A PROSPECTIVE RANDOMIZED CLINICAL TRAIL OF THREE DIFFERENT DOSES OF ROCURONIUM BROMIDE FOR INTUBATION IN ADULTS

Dissertation Submitted in partial fulfillment of

M.D. DEGREE EXAMINATION

M.D. ANAESTHESIOLOGY—BRANCH X

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU.

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

CHENNAI, TAMILNADU

MARCH 2O1O

CERTIFICATE

This is to certify that this dissertation titled **"A PROSPECTIVE RANDOMIZED CLINICAL TRAIL OF THREE DIFFERENT DOSES OF ROCURONIUM BROMIDE FOR INTUBATION IN ADULTS"** has been prepared by Dr.T.Manoharan under my supervision in the department of anaesthesiology, Chengalpattu Medical College & Hospital, Chengalpattu during the academic period 2007-2010 and is being submitted to the Tamil Nadu DR.M.G.R. Medical University, Chennai in partial fulfillment of the University regulation for the award of the Degree of Doctor of Medicine (Branch-X MD Anaesthesiology) and his dissertation is a bonafide work.

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DECLARATION

I, Dr.T.Manoharan, solemnly declare that the dissertation **"A PROSPECTIVE RANDOMIZED CLINICAL TRAIL OF THREE DIFFERENT DOSES OF ROCURONIUM BROMIDE FOR INTUBATION IN ADULTS"** is a bonafide work done by me in the Department of Anaesthesiology, Chengalpattu Medical College & Hospital, Chengalpattu, after getting approval from the Ethical Committee, under the able guidance of Prof.Dr.R.S.VIJAYALAKSHMI,MD.,DA., Professor and HOD, Department of Anaesthesiology, Chengalpattu Medical College, Chengalpattu.

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Date:

ACKNOWLEDGEMENT

I wish to express my sincere thanks to **Dr.P.Parasakthi** M.D., Dean Incharge, Chengalpattu medical college, Chengalpattu and **Dr.R.Jeganathan, M.D.,D.C.H.,** Dean in charge, Chengalpattu medical college hospital, Chengalpattu for kindly permitting to utilize the hospital facilities.

I wish to express my grateful thanks to:

Prof. Dr. R.S.Vijayalakshmi, M.D.,D.A., Professor & Head of the department of anaesthesiology, Chengalpattu medical college, Chengalpattu for her immense help, encouragement and constant supervision.

Prof.Dr.N.Krishnan, M.D.,D.A., Additional Professor of anaesthesiology for his valuable guidance, supervision and immense help during every phase of this study.

Prof.Dr.U.G.Thirumaaran, M.D., Additional Professor of anaesthesiology for his valuable suggestions, great care and attention he had so willingly extended in guiding to prepare this dissertation.

Prof.Dr.Kumudha Lingaraj, M.D.,D.A., Associate Professor of anaesthesiology for her sagacious advice and constant help throughout my period of study.

I thank **Dr.V.Gnanaganesh**, M.D.,D.A., Assistant. Professor of anaesthesiology who has been pillar of strength, support and inspiration to me and for having incultated a sense of confidence within me.

I owe great debt of gratitude to all the Assistant Professors and Tutors for their able help and support. They have been a source of great encouragement throughout my postgraduate course.

I thank the ethical committee members for the approval of my study.

I can never forget theatre personnel for their willing cooperation and assistance.

I thank all the patients who took part in my study and their relatives.

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INTRODUCTION

In the triad of anaesthesia, reflex suppression and facilitation of tracheal intubation is achieved by administering neuromuscular blocking agents. An ideal muscle relaxant should have rapid onset, profound muscle relaxation and short duration of action, so that patient's own respiratory function can be restored, should intubation proved to be impossible.[1] Succinylcholine is the only available muscle relaxant for rapid tracheal intubation.[2] Its use is associated with multiple complications like bradycardia, hyperkalemia, asystole, raised intraocular pressure, malignant hyperthermia,etc.[3,4] Therefore need exists for a nondepolarizing muscle relaxant with a rapid onset of action.

Rocuronium bromide is a new steroidal nondepolarizing neuromuscular blocking agent shown to have rapid onset of action.[5]

It has the fastest onset as compared to all other available nondepolarizing neuromuscular blockers, having an onset time similar to succinylcholine.[6]

The onset time,duration and intubating conditions are influenced by the dose of rocuronium.

AIM

This study is aimed at comparing intubating conditions in **80 seconds** by using three different doses of rocuronium bromide in adults by assessing the following parameters:

1. The onset time and duration of neuromuscular blockade
2. Intubating conditions and
3. Haemodynamic changes

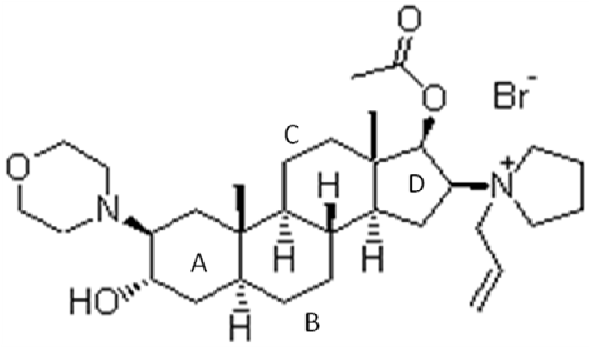
PHARMACOLOGY OF ROCURONIUM BROMIDE

Org 9426 was synthesized and studies were undertaken in Organon Teknika Laboratories. It was later renamed as "Rocuronium Bromide" and introduced into clinical practice in 1994.

CHEMISTRY:

Rocuronium is the 2- morpholino, 3- desacetyl, 16- N-allyl –pyrolidino derivative of vecuronium bromide. It is a steroidal muscle relaxant of intermediate duration of action. The decreased potency of rocuronium bromide is due to the replacement of the methyl group attached to the quaternary nitrogen of vecuronium and pancuronium by an allyl group and the absence of acetylcholine –like fragment in the A ring. The replacement of an acetate group attached to the A ring by hydroxy group makes it stable in solution.

MOLECULAR STRUCTURE



Esmeron® 50 mg
Rocuronii bromidum
Ad inject. intraven.
1 ml = 10 mg
N.V. Organon, Oss.
28839/109

PRESENTATION :

It is supplied as a ready-to-use solution, in ampoules or vials of 25mg(2.5 ml), 50mg(5 ml) and 100mg(10 ml). It should be stored at 2^0C to 8^0 C in the dark. It can be stored at 8^0C to 30^0 C for 12 weeks.

ROUTES OF ADMINISTRATION AND DOSAGE:

Intravenous or intramuscular routes.

ED_{95} dose is 0.3mg/kg . The standard dose required for intubation at 60seconds is 0.6mg/kg. It has a lag time of 25.8 seconds and onset time of 88.9 seconds. Intubating conditions can be improved by using high doses of 0.9mg/kg or 1.2mg/kg.

The clinical duration of action for the $1\times ED_{95}$,$2\times ED_{95}$ and $3\times ED_{95}$ doses are 15 minutes, 37 minutes and 53 minutes respectively. It is short acting with a dose of 0.3mg/kg($1\times ED_{95}$) and intermediate duration of action with 0.6-0.9mg/kg. When more than 1mg/kg is used for intubation, onset is very quick (less than 45 seconds) but the duration of action is prolonged (more than 1 hour)

For continuous infusion the dose is 5-10µg/kg/min (0.3-0.6 mg/kg/hour).[7] The infusion rate is adjusted to maintain twitch response at 10% of control twitch height.

PHARMACOKINETICS:

Rocuroniun is 30% bound to plasma proteins. It has a smaller volume of distribution which reflects its lower lipophilicity when compared to vecuronium.

TABLE-I

Pharmacokinetics of Rocuronium bromide

Age Group	Volume of distribution at steady state (ml/kg)	Clearance (ml/kg/min)	Elimination half life (min)
Adult	207	2.89+/-0.25	70.9 +/-4.7
Elderly	399+/-122	3.67+/-1	97+/-69.1
Children	224	2.67	46-55

Metabolism :

The effect of rocuronium is terminated primarily due to liver uptake by a carrier mediated active transport system and excretion through the bile (>70%) either degraded or undegraded.[8] The major putative metabolites 17-desacetyl rocuronium and 16N Desallyl rocuronium are pharmacologically inactive.

Liver disease increases the volume of distribution of rocuronium and could result in a longer duration of action especially with repeated doses or prolonged IV administration. A small fraction of the administered dose (<20%) is excreted by the kidneys.

PHARMACODYNAMICS.

Cardiovascular effects:

Rocuronium has only minimal cardiovascular effects as evidenced by no changes in heart rate and arterial blood pressure with doses of 2-3×ED_{95}.[19,20] The heart rate tends to increase with doses greater than 5×ED_{95}. The autonomic safety ratio for vagal block is about 10 times less than that of vecuronium.

Histamine releasing property

Rocuronium, being an aminosteroid is not associated with any increase in plasma histamine levels after rapid intravenous bolus injection of doses upto 4× ED_{95}.[21]

Anaphylactic or anaphylactoid reactions

It is devoid of any significant histamine release. In terms of allergy, rocuronium appears to be very close to those aminosteroids relaxants with a good safety profile.

Cholinesterase inhibition

Inhibition of cholinesterase by certain muscle relaxants may lead to prolongation of effect of drugs dependant on cholinesterases for their metabolism, like suxamethonium and mivacurium. Atracurium and vecuroniun have very little activity on choliesterase activity. The anticholinesterase activity of rocuronium is lower than that of vecuronium.

Central nervous system

Rocuronium has no effects on central nervous system since it does not cross the blood- brain barrier. There is no change in intracranial pressure.[46]

Intra ocular pressure :

Rocuronium has no significant effect on intra- ocular pressure. Rocuronium appears to be safe for use in rapid- sequence induction of anaesthesia for perforating eye injuries.[47]

Placental transfer :

Rocuronium does not cross the placenta in significant amounts.[48]

DRUG INTERACTIONS :

Intravenous anaesthetic agents in standard doses like thiopentone, propofol, etomidate, midazolam, fentanyl and droperidol do not have any clinically significant effect on the action of rocuronium. However, high doses of these drugs have a potentiating effect.

Enflurane and isoflurane potentiate the effect of rocuronium.[49] Halothane appears to produce less potentiation of the block. Nitrous oxide does not have an effect on the depth of the block, although it causes some prolongation in recovery. The action of rocuronium can be increased in the presence of hypokalemia (eg;-patients on diuretics), hypermagnesemia (eclamptic patients on Magnesium sulphate therapy), hypocalcemia, hypoproteinemia, dehydration, acidosis, hypercapnia , hypothermia and cachexia.[18]

Chronic administration of anticonvulsant drug phenytoin decreases the duration of action and increases the dose requirement of rocuronium. Single doses of commonly used antibiotics, metronidazole, cefuroxime, netilmycin and aminoglycosides do not have a significant effect on the action of rocuronium.

ROCURONIUM BROMIDE IN SPECIAL PATIENT GROUPS

Paediatrics :

In children, the onset of action is faster and the duration of action of rocuronium tend to be shorter. The action may be prolonged in neonates and infants due to increased volume of distribution and immature organ function.[22] United States and Germany have strongly recommended the use of rocuronium instead of succinylcholine in paediatric patients.[23] Rocuronium may be used for rapid sequence induction, as succinylcholine is relatively contraindicated because of the possible presence of undiagnosed muscle dystrophy especially in boys.[24,25]

Recommended doses: 2 -12 years: 0.9 to 1.2mg/kg

Infants : 0.6 mg/kg

Neonates:0.45 mg/kg

Geriatrics :

The duration of action is prolonged in geriatric patients due to reduced volume of distribution, reduced organ based elimination and reduced plasma clearance.[26] Both the onset and recovery are slower in the elderly.

Obstetrics :

It does not cross placental barrier in significant amounts. Insignificant amounts of rocuronium are found in the milk of lactating rats. It can safely be used during rapid sequence induction of anaesthesia in patients undergoing caeserean section, provided sufficient anaesthetic agent is used.[48] Adequate intubation conditions are obtained within 80 seconds following a 0.6 mg/kg dose; clinical duration of action is 33min. Placental transfer is limited, the average umbilical venous/maternal venous (UV/MV) ratio is 0.18. There are no untoward effects on the neonates evaluated by Apgar score(1minute & 5minutes), time to sustained respiration, total and muscular neuroadaptive capacity scores, acid–base status and blood -gas tensions in umbilical arterial and venous blood.

Obese patients :

Obese patients have metabolic alterations that may affect drug kinetics and dynamics. The onset of action is more rapid and the duration of relaxation is longer when the dose is based on actual body weight. If it is administered based on lean body mass, similar pharmacodynamic parameters are seen as in normal patients.

Hepatic dysfunction :

Plasma clearance of rocuronium is primarily due to liver uptake and biliary excretion. While its onset time is not altered, its duration of

action is significantly prolonged, but this is compensated to some extent by the larger volume of distribution.[27] It should be avoided or used in decreased doses in patients with hepatic and/or biliary disease.

Renal dysfunction :

The clearance of rocuronium was reduced in patients with renal failure when compared with healthy patients but its duration of action is not significantly altered. In severe renal impairment, it may be used in reduced doses. It is recommended that a reduced maintenance dose of 75 to 100 micrograms/kg is used in patients with renal failure.

Cardiac surgery :

Its apparent lack of clinically significant cardiovascular effects makes rocuronium a suitable choice for cardiac surgery. But it lacks the cardiac stability of vecuronium in higher doses.

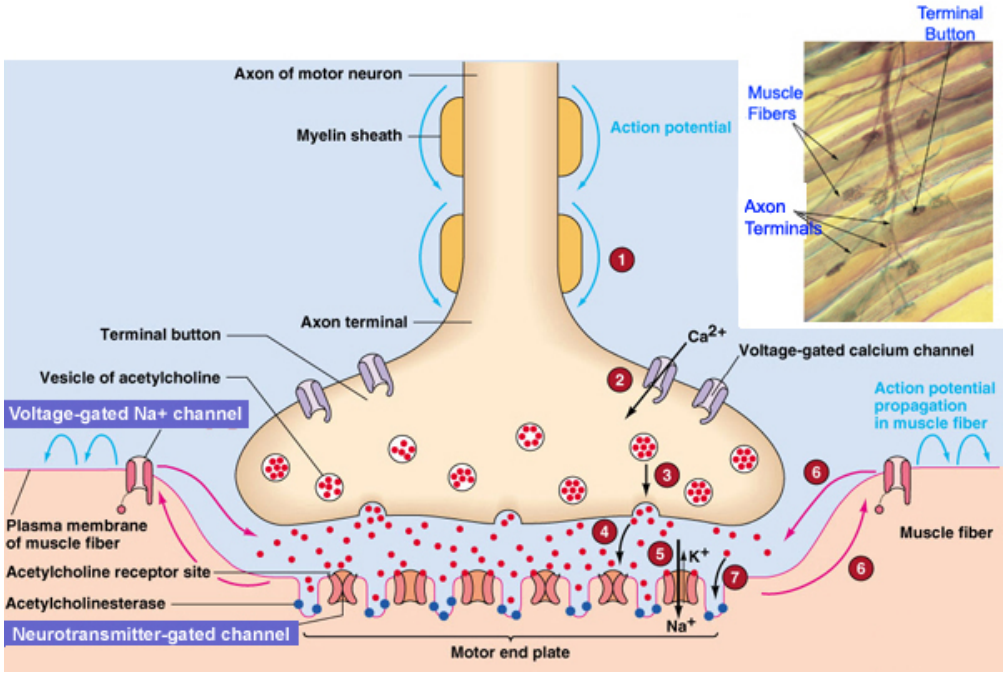
Hypothermia :

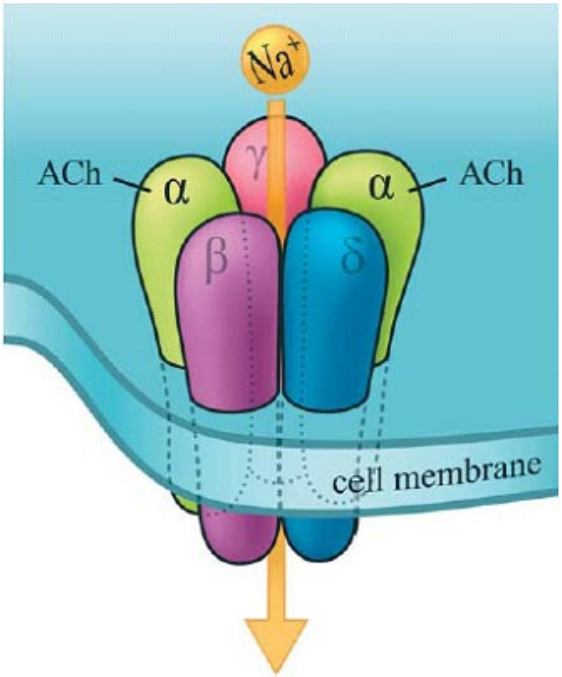
Hypothermia reduces plasma clearance of rocuronium and prolongs its duration of action significantly, producing slower recovery.

