"Comparison between Adductor Pollicis and Orbicularis Oculi as indicators of adequacy of muscle relaxation for tracheal intubation following Rocuronium induced Neuromuscular Block" - Randomized Comparative Clinical trial at KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE.

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DISSERTATION

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This is to certify that the dissertation entitled **"Comparison between Adductor Pollicis and Orbicularis Oculi as indicators of adequacy of muscle relaxation for tracheal intubation following Rocuronium induced Neuromuscular Block" - Randomized Comparative Clinical trial at KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE** *is a bonafide research work done by* **the Candidate Reg. No.-BA0109002,** *Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.*

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ABBREVIATIONS

Ach R	Acetyl Choline Receptor
AMG/ACG	Acceleromyography
AP	Adductor Pollicis
ASA	American Society of Anesthesiologist
Ca	Calcium
DBS	Double Burst Stimulation
ED	Effective Dose
I.P no.	In Patient number
Mg	Milligram
Mamps/mA	Milli Amperes
mSec/ms	Milli second
nAch r	Nicotinic Acetyl Choline receptor
NDMR	Non Depolarizing Muscle Relaxant
NMB	Neuro Muscular Block
OO	Orbicularis Oculi
PTC	Post Tetanic Count
PTF	Post Tetanic Facilitation
Sl.no.	Serial Number
TOF	Train Of Four
TOFR	Train Of Four Ratio
Wt	Weight

ABSTRACT

Background : The purpose of this study was to verify which muscle among the Adductor Pollicis (AP) and Orbicularis Oculi (OO) is a better predictor of optimal intubating condition after administration of Rocuronium.

Method : In this prospective, double blind, randomized study, 80 adult ASA –I and ASA – II undergoing general anaesthesia with tracheal intubation were allocated to two groups (n = 40) according to the reference muscle (AP or OO) used to determine the appropriate intubation time. Induction of anaesthesia was achieved with Inj Thiopentone 5mg/kg, Inj Fentanyl 2 mcg/kg and Inj Rocuronium 0.6mg/kg for muscle relaxation. Supramaximal Train Of Four (TOF – Guard acceleromyograph, neuro muscular monitor) stimulation of the ulnar nerve and facial nerve every 15 secs was used to monitor the neuromuscular block. After Train Of Four responses disappeared at Adductor Pollicis muscle or Orbicularis Oculi muscle, tracheal intubation and quality of intubation assessment was performed by an independent anaesthesiologist. Intubating conditions were scored on a Kreig et al scale.

Results : Onset time at Orbicularis Oculi was significantly shorter than Adductor Pollicis muscle ($P < 0.001$), but adequate intubating condition were significantly increased in the Adductor Pollicis (Excellent – 87.5%, Good – 12.5%, Poor – 0%) compared with Orbicularis Oculi (Excellent – 27.5%, Good – 45%, Poor – 27.5%) after a dose of 0.6mg/kg of Rocuronium ($P < 0.001$)

Conclusion : After administration of Rocuronium, twitch monitoring at Orbicularis Oculi allows a faster intubation but is associated with an unacceptable incidence of inadequate intubating condition . Adequate intubating conditions were observed with Adductor Pollicis muscle. Hence Monitoring neuromuscular activity of the Adductor Pollicis using Train Of Four to determine the appropriate tracheal intubation time and condition is more clinically relevant than monitoring the Orbicularis Oculi muscle.

KEYWORDS: *Intubating conditions, Neuro Muscular Blockade Monitoring, Orbicularis Oculi, Adductor Pollicis, Rocuronium, Train Of Four, Acceleromyography.*

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INTRODUCTION

General Anaesthesia is most common anaesthetic technique used in anaesthesia practice. Securing and maintaining a patent airway is a vital aspect of providing adequate oxygenation and ventilation during General Anaesthesia[1]. It is the prime importance of the anaesthesiologist to secure airway. Endo tracheal tube – intubation is the best and safe method to secure and prevent airway against aspiration. [2]. Laryngoscopy is known to cause increased Sympathetic response[3], which is exaggerated during inadequate intubating conditions.

