J.C., et al [13] , Lam AM., et al [27] , Mc Court et al [32].***

Rocuronium was used for emergency intubations in the present study, and the intubating conditions were good to excellent at 60 secs. This goes in concurrence with the methods and results obtained by ***Sparr [48] and Crul et al***,[12]

The mean rise in MAP and HR was higher within the groups (P = 0.001) during intubation,

and was statistically significant. This could be attributed to the adrenergic response to laryngoscopy and intubation, rather than to the effect of drugs. But the rise in MAP & HR between the groups (P = 0.3) showed no statistical significance. The hemodynamic conditions observed during intubation were comparable with the results of ***Dr. Ajeet singh et al***. This showed that the muscle relaxant administered during intubation did not alter or influence the hemodynamic state. Therefore Rocuronium, at the dose of 0.6 mg/kg (2 x ED_{95}) did not show any adverse hemodynamic response, and the hemodynamic profile was comparable to Suxamethonium.

No sign of histamine release was noted in any of the patients, in this study. Two of the patients in Rocuronium group had hypertension and tachycardia, and 1 patient experienced pain during injection. No significant adverse effects were observed in Suxamethonium group. In the study by ***Dr. Ajeet singh et al,*** complications such as laryngospasm, bradycardia, tachycardia and arrhythmias were noted in a significant number of patients in both the groups, but statistical analysis between the groups failed to show any significance.

In the present study, statistical analysis with Chi-square test showed no significant difference in the adverse effects between both the groups (P = 0.19). Hence the results of the present study with respect to adverse effects are comparable with the study of ***Dr. Ajeet singh et al***.

SUMMARY

- Rocuronium 0.6mg/kg (2 x ED_{95}) produced acceptable intubating conditions (good or excellent) in 1 minute.
- Excellent intubating conditions were observed in Suxamethonium group at 1 minute.
- Rocuronium, at the dose of 0.6 mg/kg (2 x ED_{95}) did not show any adverse hemodynamic response, and the hemodynamic profile was comparable to Suxamethonium.

CONCLUSION

Both Rocuronium and Suxamethonium produced good to excellent intubating conditions for rapid sequence intubation. Rocuronium in the dose of 0.6 mg/kg, had a comparable hemodynamic profile to Suxamethonium, and can be used as the next best alternative to Suxamethonium as a part of rapid sequence induction provided there is no anticipated difficulty in intubation. Rocuronium appears to be safe with less adverse effects and effective for rapid sequence intubation of selected patients in whom contraindications to Succinylcholine exist.

REFERENCES

1. *Agoston S*. Onset time and intubating conditions with Rocuronium, an evaluation in perspective. Eur J Anaesth 1995; 12: 31-37.
2. *Ajeet Singh, Bhatia Pradeep Kumar, Tulsiani Kishan Lal.* Comparison of onset time, duration of action and intubating conditions achieved with Suxamethonium and Rocuronium. *Indian J. Anaesth. 2004*; 48 (2) : 129-133.
3. *Awarez-Gomez J A, Fabregat J, Estelles M E et al*. Rapidez de intubation de un neuro bloqueador neuromuscular. Bromuro de rocuronium. Rev Esp Anaesthesiol Reanim 1994; 41(1): 3-6.
4. *Baker BB, Wagner JA, Hemenway WG*. Succinylcholine induced hyperkalemia and cardiac arrest. Arch Otolaryngol. 1972; 96:464–5.
5. *Bartkowski R R, Witkowski T A, Azad S S et al.* Dose response and recovery of org. 9426 under enflurane anaesthesia. Anesthesiology 1990; 73(3A) : A902.
6. *Belin RP, Karleen CI*. Cardiac arrest in the burned patient following succinylcholine administration. Anesthesiology. 1966; 27:516–8.
7. *Bowman W C, Rodger I W, Houston J et al*. Structure action relationships among some desacetoxy analogues of Pancuronium and vecuronium in anaesthetized cat. Anesthesiology 1988; 69: 57-62.
8. *Brooke MM, Donovan WH, Stolov WC*. Paraplegia: succinylcholine- induced hyperkalemia and cardiac arrest. Arch Phys Med Rehabil. 1978; 59:306–9.
9. *Cason B. Baker DG. Hickey RF. Miller RD. Agoston S*. Cardiovascular and neuromuscular effects of three steroidal neuromuscular blocking drugs in dogs (org 9616, org 9426, org 9991) Anesth Analg 1990. 70; 382-388.
10. Cooper R., Mirakur R.K. Clarke R.S.J. and Boules Z. Comparison of intubating conditions

after administration of rocuronium and Suxamethonium. British Journal of Anaesthesia 1992;69: 269-273