GENDER :

The potency of rocuronium has been reported to be slightly greater in women than in men; the ED_{95} being 0.27mg/kg and 0.39mg/kg respectively, with an increased duration of action in women.[28]

The Neuromuscular Junction





PHYSIOLOGY OF NEUROMUSCULAR JUNCTION

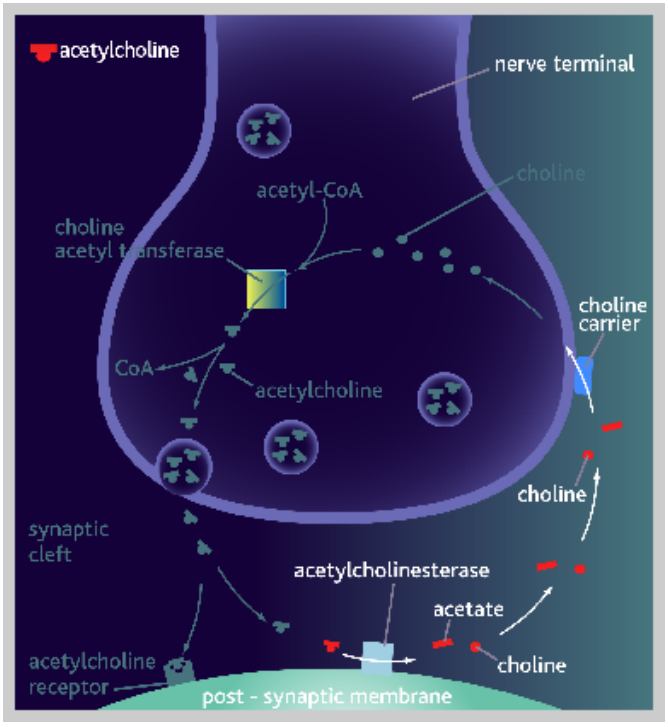
Neuromuscular Junction

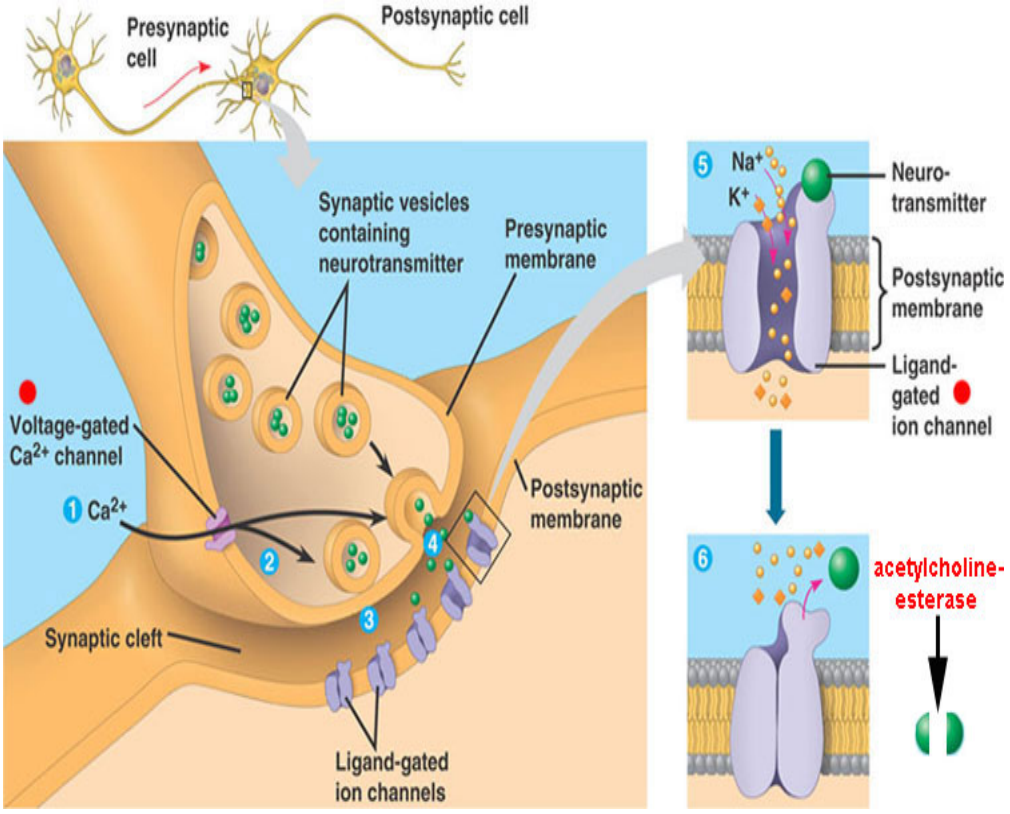
Neuromuscular junction is the synapse at which an electrical impulse travelling down a nerve is converted into muscle action potential and contraction by chemical transmitters. A motor neuron, along with all the muscle fibres supplied by it forms a motor unit, which follows all or none law of contraction.

Mechanism of neuromuscular transmission

Acetyl choline release:

An action potential travelling 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 impulse activates the calcium channels, which open up leading to calcium entry. Calcium mediated activation of calcium calmodulin dependant protein kinases lead to phosphorylation of synapsins in the vesical wall causing the vesical walls 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.


acetylcholine
nerve terminal
acetyl-CoA
choline
choline
acetyl transferase
choline
carrier
CoA
acetylcholine
choline
synaptic
cleft
acetylcholinesterase
acetate
choline
acetylcholine
receptor
post - synaptic membrane


Presynaptic
cell
Postsynaptic cell
Synaptic vesicles
containing
neurotransmitter
Presynaptic
membrane
Voltage-gated
Ca2+ channel
1 Ca2+
2
3
4
Synaptic cleft
Postsynaptic
membrane
Ligand-gated
ion channels
5 Na+
K+
Neuro-
transmitter
Postsynaptic
membrane
Ligand-
gated
ion channel
6
acetylcholine-
esterase

Acetyl choline binding to receptor :

The Ach molecule released into the synaptic cleft binds to the alpha subunit. Binding of Ach to both the α 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 perijunctional zones. This depolarization wave moving down the T tubule causes release of calcium from sarcoplasmic reticulum. The released calcium 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 acetylcholine from the receptor :

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

Non depolarizing (competitive) neuromuscular block:

Non depolarizing muscle relaxants do not alter the structural conformation of the actylcholine receptor , but prevent depolarization by combining reversibly with one or both of the α-subunits, preventing access by acetylcholine and opening of the ion channel. This results in a lower endplate potential, which does not reach the threshold necessary to initiate an action potential. This is a dynamic situation with the various molecules repeatedly combining and being released from the receptor. The neuromuscular transmission or block depends on the relative concentrations of acetyl choline and the blocking drug and their relative affinities for the postsynaptic nicotinic receptor. About 70-80% of receptors have to be occupied by a nondepolarizing drug before the response to nerve stimulation is affected.[9] Thus during recovery from a non-depolarizing block, patients with a tidal volume of atleast 5ml/kg have 80% of acetyl choline receptors may still be occupied by the drug and 50% receptors are occupied when sustained head lift for 5seconds is elicitable.

The phenomenon of fade and post-tetanic facilitation are thought to be due to block of the prejunctional nicotinic receptor. The blocking drug inhibits the positive acetylcholine feedback, which stimulates acetylcholine synthesis and mobilisation in the presynaptic nerve endings.

***Features of Nondepolarizing blockade*:**

1. No muscle fasciculation.
2. Slow onset to maximal effect and slow recovery compared to succinylcholine
3. The central muscles like diaphragm, larynx, masseter, orbicularis oculi tend to be affected earlier and recover from the block sooner than those of the peripheral muscles like adductor pollicis probably due to preferential perfusion.[10,11]
4. Presence of fade and post tetanic potentiation.
5. Despite flaccid paralysis, the muscles are still able to respond to direct stimulation.
6. The muscle block is reversed pharmacologically by anticholinesterases.
7. Low potency drugs like rocuronium and rapacurium have rapid onset of action while potent relaxants like doxacurium and pancuronium have relatively slower onset of action and a longer duration of action.[12,13]

Rocuronium produces muscle paralysis by competitive antagonism of nicotinic cholinergic receptors of skeletal muscles. Its potency is about 15-20 percent of that of vecuronium. With equipotent doses, onset of

rocuronium at the adductor pollicis muscle is much faster than that of atracurium and vecuronium.[14] It has an intermediate duration of action, a rapid recovery and shows minimal cumulation. Paralysis occurs first in the well perfused fast muscles and last in the diaphragm.[15] Onset of block is faster, but less intense at the diaphragm and adductor muscles of the larynx than at adductor pollicis muscle.[17] The diaphragm is affected later but recovers earlier than the adductor pollicis. Nondepolarizing block produced by rocuronium is antagonised by anticholinesterases.

NEURO MUSCULAR MONITORING

Muscle relaxants have come in routine use and have become vital to the care and well being of patients undergoing anaesthesia and surgery. In most instances adequacy of neuromuscular relaxation and recovery from neuromuscular blockade is judged clinically. Sudden recovery from muscle relaxant effect in the middle of the surgical procedure and postanaesthetic recurarisation are still common.Therefore, monitoring the neuromuscular blockade using neuromuscular monitor is essential. Neuromucular blocking drugs have a narrow therapeutic index and there is wide interindividual variability.So, it is wise to monitor their effect in all patients. The response of muscle to nerve stimulation should be assessed to know about the status of neuromuscular functioning precisely. By monitoring the neuromuscular blockade, sufficiency of relaxation to tracheal intubation can be determined, adequacy of surgical relaxation

can be maintained and immediate postoperative critical events like ventilatory insufficiency and hypoxemia and delayed complication like pulmonary infection could be prevented.

CLINICAL APPLICATION

The narrow margin of safety and the intention to provide a balanced adequate surgical relaxation with safe restoration of function at the end of procedure makes neuromuscular monitoring an important tool.

Intubation:

Onset of block and adequacy of intubating conditions can be assessed using TOF stimulation. Orbicularis oculi can be used for procedures where perfect immobilisation is required during intubation as in case of increased ICP or open eye injury.

Maintenance of block :

Adequate relaxation for abdominal surgery is generally correlated with 1-2 twitches of TOF. Diaphragm is relatively resistant and requires more neuromuscular blockade. Intraoperatively, the intensity of blockade may be assessed if necessary using post tetanic count.

Detecting recovery from neuromuscular blockade :

When the TOF ratio is 0.4 or less, the patient is generally unable to lift the head or arm. Tidal volume may be normal, but the vital capacity and inspiratory force will be reduced.

When the ratio is 0.6, most patients are able to lift the head for 3 seconds, open the eyes widely and stick out the tongue.

At a TOF ratio of 0.7 to 0.75, the patient can normally cogh sufficiently, and lift the head for atleast 5 seconds, but the grip strength may still be low.

When the ratio is 0.8 and higher, vital capacity and inspiratory force are normal. The patient may, however, still have diplopia and facial weakness.

TOF ratio must exceed 0.8 or even 0.9 to exclude clinically important residual neuromuscular blockade .

Residual block (TOF ratio < 0.9) is associated with functional impairment of muscles of pharynx and upper esophagus, predisposing to regurgitation and aspiration.

In long term rehabilitation in ICU:

Residual paralysis due to NMB can lead to polyneuropathy and myopathy requiring ventilatory support for a long duration after termination of muscle relaxant. Minimal use of NMB can prevent long term residual paralysis. Patient can be maintained at T1 or T2 of TOF stimuli for quick recovery.

NERVE STIMULATOR NS-100

PRINCIPLE OF NERVE STIMULATION

The current strength is the determining factor in nerve stimulation. Threshold current is the amount of current required to elicit a detectable response . It is about 15mA, when surface electrode is applied. Maximal current is the amount of current needed to induce depolarization in all the nerve fibers of the nerve bundle and evoke maximal response from the muscle.

Supramaximal current is 10—20% more than maximal current or 2.75 times more than threshold current. The resistance can be reduced by removing the hair, decornifying and de-creasing the skin.

Neuromuscular function is monitored by evaluating the muscular response to supramaximal electrical stimulation of a peripheral motor nerve. The response of the whole muscle depends on the number of nerve fibers activated. If a nerve is stimulated with sufficient intensity, all the muscle fibres supplied by that nerve will react and the maximum response will be triggered. After administration of a neuromuscular blocking drug, the response of the muscle decreases in parallel with number of fibres blocked. The reduction in response during constant stimulation reflects the degree of neuromuscular blockade.

The stimulating wave form should be rectangular (square wave) and monophasic, so that current is maintained throughout the stimulus.

The frequencies of stimulus is expressed in Hertz(hz). 1 Hz= 1 cycle/sec.The usual frequency for various types of stimulations ranges from 0.1 Hz—100Hz

Surface gel coated electrodes for electrocardiogram can be used. With large electrodes conducting area is large, obtaining a supramaximal stimulus will be difficult. Small paediatric electrodes can be used to avoid stimulation of neighbouring nerves. Needle electrodes may be used in thick skinned and obese patients.

Sites of nerve stimulation

Electrode	**Nerve**	**Muscle**	**Response**
Ulnar aspect of wrist	Ulnar Nerve	Adductor pollicis	Adduction of thumb
Behind ascending ramus	Facial N	Superficial facial muscles	Movements of muscles of facial expression
Beneath zygomatic arch	Mandibular N	Masseter	Jaw contraction
Laterally above zygomatic arch	Facial N	Orbicularis oculi	Eye blink
Head of fibula	Superficial peroneal.N	Tibialis anterior	Dorsiflexion of foot
Behind lateral malleolus	Post. Tibial N.	Extensor hallucis	Dorsiflexion of great toe

TRAIN OF FOUR STIMULUS

In TOF, four supramaximal stimuli are given every 0.5 seconds, that is at a frequency of 2 Hz. Each set (train) of stimuli is repeated every tenth to twelfth second, when used continuously.

Each stimulus in the train cause the muscle to contract if neuromuscular transmission is normal. With neuromuscular blockade, there is a decrease in amplitude of response.

a. With a partial non-depolarizing block, there is a fade in the response, that is the amplitude of the response decreases gradually from the first to the fourth response.

   Dividing the amplitude of the fourth response by the amplitude of the first response provides the TOF ratio. The ratio is inversely proportional to the degree of NMB.

b. With a depolarizing block , there is a decrease in amplitude of all the four responses compared to the control. No fade occurs in the TOF response.

USES:

1. To judge the onset of blockade : Tracheal intubation may be attempted when the response to single twitch or TOF is noted to weaken visibly.

2. To judge the depth of block : Intraoperatively, depth of neuromuscular blockade is assessed by monitoring the response to TOF

   Intense blockade—no response to TOF

   Moderate or surgical blockade- 1or 2 response to TOF is present

Number of responses detected	Degree of neuromuscular blockade
1	95%
2	90%
3	80%
4	75%

3. To judge the adequacy of recovery from block : When the third or fourth response to TOF stimulation appears, adequate recovery can be achieved within 5 minutes of neostigmine administration.

4. TOF monitoring is far less painful than tetanic stimulation. It can be performed in awake sedated patient.

Other Patterns of stimulation

1. Single twitch stimuli

In this, supramaximal stimuli are applied to a peripheral motor nerve at frequencies ranging from 0.1Hz to 1 Hz. A control twitch height should be measured before administering muscle relaxant. Twitch height

remains normal until 75% of receptors are blocked and disappears when 90% of acetylcholine receptors are blocked. This method can be used to ascertain adequacy of muscle relaxation for tracheal intubation.

2. Tetanic Stimulation

Used to evaluate residual neuromuscular blockade. During normal neuromuscular transmission and a pure depolarizing block, the muscle response to 50-Hz tetanic stimulation for 5 seconds is sustained. During a partial nondepolarizing block, the response will not be sustained ie.,fade occurs. Post tetanic potentiation is the enhancement of response to single twitch stimuli , which is applied two minutes after the appearance of fade to tetanic stimulation. Tetanic stimulation is painful and should not be applied on conscious patient.

3. Post tetanic count

The principle of post tetanic facilitation is used where 50 Hz tetanic stimulation is applied for 5 seconds, then after an interval of 3 seconds, a supramaximal stimuli is delivered every second. The number of evoked post tetanic twitch detected is called post tetanic count (PTC). The main application of PTC is to evaluate the degree of neuromuscular blockade when there is no response to single twitch or TOF after administering large dose of non-depolarizing block. PTC is useful to maintain profound muscle relaxation whenever sudden patient movement

must be avoided as in ophthalmic surgery and intubation in raised ICP where the PTC count should be “O” (Zero). PTC helps to estimate the time interval to recover from intense muscle blockade. The PTC correlates inversely with the time required for a return of single twitch or TOF responses.For intermediate-duration drugs, the time from a PTC of 1 to reappearance of twitch is 15 to 20 minutes.

PTC- 0/1	-	Intense block
3	-	Less intense block
8-10	-	Surgical block

4. Double burst stimulation:

Double burst stimulation (DBS) was developed to allow the clinician to detect subtle degree of NMB without the use of recording devices. Two short burst of tetanic stimuli delivered at a frequency of 50 Hz are repeated by a 750 ms interval. Each burst consists of series of 3 and 2 impulse ($DBS_{3,2}$) or 3 and 3 impulses ($DBS_{3,3}$). A good correlation between $DBS_{3,3}$ ratio and TOF ratio had been demonstrated. During recovery and immediately after surgery, tactile evaluation of the response to $DBS_{3,3}$ is superior to tactile evaluation of the response to TOF stimulation.

Methods for Recording of Evoked Responses :-

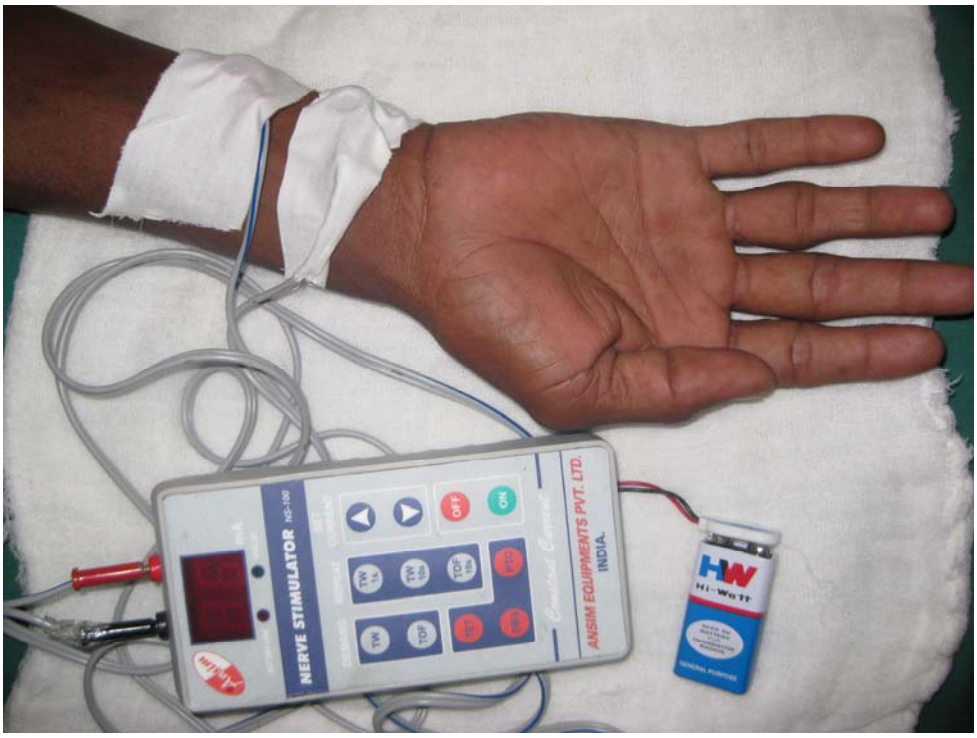
1). Visual and Tactile measurement

The simplest way of recording the response is to look and feel for it

2). Mechanomyography

3). Electromyography

4). Acceleromyography



characteristic	Depolarizing NMB (partial)	Nondepolarzing NMB (partial)
Tetanic stimulation	No fade	Fade
Post-tetanic facilitation	None	Yes
Train –of-four	No fade	Marked fade

REVIEW OF LITERATURE

Rocuronium, a non-depolarizing neuromuscular blocker was brought into clinical practice in the mid ninties.

Dose of Rocuronium may influence the onset and duration of action. Literature was reviewed to compare the intubating conditions with varying doses of rocuronium.

1.*Jamshid Ali, Showkat Ahmad Gurckoo , Asaf Shora and Shagufta Qazi in 2008,* studied intubating conditions of rocuronium bromide and succinylcholine during rapid sequence induction of anaesthesia in adult patients. The main variables assessed in these patients were intubating conditions at 60 or 90 seconds after administration of neuromuscular blocking agent according to four point scale of **Cooper et al**. They concluded that it was safe to use rocuronium for rapid sequence induction, but intubating conditions after 0.6mg/kg rocuronium at 60secs of assessment were not satisfactory in a significant number of cases. Therefore,they suggested that higher doses of rocuronium (0.9—1.2mg/kg) should be used for rapid sequence induction of anaesthesia especially if the anticipated surgical time is prolonged.

2.*Claudia A.Y. Cheng Fanzca and Cindy S.T.Aun MD.,21,May 2001***,** compared rocuronium(0.6mg/kg&0.9mg/kg) and suxamethonium for rapid tracheal intubation in children. Differences between

suxamethonium and rocuronium 0.6 mg/kg and between the two doses of rocuronium were statistically significant (P=0.016 and 0.007, respectively).They concluded rocuronium 0.9 mg/kg provides similar intubating conditions to suxamethonium 1.5 mg/kg during "modified rapid sequence induction" using alfentanil and thiopentone in children (P=0.671). Rocuronium 0.6 mg/kg was inadequate.

3. *K.C.Mc. Court, L.Salmela, R.K.Mirakhur and M.Carroll ,1998;53(9):867-71* compared rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia

This study was designed to compare the tracheal intubating conditions during rapid sequence induction of anaesthesia using rocuronium 0.6 (n = 61) or 1.0 $mg.kg^{-1}$ (n = 130) or suxamethonium 1.0 $mg.kg^{-1}$ (n=127) as the neuromuscular blocking drugs. Anaesthesia was induced with fentanyl 1-2$\mu g.kg^{-1}$ and thiopentone 5 $mg.kg^{-1}$ (median dose) and intubating conditions were assessed 60 seconds after the administration of the neuromuscular blocking drug by an observer, who was not aware of the drug given. Intubating conditions were graded on a three-point scale as **e**xcellent, **g**ood or **p**oor, the first two being considered as clinically acceptable. The study was carried out in two parts. At the end of the first part a comparison between the two doses of rocuronium was carried out when at least 50 patients had been enrolled in each group. The results showed the intubating conditions to be

significantly superior with the 1.0 $mg.kg^{-1}$ dose of rocuronium ($p<0.01$). Final comparison between the 1.0 $mg.kg^{-1}$ doses of rocuronium and suxamethonium showed no significant difference in the incidence of acceptable intubations (96 and 97%, respectively). The incidence of excellent grade of intubations was, however, significantly higher with suxamethonium (80% vs. 65%; $p=0.02$). It was concluded that rocuronium 1.0 $mg.kg^{-1}$ could be used as an alternative to suxamethonium 1.0 $mg.kg^{-1}$ as part of a rapid sequence induction provided there is no anticipated difficulty in intubation. The clinical duration of this dose of rocuronium was, however, 50-60 minutes.

4. *Anestesiol. vol.54 no.2 Campinas Mar./Apr. 2004 Maria Cristina Simões de Almeida, TSA, M.D.I; Rogério Silveira Martins, TSA, M.D.II; Ana Lúcia Costa Martins, M.D.I*

This study aimed at comparing intubation conditions after 0.6 mg.kg-^{1} rocuronium at 60 seconds in children, adults and elderly patients.

METHODS: 60 ASA I,II,III patients aged 1 to 88 years who were divided in three groups according to age: Group 1 (G1) children up to 12 years of age; Group 2 (G2), adults aged 18 to 65 years; Group 3 (G3) patients above 65 years of age.

CONCLUSIONS: In the conditions of their study, 0.6 $mg.kg^{-1}$ rocuronium was sufficient for tracheal intubation in 60 seconds in adult

and elderly patients. It was, however, insufficient for clinically acceptable intubating conditions in 60 seconds in 100% of children.

Patients were premedicated with 7.5 to 15 mg midazolam oral (adults and elderly), or 0.5 to 1 $mg.kg^{-1}$ for children (maximum 15 mg orally). After preoxygenation with 100% O_2 for 3 minutes, anesthesia was induced with fentanyl(3 to 5 $\mu g.kg^{-1}$) and propofol 3 to 4 $mg.kg^{-1}$ (children) or 2 to 3 $mg.kg^{-1}$ (adults and elderly) . All patients received rocuronium in the fixed dose of 0.6 $mg.kg^{-1}$ in 5 seconds and tracheal intubation was performed 60 seconds after rocuronium injection. For 0.6 $mg.kg^{-1}$ rocuronium, optimal time to obtain best intubating condition is approximately 70 seconds. Other authors, however, have emphasized that tracheal intubating conditions with 0.6 $mg.kg^{-1}$ rocuronium are poorer than those obtained with 1$mg.kg^{-1}$ succinylcholine . So,the current trend is to administer 0.9 to 1.2 $mg.kg^{-1}$ rocuronium when the aim is to replace succinylcholine.

For fast and safe induction, it is important that, in addition to laryngeal muscles,diaphragm and intercostal muscles are also blocked to prevent tracheal tube or cuff reactions like bucking or coughing after its placement.

5.Ali A. Sheikh N A, Khawaja S, Saleem J and Kaul S U., in March 2008, studied to find out whether rocuronium produces intubating conditions as good as suxamethonium in Rapid Sequence Induction

(RSI) in elective caesarean section. In their study, they found that clinically acceptable intubating conditions (good and excellent) were similar with both groups, although the rate of excellent intubating conditions was higher with suxamethonium that was not statistically significant. Their study showed that rocuronium 1.0 mg/kg provides equally good intubating conditions when compared with suxamethonium 1.5 mg/kg in elective caesarean section in 60 seconds using RSI.

6.*Mazurek A J ; Hann S*. compared rocuronium versus succinylcholine for rapid sequence induction and concluded that larger doses of rocuronium may be an alternative to suxamethonium.

7.*MC Donald PF, Sanisbary DA*, evaluated onset time and intubating conditions of rocuronium bromide in children and concluded that intubating conditions are achieved faster with rocuronium compared to other non depolarizing relaxants.

8.*DE Mey J.C DE Brock M, et al., in 1994* evaluated the onset and intubating conditions of rocuronium bromide in three doses of 0.6 mg/kg, 0.75 mg/kg and 0.9 mg/kg. They found acceptable intubating conditions with 0.6 mg/kg dose at 60 seconds. The onset time ranged from 1 to 1.7 minutes. Increasing the dose, improved intubating conditions and reduced onset time.The duration of action with 0.6 mg/kg was 27.3 ± 8.2 minutes,

with 0.75 mg/kg was 43.6 ±12.0 minutes and 0.9 mg/kg was 53.0 ±15.2 minutes.

9.*Stoddart* compared intubating conditions of rocuronium 0.6mg/kg with suxamethonium 1 mg/kg for tonsillectomy patients and onset time was 92 seconds and 42 seconds respectively.

10.*J. Viby – Mogenson* observed that the average clinical duration of action of intubating dose is shorter in children than adults which may be due to large volume of distribution of control compartment in children.

11.*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 the relaxant to have moderate potency with rapid onset time, intermediate duration of action and rapid recovery.

12.*Crul JF, Vanbelleghem V, et al.,* in 1995 studied intubating conditions of rocuronium bromide with alfentanil and propofol at 45 seconds, with a dose of 0.6 mg/kg.They obtained excellent intubating conditions in 60% and good conditions in 60%. In a dose of 0.9mg/kg, they obtained excellent intubating conditions in 89% and good conditions in 11%.

13.*Jean Paul Cantineau, et al* (1994) found that the diapharam is more resistant than the adductor pollicis to rocuronium 0.6 mg/kg. The onset time for muscle relaxation after 0.6 mg/kg rocuronium was shorter for the adductor pollicis muscle than for the diaphragm (80+/- 20 Vs 120

+/-62sec). Time for 10%, 25%, 75% and 90% recovery of twitch height were 34+/- 10, 40+/-10, 56+/-20 and 64+/-21 minutes, respectively for the adductor pollicis and significantly shorter for the diaphragm, 17+/-10, 23+/-9, 33+/-13, 35+/-10 minutes respectively. The intubating dose of 0.6mg/kg is close to ED_{95} of 0.5mg/kg for the diaphragm.

14. *Peter M.C Wright., et al* (1994) 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 action 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 1.2 mg/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 succinycholine at the adductor pollicis but is significantly delayed compared with that of succinycholine at the laryngeal adductors.