11. *Cooper AR. Mirakhur RK. Maddineni VR.* Neuromuscular effects of rocuronium bromide (org 9426) during fentanyl and halothane anaesthesia. Anaesthesia 1993; 48: 103-105.
12. *Crul J F, Vanbelleghem V, Buyse L et al.* Rocuronium with alfentanil and propofol allows intubation within 45 secs. Eur J Anaesth 1995; 12 (1): 111-12.
13. DeMay JC, Debrock M, Rolly G. Evaluation of the onset and intubation conditions of rocuronium bromide. Eur J Anaesth. 1994; 11:37–40.
14. *De Mey J C, Van Overschelde H, De Laat M et al*. The influence of dose on the profile of onset of neuromuscular blockade after a bolus dose of rocuronium. Br J Anaesth 1995; 71(1): A285.
15. *Dubois M Y, Lea D E, Kataria B et al.* Pharmacology of rocuronium with and without prior administration of suxamethonium. Jour of clinical anaesthesiology 1995; 7(1): 44-8.
16. Dufour DG, Larose DL, Clement SC. Rapid sequence intubation in the emergency department. J Emerg Med 13:705-710, 1995.
17. Feldman J. Cardiac arrest after succinylcholine administration in a pregnant patient recovered from Guillain-Barre´ syndrome. Anesthesiology. 1990; 72:942–4.
18. *Folders F. F, Nagashima H, Nguyan H D et al*. The neuromuscular effect of org. 9426 in patients receiving balanced anaesthesia. Anesthesiology 1991; 75: 191-96.
19. Greenan J: The cardio-oesophageal junction. Br J Anaesth 33: 432, 1961.
20. Gronert GA, Theye RA. Pathophysiology of hyperkalemia induced by succinylcholine. Anesthesiology. 1975; 43(1):89–99.
21. Habre W, Sims C; Masseter spasm and elevated creatine kinase after intravenous induction in a child. Anaesth Intensive Care 24: 496, 1996.
22. Henderson WAV. Succinylcholine-induced cardiac arrest in unsuspected Duchenne

muscular dystrophy. Can Anaesth Soc J. 1984; 31:444–6.

23. Kirkegaard Nielson H., James E. Caldwell, Peter D. Berry. Rapid tracheal intubation with rocuronium. Anaesthesiology 1999;91:131-136.

24. Kalow W. Succinylcholine and malignant hyperthermia. Federation Proc. 1972; 31:1270–5.

25. Kovarik WD, Morray JP. Hyperkalemic cardiac arrest after succinylcholine administration in a child with purpura fulminans. Anesthesiology. 1995; 83:211–3.

26. *Krieg N, Mazur L, Booij LHDJ et al*. Intubation conditions and reversibility of a new nondepolarizing neuromuscular blocking agent Acta Anaesthesiol Scand 1980; 24: 420-25.

27. *Lam AM, Pavlin EG, Visco E and Taraday J*. Rocuronium versus succinylcholine – atracurium for tracheal intubation and maintenance relaxation during propofol anaesthesia J Clin Anaesthesia 2000 Sep; 12(6): 449-53.

28. *Land I, Stovner J*. Experimental and clinical experiences with a neuromuscular relaxant R05-3816, diallylnor – toxiferine. Acta Anaesthesiol Scand 1962; 6: 85-97.

29. Linter SPK, Thomas PR, Withington PS, Hall MG. Suxamethonium associated hypertonicity and cardiac arrest in unsuspected pseudohypertrophic muscular dystrophy. Br J Anaesth. 1982; 54:1331–2.

30. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia of adult patients. Anesthesiology. 1993; 79:913–8.