15.*Cooper R, Mirakhur RK, et al.,* in 1992 compared the intubating conditions after administration of rocuronium 0.6mg/kg and suxamethonium 1 mg/kg at 60 seconds. In the rocuronium group, the intubating conditions were excellent in 14/20, good in 4/20 and fair to poor in 2/20 . In the suxamethonium group, the intubating conditions were excellent in 19/20 and good in 1/20.They recorded an onset time of 88.9 seconds and duration of 30.5 $\pm$ 7.5 minutes for rocuronium in a dose of 0.6 mg/kg

16.*Muir AW, Anderson KA, et al.,* in 1994 studied the interactions between rocuronium bromide and some drugs used during anaesthesia. They concluded that halothane, isoflurane and enflurane significantly reduced the dose requirement of rocuronium. The duration of action was markedly potentiated by enflurane and only slightly by halothane. Nitrous oxide did not affect the dose or duration of rocuronium. Among I.V anaesthetics, thiopentone and ketamine moderately potentiated the action of rocuronium. Propofol and alfentanil had a minimal effect. Morphine and chlorpromazine produced some potentiation of action of rocuronium. Streptomycin appears to potentiate its effect too.

17.*Kirkegaard – Nielsen H., et al.,* (1999) studied rapid tracheal intubation with rocuronium using a probability based approach. 80 adult patients anaesthetized with fentanyl 2 µg/kg and propofol 2mg/kg randomly received rocuronium 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 1.04 mg/kg respectively. Estimated time to obtain 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, rocurionium 1.04 mg/kg gives 95% probability of successful intubation at 60 seconds.

18.*Levy JH, Davis G, et al.,* in 1994 determined the haemodynamics and histamine release of rocuronium bromide over 2,3 and 4 x ED_{95} doses. They found no statistically significant differences among the groups with respect to heart rate, systolic blood pressure, mean arterial pressure and histamine release at peak effect for the initial 6 minutes after the bolus dose. They concluded stability even when used in doses upto 4 x ED_{95}

19.*Andrews JI., 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 1 mg/kg or succinylcholine 1mg/kg . Intubating conditions were assessed at one minute and intubation was performed. They concluded that rocuronium 1mg/kg given along with propofol in a rapid sequence induction of anaesthesia is clinically equivalent to succinylcholine 1mg/kg.

20.*Magorian T, Flannery KB, et al.,* in 1993 evaluated the onset time and duration of action of rocuronium in 3 dosage schedules. A dose of 0.6 mg/kg had a onset time of 89 seconds with a duration of action ranging from 23 to 75 minutes with a mean of 37 minutes. In a 0.9 mg/kg dose, the onset time was 75 seconds and duration of action ranging from 25 to 88 with a mean of 53 minutes. In a 1.2 mg/kg dose, onset time was 55 seconds & a duration of action ranging from 38 to 150 with a mean of 73 minutes.

MATERIALS AND METHODS

This study was conducted in 60 patients who met the study criteria and underwent general anaesthesia with endotracheal intubation.

DESIGN OF STUDY:-

It is a Comparative Prospective Randomized clinical trial study. The study was approved by the Ethical Committe and done during the period from May 2009 to August 2009 in the department of anaesthesiology, Chengalpattu medical college hospital, Chengalpattu. The surgeon was also duly informed of the study.

The inclusion criteria were:-

1. Patients of ASA grade I and II of either sex
2. MPC I and II
3. Age group of 25 to 45 years
4. Elective surgeries posted under G.A.

The exclusion criteria were :-

1.Known or anticipated difficult airways

2.Patients with neuromuscular disease

3.Drugs known to interact with neuromuscular blocking agents

4.Family H/O Malignant Hyperthermia

5.Renal or Hepatic disorder

6.Known allergy to drugs

Sixty patients who fulfilled the eligibility criteria were enrolled for the study. Preoperatively informed, written consent was obtained from these patients. These patients were systematically randomized into three groups of twenty each.

Group 1 ----- Thiopentone 5mg/kg + Rocuronium 0.6 mg/kg

Group 2----- Thiopentone 5mg/kg + Rocuronium 0.9 mg/kg

Group 3----- Thiopentone 5mg/kg + Rocuronium 1.2 mg/kg

PREOPERATIVE EVALUATION

In all patients, age, I.P.No., baseline vital parameters were recorded. History regarding previous anaesthesia, surgery, any significant medical illness , medications and allergy were recorded.

Complete physical examination and airway assessment was done.

Following laboratory investigations were done:-

Haemoglobin % Urine- Albumin and sugar, Packed cell volume Blood- urea, sugar, creatinine, Liver Function Tests, E.C.G. X-Ray Chest

ANAESTHESIA PROTOCOL

Pre operative visit was done to allay anxiety and good rapport was established with the patient and the procedure was explained to the patient.

PREMEDICATION

All patients received Inj. Pentazocine 0.5mg/kg and Inj. Glycopyrollate 10µg/kg I.M. 45 minutes prior to surgery.

INDUCTION OF ANAESTHESIA

After shifting the patient to operation theatre, intravenous line was secured using 18G cannula in a vein in the dorsum of hand and maintenance intravenous fluids were started.

Following monitors were connected to the patients :

1.Non invasive blood pressure

2. Electro cardiogram monitor

3. Pulse oximeter

4. Neuromuscular monitor

For stimulation of the ulnar nerve ,the electrodes are best applied at the volar side of the wrist The Ulnar nerve motor point is located 15—

25mm proximal to the pisiform bone on the thumb side of the flexorcarpiulnaris tendon.

The distal electrode was placed about 1cm proximal to the point at which the proximal flexion crease of the wrist crosses the radial side of the tendon to the flexor carpi ulnaris muscle. The proximal electrode was placed 2-5 cm proximal to the distal electrode[29]. With this placement of electrodes, electrical stimulation normally elicits only finger flexion and thumb adduction. Polarity of the electrodes is less crucial when both electrodes are close to each other at the volar side of the wrist; however, placement of the negative electrode distally normally elicits the greatest neuromuscular response.

The patient was preoxygenated for 3 minutes and then induced with Inj.Thiopentone 5mg/kg 2.5% solution given over 15 seconds. Following loss of consciousness , the ulnar nerve was stimulated at the wrist using peripheral nerve stimulator.The current strength was progressively increased and the single twitch elicited. When the maximal thumb adduction was obtained the current strength was noted and one and half times the strength was used for elicitation of Train Of Four Stimulus.The HR and B.P. with supramaximal stimulus were noted.

A bolus i.v. dose of Inj.Rocuronium 0.6mg/kg(2× ED_{95}) or Inj.Rocuronium 0.9mg/kg(3× ED_{95}) or Inj.Rocuronium 1.2mg/kg(4× ED_{95}) depending on the group was given over a period of in 5 seconds.

Patient was ventilated with 100% oxygen. TOF was elicited every 10 seconds and the trachea was intubated after 80 seconds with appropriate size endotracheal tube after doing a proper laryngoscopy. Endotracheal tube was secured after confirming bilateral air entry. The conditions of intubation were evaluated and scored according to the scoring system described by Cooper et al.

The time from the end of injection of the relaxant to the time when all four responses of TOF were abolished was taken as onset time.

After intubation and observation of the intubating conditions and haemodynamic profiles, anaesthesia was maintained with 33.3% oxygen and 66.7% nitrous oxide using closed circuit system with controlled ventilation. B.P. and Pulse Rate were recored 1minute, 3minuutes and 5minutes after injection of the relaxant. Volatile anaesthetics were not used in this study.

Neuromuscular function was monitored using TOF stimuli every 5minutes. The interval between the administration of the bolus dose of the relaxant and the reappearance of the two responses to TOF was taken as the duration of action.

OBSERVATIONS AND RESULTS

The following observations were recorded :-

1. The mean onset of neuromuscular blockade and duration of action were calculated for all the three groups.

2. The heart rate, systolic pressure, diastolic pressure, mean arterial pressure were recorded before induction, during intubation and 1minute, 3minutes and 5 minutes after intubation and compared between the three groups

3. Intubating conditions were scored by a scoring system used by Mirakhar R.K. , Cooper A.R. and Clark R.S.J[30]. (Table II and Table III). The scores for jaw relaxation, vocal cord position and response to intubation and the total scores are compared between the 3 groups .

TABLE II

Scoring of Intubating Conditions

Score	Jaw relaxation	Vocal Cords	Response to intubation
0	Poor (impossible)	Closed	Severe coughing or bucking
1	Minimal(difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None

TABLE III GRADING

Intubating Conditions	Score
Excellent	8—9
Good	6—7
Fair	3—5
Poor	0—2

STATISTICAL EVALUATION

All recorded data were entered using MS Excel software and analyzed using STATA software for determining the statistical significance. Analysis of Variance (ANOVA) was used to study the significance of mean of various study parameters among the three groups. Student's 't' test was used to compare the two groups on mean values of various parameters. The p-value taken for significance is 0.05.

The study was conducted on 60 patients randomly allocated into 3 groups as given below :-

DRUG AND DOSAGE SCHEDULE

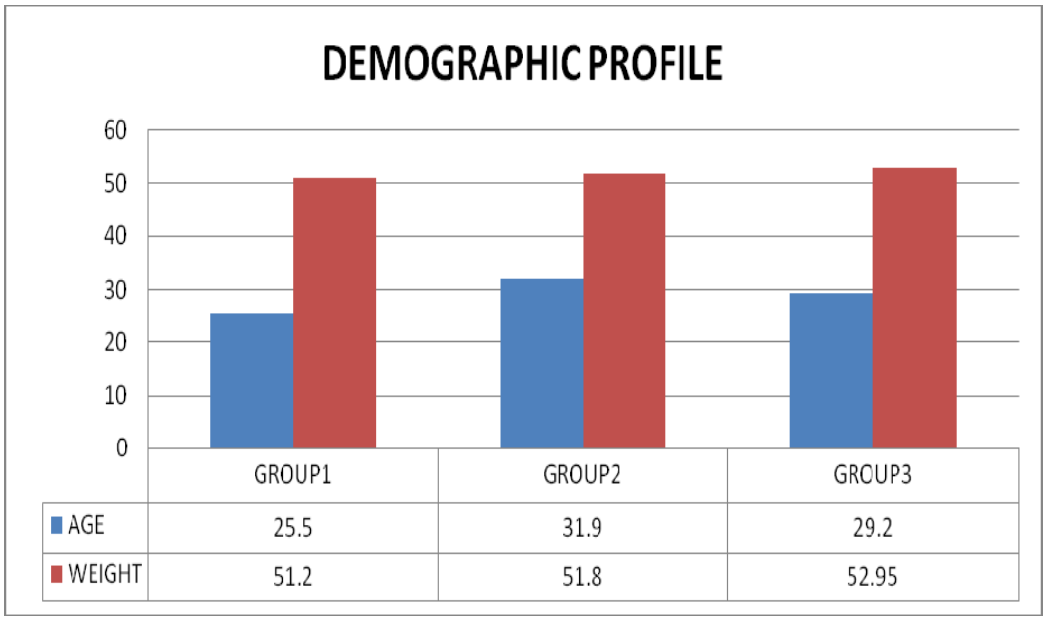
Group	Number of cases	Drug & Dosage
1	20	Rocuronium 0.6mg/kg
2	20	Rocuronium 0.9mg/kg
3	20	Rocuronium 1.2mg/kg

Statistical analysis :

TABLE IV Demographic profile

	GROUP 1	GROUP 2	GROUP 3	P
GENDER (M/F)	5/15	13/7	15/5	
AGE(YEARS) MEAN±SD	25.5±6.6	31.9±7.1	29.2±6.7	<0.05
WEIGHT (KG) MEAN±SD	51.2±10.8	51.8±14.1	52.95±8	>0.05

More female patients are present in Group-1 and more male patients in Group-3. More younger patients in Group-1. The age difference among the groups observed is statistically significant ($p < 0.05$). But there is no significant difference between the three groups regarding weight of the patient.


DEMOGRAPHIC PROFILE
60
50
40
30
20
10
0
GROUP1
GROUP2
GROUP3
AGE
25.5
31.9
29.2
WEIGHT
51.2
51.8
52.95

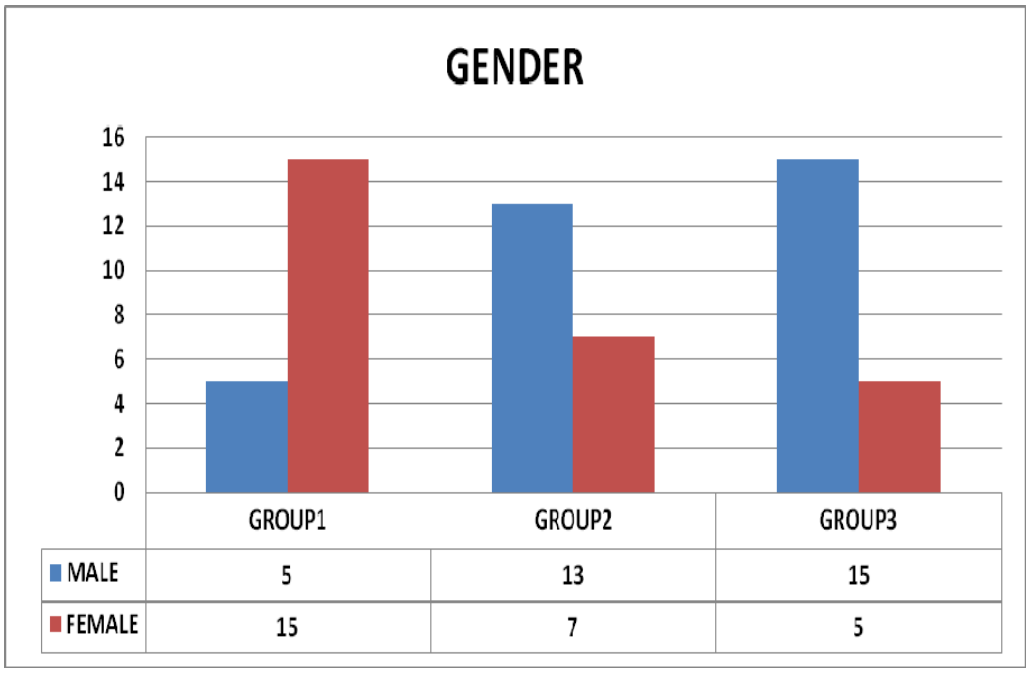
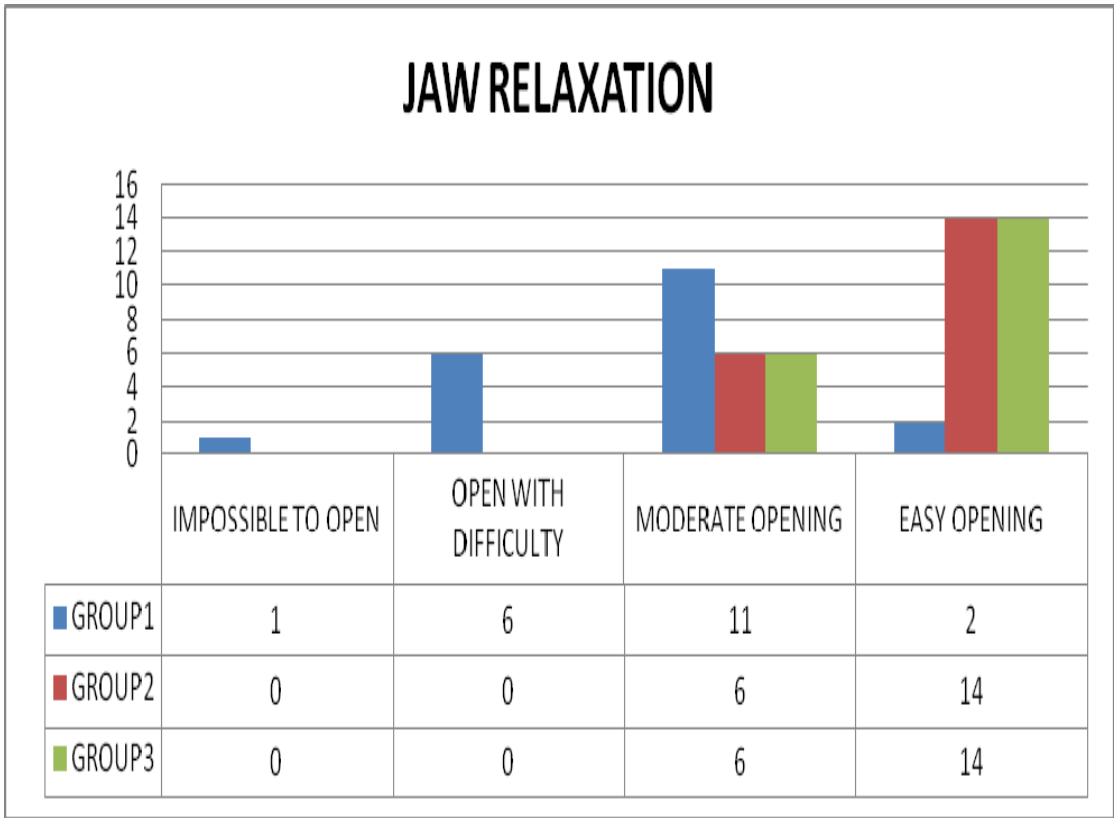
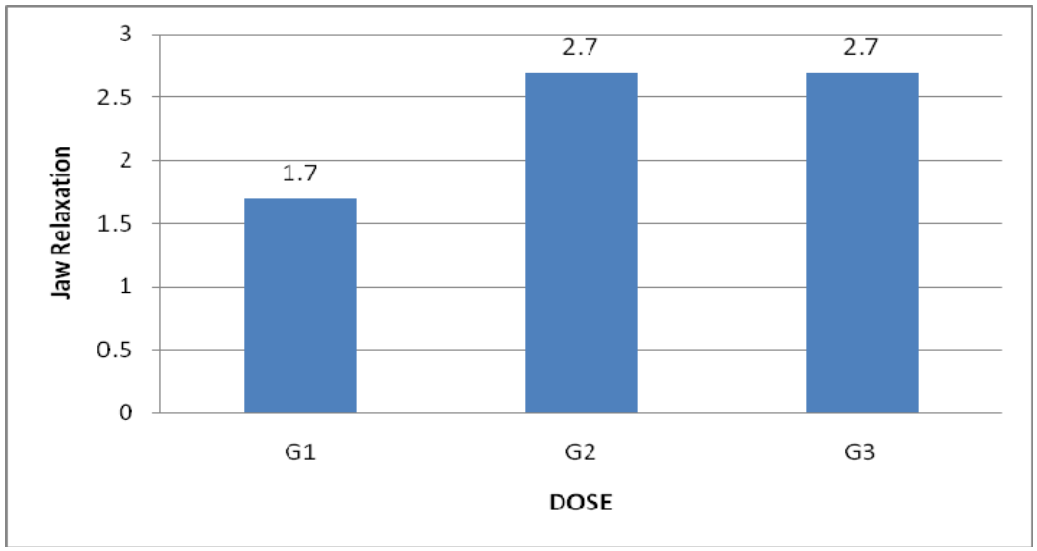

GENDER
16
14
12
10
8
6
4
2
0
GROUP1
GROUP2
GROUP3
MALE
5
13
15
FEMALE
15
7
5

TABLE V **Jaw relaxation**

	IMPOSSIBLE TO OPEN	OPEN WITH DIFFICULTY	MODERATE OPENING	EASY OPENING	MEAN ±SD
GROUP1	1	6	11	2	1.7± 0.7
GROUP2	0	0	6	14	2.7± 0.5
GROUP3	0	0	6	14	2.7± 0.5



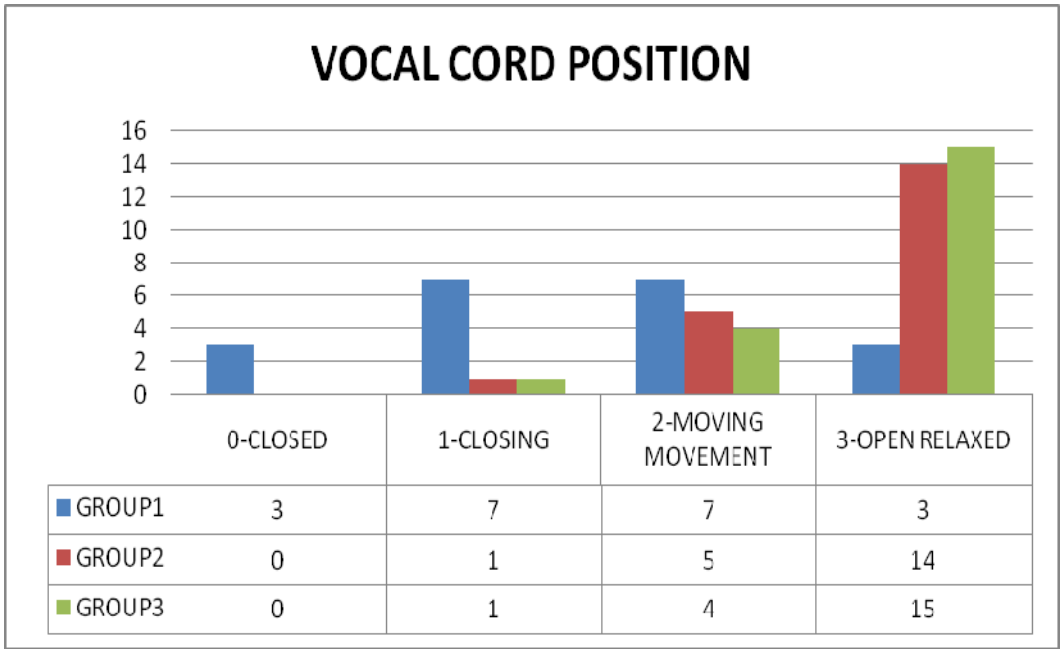
Mean Jaw Relaxation



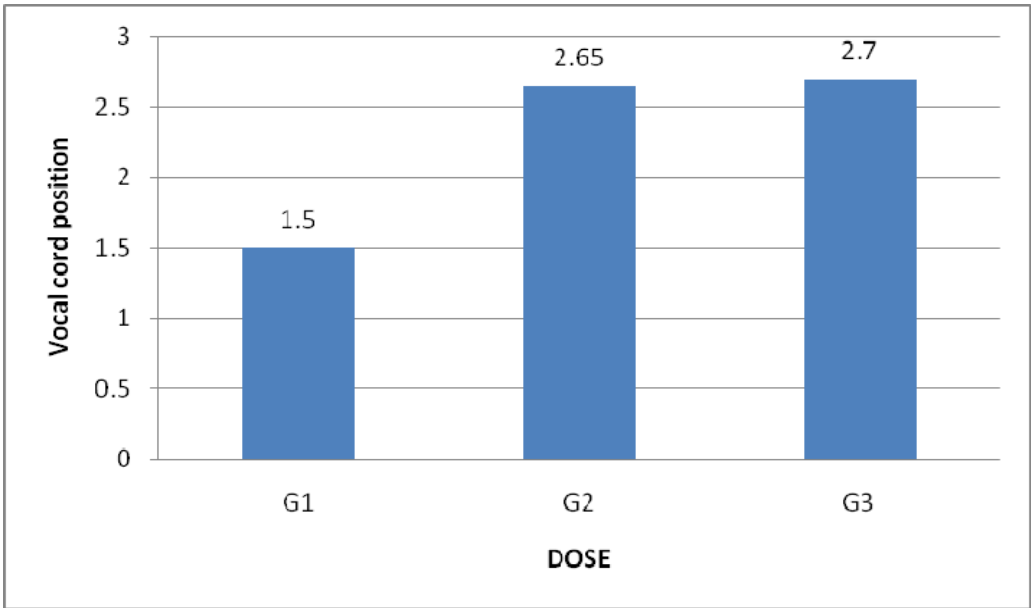
There is significant difference among the three groups on Mean Jaw Relaxation (p <0.05), but there is no significant difference between group-2 and group-3.

TABLE VI Vocal Cord Position

	0-CLOSED	1-CLOSING	2-MOVING MOVEMENT	3-OPEN RELAXED	MEAN ±SD
GROUP 1	3	7	7	3	1.5± 0.9
GROUP 2	0	1	5	14	2.7 ±0.6
GROUP 3	0	1	4	15	2.7± 0.6



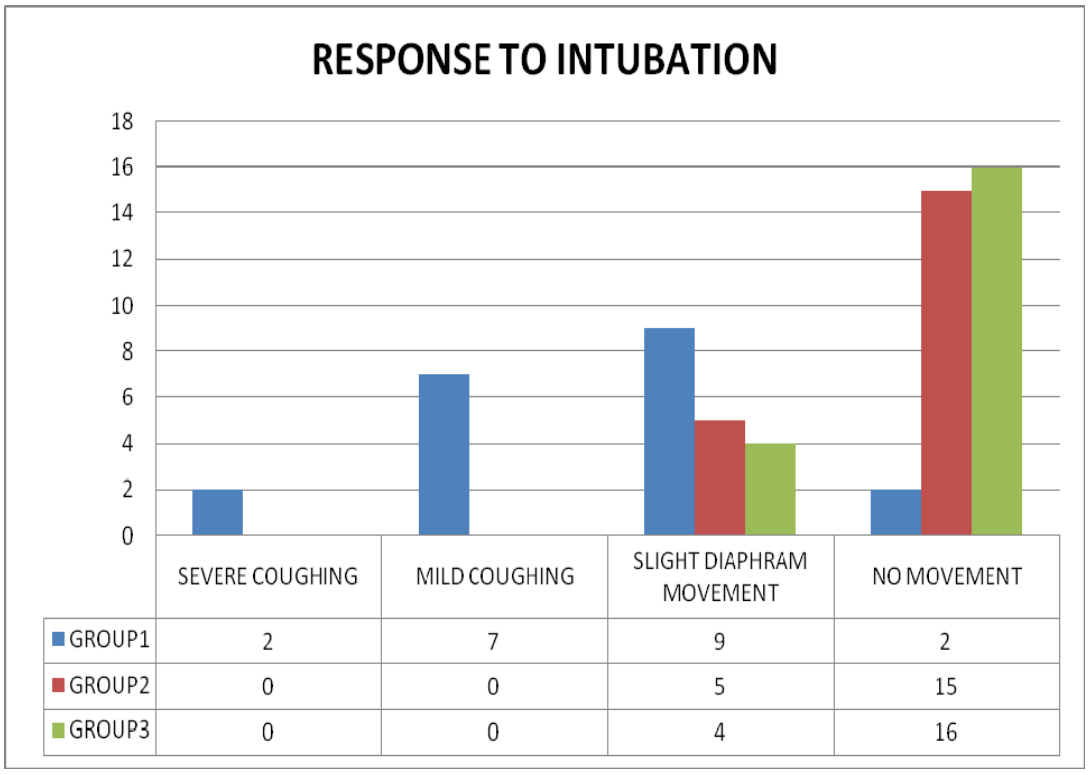
Vocal cord position



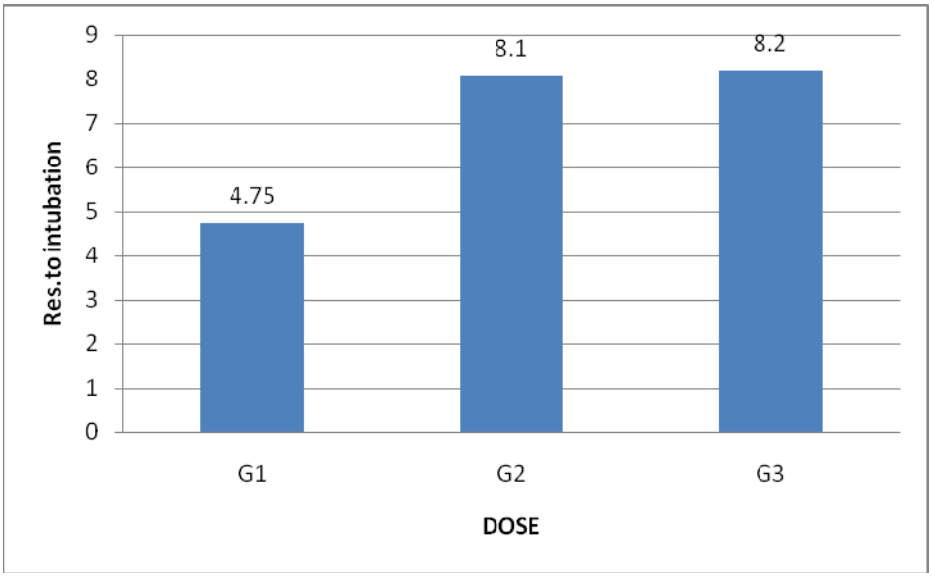
There is significant difference among the three groups on Mean vocal cord position ($p < 0.05$), but there is no significant difference between group-2 and group-3.

Table VII **Response to Intubation**

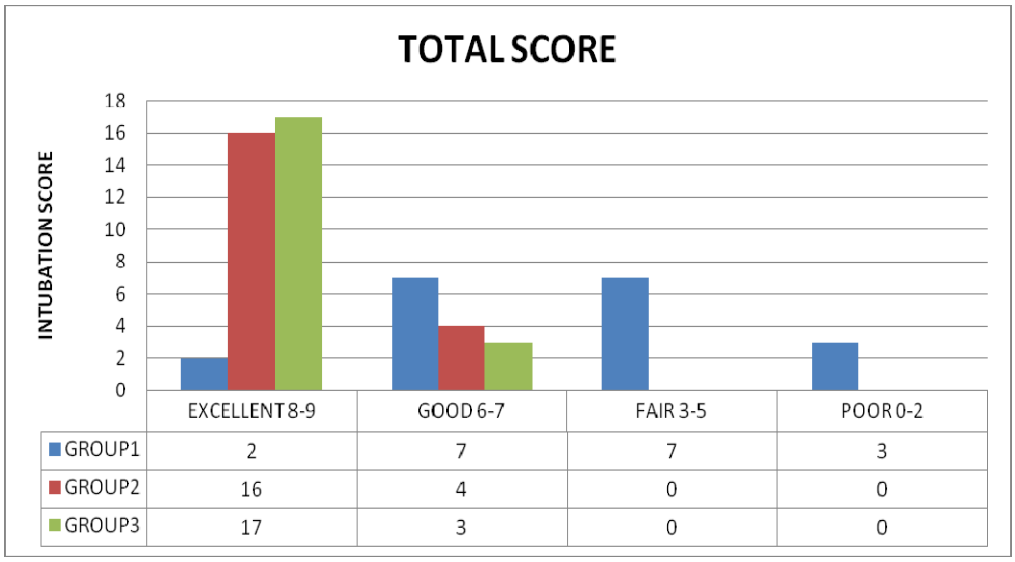
	SEVERE COUGHING	MILD COUGHING	SLIGHT DIAPHRAGM MOVEMENT	NO MOVEMENT	MEAN ±SD
GROUP 1	2	7	9	2	1.6± 0.8
GROUP 2	0	0	5	15	2.8 ±0.4
GROUP 3	0	0	4	16	2.8± 0.4



Response to Intubation



There is significant difference among the three groups on Mean Response to intubation (p <0.05), but there is no significant difference between group-2 and group-3.