31. Mallampati SR,Gatt SP, GuginoLD *et al*. 1985.A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J* 32: 429±34.

32. *Mc Court K C, Salmela L, Mirakhur R K et al*. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia: Anaesthesia

1998; 53; 867-71.

33. Minton MD, Grosslight K, Stirt JA et al: Increases in intracranial pressure from Succinyl choline: Prevention by prior non depolarizing blockade, Anesthesiology 65: 165, 1986.

34. Mirakhur R.K., Cooper A.R. and Clarke R.S.J. Onset and intubating conditions of rocuronium bromide compared to those of suxamethonium. European Journal of Anaesthesiology 1994; (Suppl. 19): 41-43

35. *Muir A W, Houston J, Green K L, Marshall R J et al*. Effects of a new neuromuscular blocking agent (org 9426) in anaesthetized cats and pigs and in isolated neuromuscular preparations. Br J Anaes 1989; 63: 400-410.

36. *Muir AW, Houston J. Marshall RJ. Bowman WC. Marshall IG*. A comparison of neuromuscular blocking and autonomic effects of two new short-acting muscle relaxants with those of succinyl choline in the anaesthetized cat and pig. Anesthesiology 1989; 70. 533-540.

37. *Nash CL, Haller R, Brown RH.* Succinylcholine, paraplegia, and intraoperative cardiac arrest. J Bone Jt Surg. 1981; 63:1010–2.

38. Pandey K, Badola RP, Kumar S: Time course of intra-ocular hypertension produced by suxamethonium. Br J Anaesth 44: 191, 1972.

39. Pantuck, E.J. (1993) Plasma cholinesterase: gene and variation. Anesth. Analg. 77, 380-6.

40. *Prien T, Zahn P. Meriges M, Brussel T*. 1 x ED90 dose of rocuronium bromide: Tracheal intubation conditions and time course of action. Eur J Anaesth 1995; 12(11): 85-90.

41. *Puhringer F K, Khuenl, Brandy K S, Koller J et al*. Evaluation of intubating conditions of rocuronium and succinyl choline in outpatient surgery. Anaesth Analg 1992; 75: 37-40.

42. Rubin MA, Sadovnikoff N. Neuromuscular blocking agents in the emergency department.

J Emerg Med. 1996; 14:193–9.

43. Sakles JC, Laurin EG, Rantapaa AA, Panacek EA. Airway management in the emergency department: a one-year study of 610 tracheal intubations. Ann Emerg Med. 1998; 31:325–32.

44. Sakles JC, Laurin EG, Rantapaa AA, Panacek EA. Rocuronium for rapid sequence intubation of emergency department patients. J Emerg Med. 1999; 17:611–6.

45. Schwartz DE, Kelley B, Caldwell JE. Succinylcholine-induced hyperkalemic arrest in a patient with severe metabolic acidosis and exsanguinating hemorrhage. Anesth Analg. 1992; 75:291–3.

46. Sellick BA. Cricoid pressure to control regurgitation of stomach contents during induction of anesthesia. Lancet 2:404-406, 1961.

47. *Smith, G., Dalling, R and Williams, T.I.R*. (1978) Gastro-oesophageal pressure changes produced by induction of anesthesia and Suxamethonium. Br. J. Anaesth. 50, 1137-43.

48. *Sparr H J, Luger T J, Heidegger T et al.* Comparision of intubating conditions after rocuronium and Suxamethonium following rapid sequence induction with thiopentone in elective case. Acta Anaesthesiol Scand 1996; 4: 40 (4); 425-30.

49. Sumikawa K, Mitsuya K. Succinylcholine-induced cardiac asystole in a patient with acute hypokalemia. Med J Osaka Univ. 1978; 28(3-4):359–62.

50. Tobey RE. Paraplegia, succinylcholine, and cardiac arrest. Anesthesiology. 1970; 4:359–64.

51. Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. Anesthesiology. 1967; 28:467–70.

52. Tryba M, Zorn A, Thole H, Zenz M. Rapid-sequence orotracheal intubation with rocuronium: a randomized double-blind comparison with Suxamethonium-preliminary communication. Eur J Anesth. 1994; 11:44–8.