GROUP I V_S GROUPII	P=0.001	- Significant
GROUP I V_S GROUPIII	P=0.001	- Significant
GROUP II V_S GROUPIII	P=0.79	**-Not significant**

MEAN ± STANDARD DEVIATION (MINIMUM-- MAXIMUM)

TABLE VIII HR

TIME	GROUP 1	GROUP 2	GROUP 3	P VALUE
BASELINE	90.3± 10.3 (70–108)	90.2± 11.3 (76–120)	90.15± 9.9 (76–110)	>0.05
INDUCTION	94 ± 9.1 (76–112)	93±11.9 (80– 126)	94.3±9.7 (80–112)	>0.05
INTUBATION	108± 11 (90–126)	96.4±12.9 (82–128)	99.15±10.3 (84–120)	<0.05
1 MIN	110±11.7 (94– 130)	93.05±10.4 (80–114)	95.65±9.5 (80–116)	<0.05
3 MIN	108.25±12.6 (90–136)	90.5±11.2 (78–119)	90.3±8.7 (80–110)	<0.05
5 MIN	99.9±11.2 (86–126)	86.4± 10.3 (74 –122)	85.65± 6.4 (74 –98)	<0.05

There is 5-40% increase in Heart Rate from baseline on monitoring the patients in Group-1 ,5-20% in Group-2 and Group-3. The higher HR observed at 1st minute in Group-1 and at intubation in Group 2& Group 3. Among the three groups, there is no statistical significant difference at Baseline and Induction ($p > 0.05$). Whereas, there is highly significant difference in mean HR among the three groups at intubation, 1st 3rd and 5th minute. There is no significant difference between Group 2&Group 3.

TABLE IX SYSTOLIC BLOOD PRESSURE

TIME	GROUP 1	GROUP 2	GROUP 3	P VALUE
BASELINE	118.5±7.9 (102–136)	121.95± 5.4(106– 130)	120.8± 6.8 (106–130)	>0.05
INDUCTION	117.2± 10.2 (100 – 136)	119.05±6.9(100–130)	117.5±9.4 (100–134)	>0.05
INTUBATION	135.1±8.7 (118–160)	123.4±4.8 (112–132)	126.05±7.0 (112 –138)	<0.05
1 MIN	134.2±6.7 (120–142)	121.55±6.9(110–138)	123.4±6.0 (110–130)	<0.05
3 MIN	130.1±5.1 (116–136)	118.95±7.0 (110 – 133)	120.1± 5.9 (106–128)	<0.05
5 MIN	124.2± 7.5 (106–138)	116.45±6.0 (103–128)	117.1±4.7 (106–122)	<0.05

There is 10-35% increase in Systolic blood pressure from baseline on monitoring the patients in Group-1 ,10-20% in Group-2 and Group-3. The higher Systolic blood pressure observed at intubation in Group-1 , Group 2 and Group 3.There is no statistical significant difference among the three groups at Baseline and Induction ($p > 0.05$). Whereas, there is highly significant difference among the three groups in mean SBP, at intubation, 1st 3rd and 5th minute. . There is no significant difference between Group 2 & Group 3

TABLE X DISASTOLIC BLOOD PRESSURE

VARIABLE	GROUP 1	GROUP 2	GROUP 3	P VALUE
BASELINE	75±6.1 (60–86)	77.4± 6.9 (68– 90)	74.8± 7.3 (64 –90)	>0.05
INDUCTION	73.9±9.3 (58–90)	76.70±7.9 (60–90)	73.55 ±8.0 (60–88)	>0.05
INTUBATION	85.45±8.9(68 – 109)	79.05±6.5 (70–92)	77.9± 5.6 (70–90)	<0.05
1 MIN	85.2±6.8 (70–98)	77.6± 5.5 (70–90)	76.4±5.2 (70–90)	<0.05
3 MIN	83.8±6.9 (76–98)	76.6±6.2 (68–90)	74.1± 4.3 (66–86)	<0.05
5 MIN	80.6±6.9 (67–94)	75±5.9 (66–90)	72.1±4.4 (64–80)	<0.05

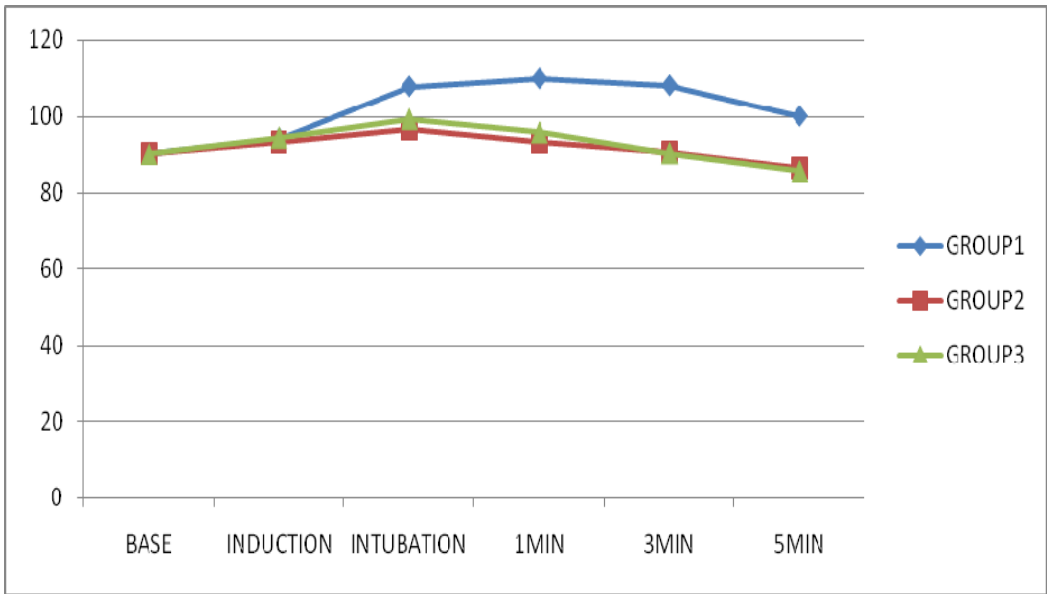
There is 10-25% increase in Diastolic blood pressure from baseline on monitoring the patients in Group-1, much less increase in Group-2 and Group-3. The higher Diastolic blood pressure observed at intubation in Group-1 , Group 2 and Group 3.There is no statistical significant difference among the three groups at Baseline and Induction (p >0.05). Among the three groups, there is highly significant difference in mean DBP at intubation, 1st ,3rd and 5th minute. There is no significant difference between Group 2 & Group 3.

TABLE XI MEAN ARTERIAL PRESSURE

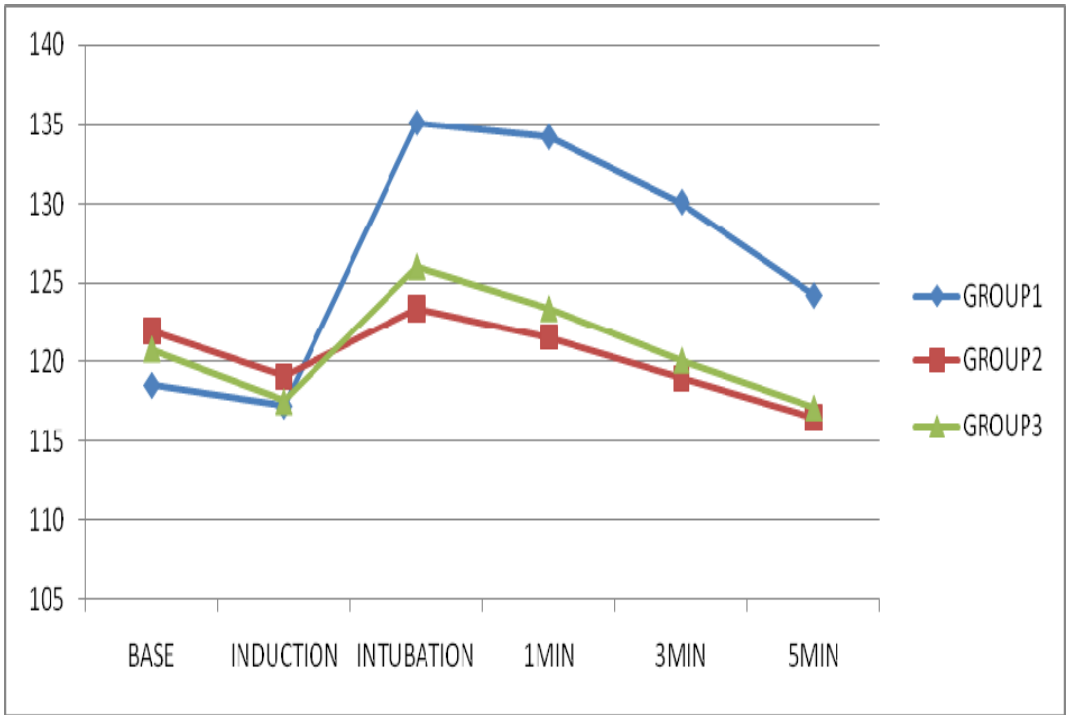
VARIABLE	GROUP 1	GROUP 2	GROUP 3	P VALUE
BASELINE	88.15±8.2 (67–103)	92.3± 5.6 (82 –101)	90.1± 6.5(80–103)	>0.05
INDUCTION	87.7 ± 9.8 (67–104)	90.85±6.9 (77–102)	88.1± 8.0(76–102)	>0.05
INTUBATION	98.45±12.1 (72–126)	92.4±6.9 (77–103)	92.45±6.0(77–103)	>0.05
1 MIN	99.3±9.5 (67–111)	92.05 ±4.9(84–103)	90.55±6.8(69–102)	<0.05
3 MIN	97.25±9.7 (62–109)	89.55±7.8 (66–103)	89.25± 4.2(79–99)	<0.05
5 MIN	93.85±8.48 (69–109)	88.9± 4.7 (80–97)	87.35±3.5 (82–94)	<0.05

There is 10-25% increase in MAP from baseline on monitoring the patients in Group-1, much less increase in Group-2 and Group-3. The higher MAP observed at 1st minute in Group-1 and at intubation in Group 2& Group 3.There is no statistical significant difference among the three groups at Baseline, Induction and Intubation (p >0.05). There is highly significant difference in mean MAP among the three groups, at 1st, 3rd and 5th minute. . There is no significant difference between Group 2 & Group 3.

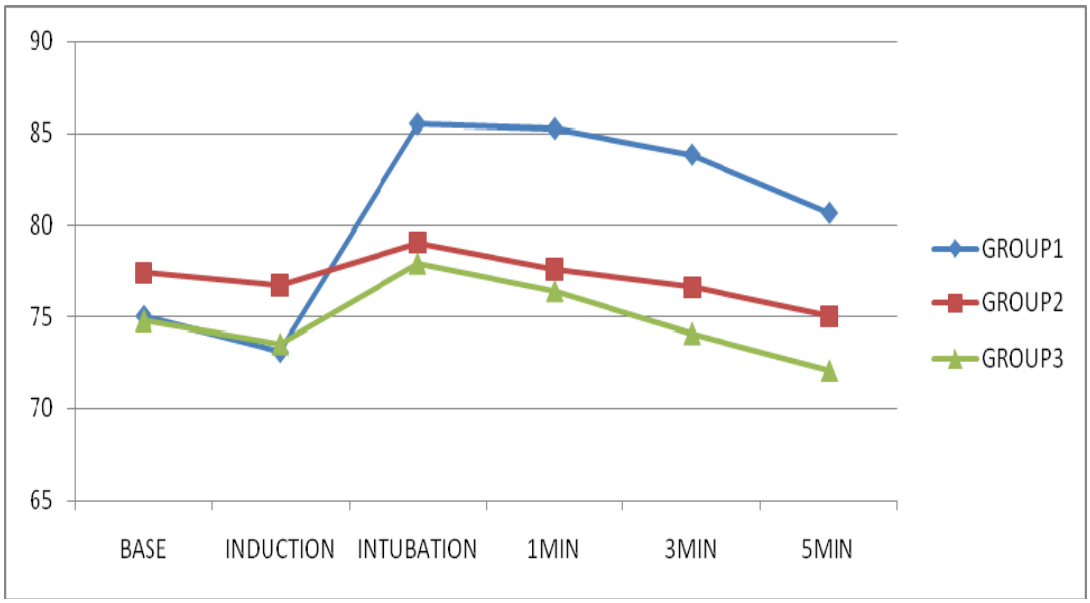
Distribution of mean Heart rate response



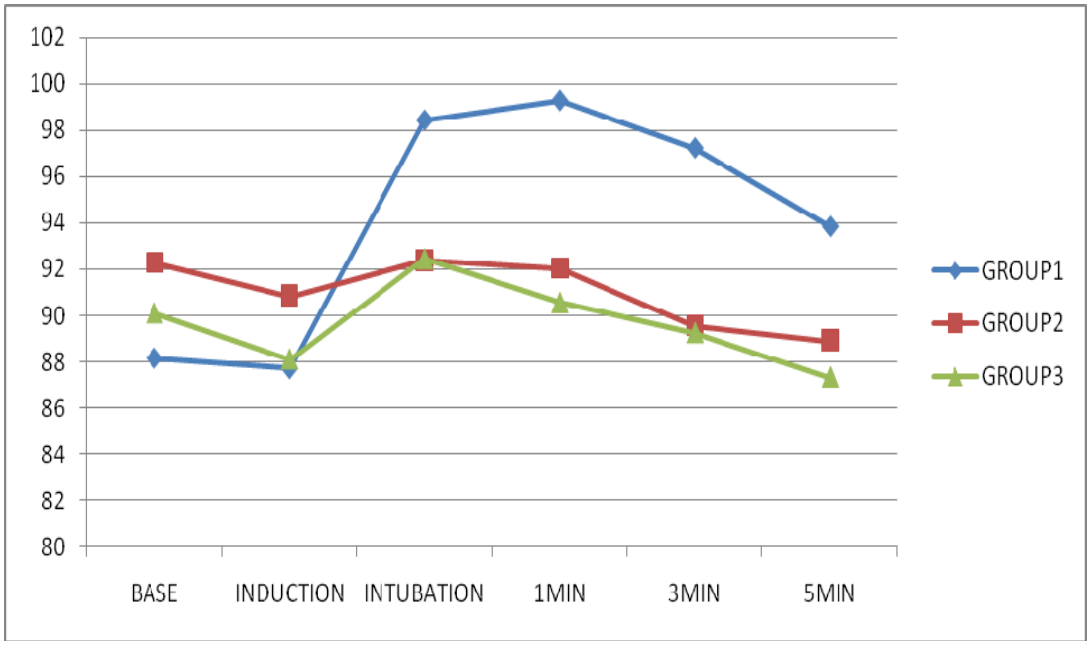
Distribution of mean SYSTOLIC BLOOD PRESSURE response



Distribution of mean DIASTOLIC BLOOD PRESSURE response



Distribution of MEAN ARTERIAL PRESSURE response

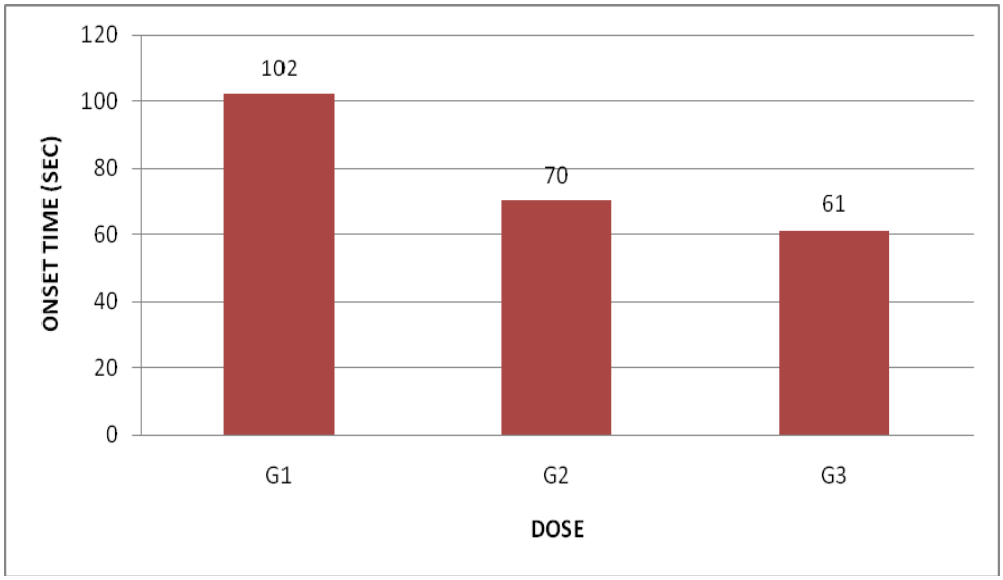


The mean onset of time and duration of action were calculated for all the three groups and the results were tabulated as shown in Table

TABLE XII Onset Time and Duration of 1st Dose

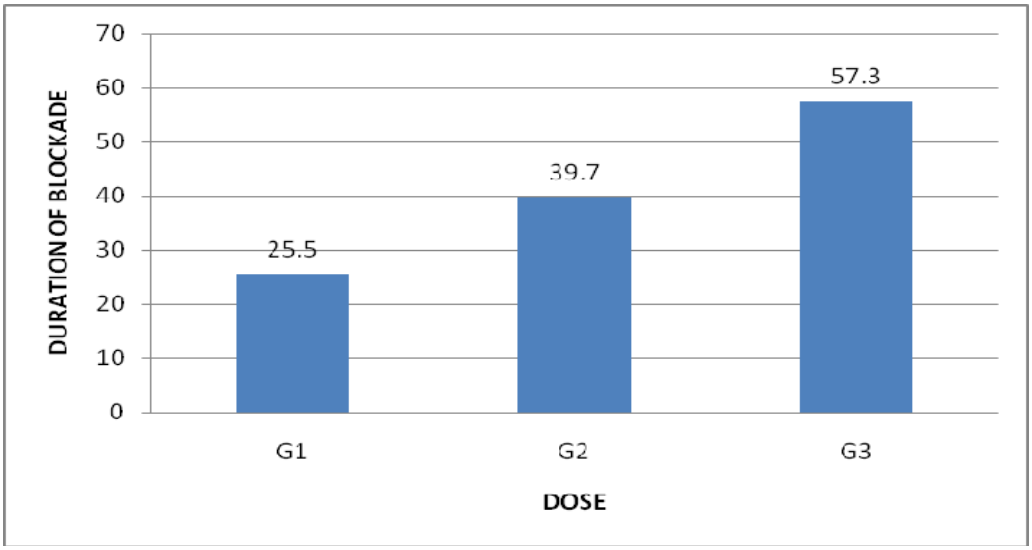
Mean			
Parameter	Group 1 N=20	Group 2 N=20	Group 3 N=20
Onset(Seconds)	102	70	61
Duration(minutes)	25.5	39.7	57.3

Mean Onset time



There is significant difference among three groups on mean onset time ($p < 0.05$), but there is no significant difference between the group 2 and group 3.

Mean Duration of Blockade



There is significant difference among the three groups (P <0.05) and also significant difference between group 2 and group 3 (p <0.05).

RESULTS

1. Statistical analysis showed that there was significant difference between distribution of age and sex among the three study groups (Table IV).

2. Jaw relaxation: On analyzing the jaw relaxation, it was impossible to open in one case and open with difficulty in six cases in Group 1. These kind of problems did not occur in Group 2 & Group 3 (Table V).

Statistical analysis showed that the mean score for jaw relaxation was significantly higher in Group 2 & Group 3 (ie; 2.7± 0.47, 2.7 ± 0.47) than Group 1 (ie; 1.7± 0.73).

3. Vocal cod position : Regarding vocal cord position ,the closed status (score 0) was seen in three cases in Group 1 whereas no such case had been encountered in Group 2 & Group 3 (Table VI).

Mean score for vocal cord position was significantly higher in Group 2 & Group 3 when compared to Group 1 (1.5 ±0.94, 2.65 ± 0.58, 2.7 ± 0.57 in Group 1, 2 & 3 respectively)

4. Response to intubation : With regard to response to intubation, two cases had severe coughing /bucking and seven cases had mild coughing

in Group1 .These untoward events did not happen in Group 2 & Group 3 (Table VII).

Mean score for response to intubation was significantly higher in Group 2 & Group 3 when compared to Group 1(1.55 ± 0.82, 2.75 ± 0.44, 2.8 ± 0.41 in Group 1,2 &3 respectively)

5. Intubation score : The analysis of intubation scores to assess conditions at intubation shows that higher doses result in a statistically significant increase in the ease of intubation. Mean total intubating score in Group 2 & Group3 were identical which is significantly higher than Group1 (4.75± 2.19, 8.1 ± 1.16, 8.2 ± 1.15 in Group 1,2 & 3 respectively)

6. Acceptable intubating conditions (excellent and good scores) were observed in 19 patients in Group 2 and Group 3. 4 patients had poor intubation score and 7 patients had fair intubation score in Group 1. No significant differences in intubating conditions between rocuronium 0.9mg/kg and 1.2mg/kg.

7. Statistical analysis revealed that mean Heart Rate,Systolic Blood Pressure, Diastolic Blood Pressure ,Mean Arterial Pressure during intubation in Group 1 was significantly higher than in Group2 and Group3.(108 ± 11, 135.1 ± 8.7, 85.45 ± 8.9, 98.45 ± 12.1 in Group1, 96.4 ± 12.9 ,123.4 ± 4.8, 79.05 ± 6.5, 92.4 ± 6.9 in Group 2 & 99.15 ± 10.3,

126.05 ± 7, 77.9 ± 5.6, 92.45 ± 6.0 in Group 3 respectively (Tables VIII, IX, X, XI)

8. Mean Heart Rate at the end of 5 minutes was higher in Group 1 compared to Group 2 and Group 3.(99.9 ± 11.2, 86.4 ± 10.3 ,85.65 ± 6.4 in Group, 2 and 3 respectively)

9. The analysis showed that the onset of blockade is inversely proportional to the dose of rocuronium. The onset time for the intubating dose was significantly lower in Group 3 and between Group1 &2 ,the onset time was significantly lower in Group 2 (102.25 ± 29.93sec in Group1, 70 ± 20.13 sec in Group2 and 61.2 ± 12.95 sec in Group 3)

10. The duration of neuromuscular blockade increases as the dose increases. Duration of action of the intubating dose was significantly higher in Group 3 when compared to Group 1 & 2. (25.5 ± 3.59 minutes in Group1, 39.75 ± 4.43 minutes in Group 2 and 57.25 ± 7.51 minutes in Group 3) (Table XII)

DISCUSSION

In this study, three different doses of rocuronium (0.6mg/kg, 0.9mg/kg and 1.2mg/kg) were used for intubation and various parameters like onset time, duration of neuromuscular blockade, intubating conditions and haemodynamic changes were compared.

The onset time and duration of neuromuscular blockade were studied by electrical nerve stimulation The most commonly used pattern of electrical nerve stimulation for evaluation of neuromuscular function is the train-of-four. The study was conducted by using the peripheral nerve stimulator NS-100 to elicit TOF response and visual recording of the evoked responses were made.

The time from the end of injection of the relaxant to the time when all four responses of TOF were abolished was taken as onset time.

Neuromuscular function was monitored using TOF stimuli every 5minute after giving the bolus dose of the relaxant. The interval between the administration of the bolus dose of the relaxant and the reappearance of the two responses to TOF was taken as the duration of action.

There was significant difference in onset time among the three groups. Group 3 showing fastest onset 61.2 ± 12.95 seconds compared to Group 2 (70 ± 20.13 sec) and Group 1(102.25 ± 29.93 sec).

Magonian et al. reported an onset time with succinylcholine (50.0 ± 17.0 sec), 89.0 ± 33.0 sec. and 75.0 ± 28.0 sec after 0.6mg/kg and 0.9mg/kg rocuronium respectively.[36]

On the other hand Latorre et al reported an onset time of 48.0 ± 16.0 sec after 1 mg/kg succinylcholine and onset time of 3.0 minutes after 0.6mg/kg rocuronium.[37]

However Weirda et al. reported an onset time of 172.0 sec after rocuronium 0.6mg/kg.[38]

A clinical duration of 17.4 ± 3.2 min after 0.6 mg/ kg rocuronium was reported by Booji et al[39],while we found duration of 25.5 ± 3.59 min after 0.6mg/kg rocuronium.

Mirakhur et al[40] and Weirda et al. reported a clinical duration of 30.0 min and 33.0 min respectively after 0.9mg/kg rocuronium. This duration is close to our observation of 39.75 ±4.43 min with 0.9 mg/ kg of rocuronium.

So,eventhough the onset time is faster in group3(1.2mg/kg) there is prolongation of the duration of neuromuscular blockade for the first dose of rocuronium and this is an added disadvantage to this group.

Cheng CA et al found that rocuronium 0.9mg/kg provides similar intubating conditions to suxamethonium 1.5 mg/kg using alfentanyl and thiopentone while rocuronium 0.6 mg/kg was inadequate.[34]

Aboulish E and colleagues found that rocuronium 0.6 mg/kg with thiopentone 6mg/kg provides good to excellent intubating conditions at 80 seconds and found that rocuronium is safe for mother and foetus.[35] Times to maximum blockade for 0.9 and 1.2 mg/kg rocuronium were the shortest. .

Good to excellent tracheal intubating conditions have been reported within 60 seconds following rocuronium, 0.6-1.2 mg-kg-1 (2-4×ED_{95}) Intubating conditions as observed by Mirakhur et al[40], Copper et al[41] Huizinga et al[42] and Shukla et. al[43] were good or acceptable in 95% patients at 60 seconds and in all patients at 90 seconds. The average intubating time as reported by Mirakhur et al. was 89 seconds.

However, in our study we observed excellent to good intubating conditions in 45% in group 1, 100% in group 2 and in 100% in group 3. Our observations in rocuronium groups are very close to that observed by above authors.

It is expected to have an onset time possibly as rapid as that of succinylcholine . But, unlike succinylcholine, rocuronium has little or no cardiovascular side effects[31], and does not cause histamine release. Thus

it is ideal for rapid-sequence induction of anesthesia and may be preferable to succinylcholine in compromised patients in whom cardiovascular effects are to be avoided. Rocuronium is currently being used in rapid sequence induction[32,33] as an alternative to suxamethonium. It has a rapid onset of action, less than 1 minute for complete neuromuscular block with doses of 0.9-1.2 mg/kg.

Intubation conditions were good to excellent for rocuronium at the 0.9 mg/kg dose(100%) and at the 1.2 mg/kg dose(100 %), whereas rocuronium at the 0.6 mg/kg dose had the least number of excellent to good conditions (45%) and the most poor(15%) or not possible assessments and few patients could not be intubated.

There were important changes or intergroup differences in mean arterial blood pressure and heart rate. Patients receiving 0.6mg/kg were more likely to experience moderate coughing and bucking after tracheal tube insertion, $P < 0.05$, Table VII).

Cantineau JP, et al[11] (1994) studied the neuromuscular effect of rocuronium on the diaphragm and adductor pollicis muscles in anaesthetized patients and concluded that the diaphragm is more resistant than the adductor pollicis to rocuronium, as shown by greater ED50 and ED95 and faster recovery of the twitch height. The intubating dose of 0.60 $mg.kg^{-1}$ is close to the ED95 of 0.50 $mg.kg^{-1}$ for the diaphragm.

The adductor pollicis muscle appears to be a good reflection of paralysis of the upper airway muscles, especially when considering recovery.[44]

Patient's readiness for intubation could not be judged by the loss of four responses of TOF stimuli monitored at adductor pollicis.[45] This may be because of earlier blockade of laryngeal muscles than adductor pollicis by rocuronium. Therefore, onset time has become overestimated as a predictive parameter for the rate of development of adequate intubating conditions. However, onset time is complementary to information provided by intubation score. It is very important to note that all the patients in group 2 & 3 were intubated with good to excellent intubating conditions, when there was no diaphragmatic activity. This perhaps be acceptable even in emergency tracheal intubation in those patients in whom succinylcholine is contraindicated because of presence of other problems.

Higher doses of rocuronium (0.9- 1.2mg/kg) produces ideal intubating conditions but the duration of acion is very much prolonged

in 1.2mg/kg group. No further improvement in intubation conditions achieved by increasing the rocuronium dose from 0.9 mg/kg to 1.2 mg/kg.

CONCLUSION

Among the three doses of rocuronium bromide used for endotracheal intubation in the study, I conclude that, rocuronium bromide in the dose of 0.9mg/kg (Group 2) produced acceptable intubating conditions in 80 seconds without undue prolongation of the neuromuscular blockade.

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PROFORMA

Name Age/Sex IP NO: Wt :

DIAGNOSIS: Surgery :

Preop Assesment :

Investigations : O/E :

Haemoglobin % Urine- Albumin and sugar, Packed cell volume

Blood- urea, sugar, creatinine, Liver Function Tests, E.C.G. X-Ray Chest

Premedication:

Shifting to O.T.

I.V. line Securing

Preoxygenation :

Induction :

Muscle relaxant used

Group I : Inj. Rocuronium 0.6mg/ kg

Group II : Inj. Rocuronium 0.9mg/ kg

Group III : Inj. Rocuronium 1.2mg/ kg

Maintenance :

Onset Time of neuromuscular blockade :

Intubation at 80 sec.