53. Wang JM, Stanley TH. Duchenne muscular dystrophy and malignant hyperthermia—two case reports. Can Anaesth Soc J. 1986; 33:492–7.

54. Whittaker, M. (1980) Plasma cholinesterase variants and the anaesthetist. Anaesthesia 35, 174-97.

55. *Wierda JMKH. De Wit APM. Kuizenga K. Agoston S*. clinical observations on the neuromuscular blocking action of org 9426, a new steroidal non-depolarizing agent. Br J Anaesth 1990; 64: 521-532.

56. *Wierda JMKH, Hommes FDM, Nap HJA et al.* Comparison of time course of action and endotracheal intubating conditions of vecuronium, rocuronium and mivacurium. Anaesthesia 1995; 50: 393-96.

57. Wright PM, Andrews JI, Kumar N, Van den Brom RH, Oikkola KT, Roest GJ. A large simple randomized trial of rocuronium versus succinylcholine in rapid sequence induction of anaesthesia along with propofol. Acta Anaesthesiol Scand. 1999 Jan; 43(1): 1-8

58. Yamamoto LG, Yim GK, Britten AG. Rapid sequence anesthesia induction for emergency intubation. Ped Emerg Care 6:200-213, 1990.

A COMPARATIVE EVALUATION OF ROCURONIUM AND SUXAMETHONIUM FOLLOWING RAPID SEQUENCE INDUCTION IN EMERGENCY SURGERIES

PROFORMA

1. NAME: AGE/SEX: I.P.No:
2. WEIGHT :
3. DIAGNOSIS :
4. PROCEDURE PLANNED :
5. HISTORY IN BRIEF :

6. TIME SINCE LAST MEAL/DRINK :
7. CO-EXISTING ILLNESS : DM/HT/PT/EPILEPSY/IHD HEPATIC/RENAL DISEASE
8. EXAMINATION : PULSE RATE -
   RESP. RATE -
   BP -
   CVS -
   RS -
   AIRWAY -
9. INVESTIGATIONS : Hb% -
   BLOOD SUGAR -
   BLOOD UREA -
   S. CREATININE -
   S.ELECTROLYTES - Na^+
   - K^+

10. DETAILS OF RSI :

a) Pre-oxygenation - 3 mins.

b) Pre-medication - Glycopyrrolate 0.2mg + Pentazocine 30mg

I.V. 5 mins. before induction

c) Induction - Thiopentone 5mg/kg

d) Cricoid pressure

e) Muscle relaxant - Suxamethonium – 1.5 mg/kg

- Rocuronium - 0.6 mg/kg

f) Intubation - at 60 secs.

Cooper's Scoring System

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

g) Intubation score - 8 – 9 : excellent

- 6 – 7 : good

- 3 – 5 : fair

- 0 – 2 : poor

h) Laryngoscopy - Cormack & Lehane grade –

i) Confirmation of ETT placement - Inspection & auscultation

j) Cuff inflation and release of cricoid pressure

11. No. OF ATTEMPTS AT INTUBATION :

12. AIRWAY ADJUNCTS USED - Combitube

- LMA

- Surgical airway

13. HEMODYNAMIC RESPONSE TO INTUBATION :

	baseline	**induction**	**Intubation**	**1m**	**3m**	**5 m**
HR						
BP (MAP)						
SpO2						

14. ADVERSE EFFECTS:

- Arrhythmia
- Bradycardia
- Tachycardia
- Hypertension
- Hypotension
- Pain on injection
- Laryngospasm / Bronchospasm
- Prolonged apnoea

Anaphylactic / Anaphylactoid reactions

MASTER CHART

GROUP- I (ROCURONIUM 0.6 mg/kg)