Intubation Score: Cooper Scoring System

Score	Jaw relaxation	Vocal Cords	Response to intubation
0	Poor (impossible)	Closed	Severe coughing or bucking
1	Minimal(difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None

Total Score : Excellent (8-9)/ Good (6-7)/ Fair (3-5) / Poor(0-2)

Haemodynamic Response to Intubation :

No	Name	Age	Sex	Baseline				Induction				Intubation				1 min				3 min				5 min			
				HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP

Duration of action of Intubating dose :

Masterchart

GROUP 1

S.NO	SURGERY	ONSET TIME (sec)	DURATION OF BLOCKADE (min)	INTUBATING CONDITIONS AT 80 SEC				
				JAW RELAXATI0N	VOCAL CORDS	RESPONSE TO INTUBATION	INTUBATION SCORE	INTUBATION GRADE
1	Post auricular flap	90	25	2	2	2	6	Good
2	Inguinal herniorraphy	100	20	1	0	1	2	Poor
3	Fibroadenoma excision	80	20	2	1	1	4	Fair
4	Fibroadenoma excision	55	25	3	3	2	8	Excellent
5	Lap sterilization- TAT	60	25	3	3	2	8	Excellent
6	MTP & LAP TAT	100	30	2	2	3	7	Good
7	Hemithyroidectomy	90	25	2	2	2	6	Good
8	Open&internal fixation - elbow	110	25	0	1	1	2	Poor
9	Lumpectomy breast	80	30	2	3	2	7	Good
10	Implant removal radius	120	25	1	0	0	1	Poor
11	Fibroadenoma excision	130	25	1	1	2	4	Fair
12	Tonsillectomy	120	25	1	2	1	4	Fair
13	Fibroadenoma excision	90	30	2	2	3	7	Good
14	Adeno Tonsillectomy	60	20	2	2	2	6	Good
15	Fibroadenoma excision	100	30	2	2	2	6	Good
16	Fibroadenoma excision	110	30	2	1	2	5	Fair
17	Fibroadenoma excision	180	20	1	0	0	1	Poor
18	Interval appendiceetomy	130	25	2	1	1	4	Fair
19	Tonsillectomy	100	25	2	1	1	4	Fair
20	Fibroadenoma excision	140	30	1	1	1	3	Fair

GROUP 1

S.NO	NAME	IPNO	WEIGHT(kg)	SEX	AGE(years)	BASELINE				INDUCTION				INTUBATION			
						HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	Elavarasi	34196	45	F	20	86	110	76	88	88	108	80	89	96	120	88	99
2	Prabu	4160	48	M	23	88	126	80	95	96	124	84	97	120	140	98	112
3	Chitra	10809	40	F	25	84	120	80	93	82	120	82	95	90	128	88	101
4	Priya	13023	50	F	20	106	120	80	93	100	116	78	91	101	118	80	93
5	Prema	3376	60	F	32	79	109	77	87	86	110	80	90	100	160	109	126
6	Dhanaselan	13397	55	F	30	106	124	78	93	112	128	74	92	120	138	68	91
7	Venda	13711	80	F	35	90	136	86	103	94	136	88	104	110	140	90	107
8	Murugan	13419	75	M	35	85	126	86	99	90	128	90	103	106	138	96	111
9	Suganthi	14377	45	F	20	86	124	76	92	88	126	80	95	96	136	84	101
10	Manikandan	15073	57	M	21	104	111	71	85	102	110	70	84	116	130	84	100
11	Jayanthi	19433	43	F	26	70	120	70	87	76	110	60	87	97	140	90	106
12	Sheela	16489	46	F	21	82	120	76	91	88	128	78	95	100	132	86	91
13	Pushpalatha	16954	45	F	22	78	116	74	88	86	110	70	83	96	138	90	106
14	Barathi	88496	40	M	20	90	102	60	72	96	100	58	72	110	130	78	92
15	Parimala	18760	45	F	36	84	120	68	82	90	110	60	76	100	140	78	98
16	Prema	20857	54	F	18	98	110	76	87	106	100	70	80	120	136	80	74
17	Sathiya	20390	45	F	23	92	120	70	67	94	122	72	67	126	138	76	96
18	Kumaresan	20810	48	M	20	108	126	76	92	110	130	74	92	120	140	86	72
19	Sasikala	20683	60	F	23	98	110	70	83	100	112	60	77	120	130	80	96
20	Soundari	19971	43	F	40	92	120	70	86	96	116	70	85	116	130	80	97

GROUP 1

S.NO	IPNO	1MIN				3 MIN				5 MIN			
		HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	34196	94	120	84	96	90	126	86	99	88	118	84	95
2	4160	120	138	98	111	126	136	96	109	108	130	90	103
3	10809	96	128	90	102	108	136	94	108	94	138	94	109
4	13023	96	120	70	87	97	116	98	91	95	110	80	90
5	3376	98	140	86	104	136	136	80	99	126	126	78	94
6	13397	130	140	86	104	128	130	84	99	120	128	80	96
7	13711	118	140	92	108	110	136	90	105	100	130	88	102
8	13419	104	130	94	106	100	128	92	104	92	128	90	103
9	14377	96	130	84	100	92	132	86	102	90	130	88	102
10	15073	118	130	84	100	110	122	82	95	102	116	85	94
11	19433	100	138	88	104	98	130	80	104	90	126	76	92
12	16489	106	136	90	105	102	130	80	97	90	120	76	91
13	16954	110	140	92	108	100	130	86	101	86	126	78	94
14	88496	108	130	76	91	106	128	76	93	99	106	67	81
15	18760	105	142	80	100	96	136	76	96	90	130	70	90
16	20857	126	130	78	95	116	126	76	62	106	120	80	93
17	20390	120	140	90	67	110	130	78	95	100	128	76	69
18	20810	126	142	82	102	120	134	80	98	117	126	78	94
19	20683	124	134	82	99	120	130	80	97	108	120	76	91
20	19971	106	136	78	97	100	130	76	91	98	128	78	94

GROUP 2

S. NO	SURGERY	ONSET TIME (Sec)	DURATION OF BLOCKADE (min)	INTUBATING CONDITIONS AT 80 SEC				
				JAW RELAXATI0N	VOCAL CORDS	RESPONSE TO INTUBATION	INTUBATION SCORE	INTUBATION GRADE
1	Open reduction &internal fixation	80	50	3	3	3	9	Excellent
2	Inguinal herniorraphy	65	40	2	3	3	8	Excellent
3	Inguinal herniorraphy	70	35	3	3	3	9	Excellent
4	Bilateral Inguinal hernia -Mesh repair	120	40	3	3	3	9	Excellent
5	Ureterorenoscopy	75	30	2	3	3	8	Excellent
6	Fibroadenoma excision	45	40	3	3	2	8	Excellent
7	MTP & LAP Sterilisation	45	40	3	3	3	9	Excellent
8	K-Wire fixation- Ankle #	80	40	3	3	3	9	Excellent
9	Tonsillectomy	100	40	3	2	3	8	Excellent
10	Excision- Fibroadenoma	100	45	3	3	3	9	Excellent
11	Sebaceous cyst face-excision	70	35	2	3	2	7	Good
12	Cross Finger Flap –Index finger	70	45	2	2	2	6	Good
13	Superficial parotidectomy	60	40	3	3	3	9	Excellent
14	Endoscopic sinus surgery	80	40	2	2	2	6	Good
15	Open reduction&internal fixation-Patella fracture	65	40	3	3	3	9	Excellent
16	Pilonidal sinus –Excision	60	35	2	3	3	8	Excellent
17	Inguinal herniorraphy	65	40	3	2	2	7	Good
18	L4-L5 Discectomy	60	45	3	3	3	9	Excellent
19	Acetabular fracture- Open reduction&internal fixation	35	35	3	3	3	9	Excellent
20	Endoscopic sinus surgery	55	40	3	2	3	8	Excellent

GROUP2

S.NO	NAME	IPNO	WEIGHT kg	SEX	AGE years	BASELINE				INDUCTION				INTUBATION			
						HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	Immanuvel	14039	70	M	34	78	122	72	89	86	115	86	96	90	120	80	93
2	Anandhan	5163	60	M	32	88	120	80	93	82	122	82	95	82	122	82	95
3	Chandran	5676	48	M	29	90	130	86	101	92	130	88	102	88	128	86	100
4	Ravi	10933	60	M	30	80	126	86	99	80	126	84	98	82	128	86	100
5	Kannan	12462	65	M	40	88	128	78	95	90	130	80	97	90	122	82	98
6	Kamatchi	77208	45	F	20	86	124	80	95	90	120	76	91	92	112	78	78
7	Jagavalli	13374	55	F	25	88	122	82	95	90	118	80	93	94	124	78	89
8	Thiagu	10322	53	M	35	8	120	82	95	84	122	86	98	86	124	88	100
9	Valli	14622	45	F	20	89	127	72	91	90	126	74	92	92	132	79	93
10	Govindammal	14902	50	F	40	96	120	90	100	98	120	90	100	115	126	92	103
11	Antony	19503	85	M	39	90	126	80	95	96	120	70	86	100	130	76	94
12	Kumar	15545	55	M	35	78	122	78	93	80	120	76	91	84	124	80	95
13	Murugan	17739	70	M	39	120	130	86	100	126	120	80	93	128	124	86	98
14	Manjula	88686	40	F	35	84	120	80	93	90	110	60	77	100	120	70	77
15	Suresh	20035	20	M	20	108	106	70	82	112	100	70	80	116	116	74	88
16	Nathiya	20393	60	F	20	97	116	70	85	100	110	68	82	106	124	80	95
17	Prabaharan	21721	75	M	38	90	120	70	88	92	120	76	91	92	128	70	89
18	Murali	20868	55	M	34	110	120	68	85	112	116	70	85	114	118	74	88
19	Loganathan	21207	60	M	35	76	118	68	85	80	116	70	85	84	120	70	86
20	Uma	24251	45	F	37	86	122	70	87	90	120	68	85	94	126	70	89

GROUP 2

S.NO	IPNO	1MIN				3 MIN				5 MIN			
		HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	14039	86	118	76	90	82	120	70	86	78	122	74	90
2	5163	80	120	80	93	78	120	78	92	82	122	82	95
3	5676	84	120	80	93	84	122	82	95	82	118	80	93
4	10933	80	124	84	97	80	120	82	95	78	120	78	92
5	12462	86	126	80	95	85	128	78	95	85	128	80	96
6	77208	88	110	78	89	84	110	80	90	84	103	68	82
7	13374	83	112	76	88	82	110	80	90	83	112	82	92
8	10322	84	120	80	93	86	124	82	96	84	120	78	92
9	14622	104	133	90	103	119	133	90	103	122	120	70	88
10	14902	104	120	88	99	102	122	88	100	102	110	90	97
11	19503	100	130	76	94	92	120	76	90	86	122	74	90
12	15545	84	124	80	95	80	120	70	87	82	120	70	87
13	17739	106	120	70	86	100	110	72	85	80	112	70	84
14	88686	100	138	80	99	98	130	78	95	90	120	76	91
15	20035	114	120	72	88	110	110	70	83	90	106	68	80
16	20393	106	120	76	91	100	110	70	83	92	112	74	86
17	21721	90	120	72	88	86	122	74	90	84	116	76	89
18	20868	102	110	72	84	96	110	74	86	90	112	72	85
19	21207	86	120	70	86	80	118	68	84	74	116	66	82
20	24251	94	126	72	90	86	120	70	66	80	118	72	87

GROUP 3

S. NO	SURGERY	ONSET TIME (Sec)	DURATION OF BLOCKADE (min)	INTUBATING CONDITIONS AT 80 SEC				
				JAW RELAXATI0N	VOCAL CORDS	RESPONSE TO INTUBATION	INTUBATION SCORE	INTUBATION GRADE
1	Appendicectomy	45	45	3	3	3	9	Excellent
2	Intramedullary nailing	64	50	3	3	3	9	Excellent
3	Open reduction-Internal fixation- Radius	50	55	2	3	3	8	Excellent
4	Open reduction -DCS-Femur fracture	65	60	3	3	3	9	Excellent
5	Olecranon facture- Tension-Band wiring	45	50	3	2	3	8	Excellent
6	Hand injury –Exploration	60	65	3	3	3	9	Excellent
7	Foot metatarsal fracture –K Wire fixation	90	60	3	3	3	9	Excellent
8	Hemithyroidectomy	65	55	3	3	2	8	Excellent
9	Cholecystectomy	55	70	3	3	3	9	Excellent
10	L5-S1 Microdissectomy	50	55	2	2	3	7	Good
11	Superficial Parotidectomy	50	50	3	3	3	9	Excellent
12	Complete Thyroidectomy	80	70	3	3	3	9	Excellent
13	Appendicectomy	85	55	3	3	3	9	Excellent
14	Appendicectomy	70	50	3	2	3	8	Excellent
15	Superficial Parotidectomy	55	55	3	3	3	9	Excellent
16	Fracture Humerus- External fixation	60	55	2	3	3	8	Excellent
17	Superficial Parotidectomy	50	70	3	3	3	9	Excellent
18	Ulna & Radius fracture- Internal fixation	50	50	2	2	2	6	Good
19	Vascular malformation-Excision	65	60	2	2	2	6	Good
20	Post.cruciate ligament- Screw fixation	70	65	2	3	3	8	Excellent

GROUP 3

S.NO	NAME	IPNO	WEIGHT	SEX	AGE	BASELINE				INDUCTION				INTUBATION			
			kg		years	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	Sekar	6388	55	M	38	86	120	84	96	88	122	86	98	84	120	80	93
2	Thiyagu	10332	50	M	28	88	120	74	93	90	120	76	91	96	122	78	93
3	Karthikeyan	11209	4	M	21	86	122	76	91	90	128	74	91	94	130	78	95
4	Muthukrishnan	11305	50	M	35	90	130	80	97	92	134	84	101	92	134	86	102
5	Panchatcharam	13267	47	M	30	92	122	80	94	90	120	82	97	100	124	80	95
6	Raj	13408	47	M	26	90	126	86	99	94	130	88	102	98	130	90	103
7	Murugan	16777	50	M	20	90	106	68	80	96	100	66	77	100	112	70	84
8	Jeyanthi	16493	65	F	30	80	126	66	86	88	116	70	85	90	130	76	94
9	Lily	16136	55	F	40	78	110	76	87	82	100	70	80	86	116	80	92
10	Kumar	18168	60	M	33	78	120	66	84	88	110	60	76	90	128	70	89
11	Usha	19195	40	F	25	88	120	68	85	92	116	70	85	98	122	76	91
12	Maheswari	19476	45	F	22	96	116	70	85	100	110	65	80	15	125	70	88
13	Srinivasan	20070	55	M	35	110	130	90	103	112	122	86	98	120	134	88	103
14	Lakshmi	12824	50	F	32	106	120	70	86	110	126	72	90	114	130	76	94
15	Sakthivel	20723	70	M	39	102	110	70	83	106	106	68	80	110	116	78	90
16	Venkatesan	18032	60	M	26	101	130	80	97	108	126	70	88	116	132	74	93
17	Perumal	95518	50	M	30	76	122	70	87	80	120	68	85	90	134	78	92
18	Purushothaman	22882	45	M	22	90	116	64	81	94	114	64	80	100	124	70	88
19	Ongaran	23636	40	M	17	100	120	78	92	106	110	76	87	110	120	80	93
20	Loganathan	21207	60	M	35	76	130	80	96	80	120	76	91	90	138	80	77

GROUP 3

S.NO	IPNO	1MIN				3 MIN				5 MIN			
		HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	6388	84	120	78	92	82	118	78	91	82	118	76	91
2	10332	95	120	78	92	86	120	76	91	84	116	76	89
3	11209	94	130	76	94	90	128	74	92	88	120	70	87
4	11305	88	126	78	94	84	120	76	91	85	122	78	93
5	13267	9	120	78	92	90	122	78	93	84	122	80	94
6	13408	93	130	90	102	90	126	86	99	88	120	80	93
7	16777	96	110	70	83	86	106	66	79	84	108	70	83
8	16493	88	124	70	88	80	120	68	85	78	120	70	87
9	16136	85	120	78	92	84	120	76	91	80	116	78	90
10	18168	92	130	74	93	86	126	72	90	80	120	64	91
11	19195	90	120	70	86	86	118	74	89	80	110	68	82
12	19476	100	118	72	87	96	116	72	86	90	110	70	83
13	20070	116	130	86	101	110	126	76	92	90	120	70	86
14	12824	106	126	80	95	104	120	76	90	96	116	72	86
15	20723	108	114	76	88	104	110	76	87	98	106	74	84
16	18032	110	130	76	94	92	126	72	90	88	120	70	86
17	95518	80	130	70	90	80	120	70	86	74	120	68	85
18	22882	98	122	72	88	96	124	70	88	94	120	68	85
19	23636	106	118	78	91	100	110	70	83	92	118	70	86
20	21207	88	130	78	69	80	126	76	92	78	120	70	86