Age/ Sex	map						PR						Intubation score				Adverse effects
	Base line	Induction	Intubation 0 s	1 m	3m	5m	Base line	Induction	Intubation 0 s	1m	3m	5m	J	V	R	T	
18/M	81	76	88	89	99	99	96	107	113	94	92	88	3	3	2	8	Nil
20/M	88	77	95	97	98	96	68	82	94	96	88	76	3	3	2	8	Nil
25/M	97	83	107	102	95	96	77	89	101	103	96	89	3	2	2	7	Nil
40/M	130	118	136	133	134	130	82	97	121	115	112	96	3	3	2	8	HT, Tac
19/M	87	78	92	90	88	86	102	111	122	126	114	98	3	2	2	7	Nil
42/F	86	80	89	90	89	88	84	88	102	104	101	92	3	3	2	8	Nil
22/M	89	79	95	93	90	91	109	93	135	133	131	126	3	3	2	8	Nil
32/M	122	110	132	133	130	127	112	116	132	136	126	114	3	3	2	8	HT, Tac
37/F	95	86	104	102	100	97	89	99	4	110	102	92	3	3	2	8	Nil
29/F	89	77	95	94	93	90	92	109	111	99	96	97	3	3	2	8	Pain
25/M	94	86	99	100	98	97	88	94	102	99	94	89	3	3	2	8	Nil
35/M	110	99	121	118	116	115	92	99	108	105	99	89	3	2	2	7	Nil
20/M	80	72	94	92	90	87	68	77	86	82	80	74	3	3	2	8	Nil
52/F	111	98	122	120	119	115	94	107	119	121	109	108	3	3	2	8	Nil
29/M	104	90	118	120	116	115	78	87	94	96	91	88	3	3	2	8	Nil
42/M	100	88	111	110	108	106	80	92	98	99	91	87	3	3	2	8	Nil
28/F	97	83	108	110	109	105	84	99	104	105	98	94	3	3	2	8	Nil
32/F	83	69	98	100	99	96	98	114	124	122	111	105	3	3	2	8	Nil
24/M	87	71	101	98	96	92	87	98	106	111	107	99	3	3	2	8	Nil
31/M	104	95	128	120	115	110	74	84	97	99	91	86	3	3	2	8	Nil

MASTER CHART

GROUP- II (SUXAMETHONIUM 1.5 mg/kg)

Age/ Sex	MAP						PR						Intubation score				ADVER EFFEC
	Base line	Induction	Intubation 0 s	1 m	3m	5m	Base line	Induction	Intubation 0 s	1m	3m	5m	J	V	R	T	
28/M	97	85	103	102	100	98	84	96	112	108	105	99	3	3	3	9	Nil
22/M	99	91	107	106	103	100	78	88	106	105	100	84	3	3	3	9	Nil
35/M	96	87	105	105	102	100	77	86	99	95	88	89	3	3	3	9	Nil
40/F	70	77	93	92	90	86	68	75	88	85	80	76	3	3	3	9	Nil
29/M	88	81	93	91	90	87	70	76	84	87	81	83	3	3	3	9	Nil
32/F	101	90	110	109	105	101	85	99	108	105	101	97	3	3	3	9	Nil
22/F	91	81	96	95	93	90	88	92	99	98	94	96	3	3	3	9	Nil
33/M	109	97	119	116	115	110	92	100	109	105	101	99	3	3	3	9	Nil
37/M	103	96	106	104	103	101	82	93	98	101	97	95	3	3	3	9	Nil
29/F	78	74	95	96	94	90	99	118	124	120	117	112	3	3	3	9	Nil
25/M	82	78	93	93	92	88	66	78	85	82	80	76	3	3	3	9	Nil
35/M	103	91	109	108	107	105	72	85	97	95	90	85	3	3	3	9	Nil

	20/M	85	79	96	95	94	90		76	82	96	92	89	88		3	3	3	9	Nil
	52/F	100	91	103	102	101	100		90	105	115	110	109	105		3	3	3	9	Nil
	29/F	89	81	94	93	92	90		83	96	105	101	98	95		3	3	3	9	Nil
	42/M	99	89	106	105	104	101		78	85	95	92	89	85		3	3	3	9	Nil
	28/F	111	93	117	115	113	110		104	114	128	132	126	118		3	3	3	9	Nil
	32/F	93	82	105	104	103	100		96	106	129	125	118	109		3	3	3	9	Nil
	24/M	86	78	101	100	99	95		75	80	95	92	88	82		3	3	3	9	Nil
	31/M	84	78	102	100	98	93		80	86	99	95	91	86		3	3	3	9	Nil