Intubating conditions can be assessed clinically or using Neuro muscular monitoring[4], which is the best non invasive technique. In clinical practice Neuro muscular block is monitored by assessing the response of Adductor Pollicis after ulnar nerve stimulation or orbicularis Oculi after facial nerve stimulation using neuro muscular monitor – Train of Four (TOF). Complete relaxation of the jaw, laryngeal, Vocal cord, pharyngeal muscles, and diaphragm is needed for excellent intubating conditions in order to reduce the risk of Vocal cord trauma[5.] Response to intubation is a function of both muscular block and the level of anesthesia. It is possible to intubate a patient with less-than-complete paralysis if a sufficient depth of anesthesia is present[6] .

Neuromuscular blocking agents improve intubating conditions[7]. The dose of narcotics required for acceptable intubating conditions in the absence of muscle paralysis produce significant hypotension[8]. It has been demonstrated that poor intubating conditions are associated with an increased incidence of hoarseness of voice and vocal cord damage[9] . Giving neuromuscular blocking agents improved the quality of intubating conditions.

Onset time differs from one muscle to another. Neuro muscular block is faster at diaphragm, masseter, adductor muscles of larynx and orbicularis of the eye as compared to adductor pollicis (AP) after injection of a bolus dose of non depolarizing muscle relexant[10,11,12].

There has been discrepancies as to which muscle is better predictor for intubating conditions between Orbicularis Oculi and Adductor Pollicis. Studies states that Orbicularis Oculi (OO) and laryngeal adductor muscles have similar onset time, Sensitivity to muscle relaxants and recovery profile [10,13] , hence is a better predictor of intubating condition [14,15,16]. Where as other studies have shown monitoring Adductor Pollicis to determine tracheal intubating condition is more clinically relevant than monitoring Orbicularis Oculi muscle. [17,18] using Train of Four (TOF) watch Acceleromyography, neuro muscular monitor. Visual monitoring is a less objective method of measurement than the continuous monitoring and registration of the evoked mechanical or electromyographic response[19] .

Goodmurphy and colleagues found that OO is made up of small, round and 89% fast twitch type 2 fibers [20]. AP is made up of slow oxidative type of fibers [12]. Morphology of neuromuscular junction is also responsible for the observed difference in sensitivity of a given muscle to muscle relaxant[21].

Hence a study was under taken to know which muscle is a good indicator for tracheal intubation. The ideal condition for intubation is tested with Train Of Four (TOF) – Guard acceleromygraphic response (Organon-Teknika, Belgium) – Neuro muscular stimulator, at respective nerve supply of the muscle.

In this study comparison between Adductor Pollicis(AP) and Orbicularis Oculi (OO) as indicators for adequacy of muscle relaxation for tracheal intubation after administration of Rocuronium in KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE was done. This would determine which muscle is a better predictor for intubating condition, to lower risk of laryngeal trauma and post - operative sore throat during adequate intubating condition.

OBJECTIVES

1. To determine whether monitoring Orbicularis Oculi (OO) or Adductor Pollicis (AP) could predict adequate intubating conditions after giving Non-depolarizing muscle relaxant in adults using Train Of Four (TOF) Guard acceleromyographic response.

2. To compare the Acceleromyographic estimation of early onset of complete Neuro Muscular blockade (NMB) at Orbicularis oculi (OO) muscle and Adductor pollicis (AP) muscle.

REVIEW OF LITERATURE

In the 18th century tubes were passed into trachea during resuscitation from drowning, but these tubes were passed without direct visualization and were not for delivery of anaesthetic agents. Endotracheal anaesthesia was introduced to the clinical practice in early part of 20th century**.**

Though endotracheal anaesthesia was practiced with metal tubes and chloroform anaesthesia, true concept of endotracheal intubation was actually introduced by Sir Ivan Magill during the World War I. Sir Ivan Magill along with Stanley Rowbotham developed this technique out of necessity.

Concept of balanced anaesthesia was introduced by John S Lundy in 1926 which incorporated premedication, regional anesthesia and general anesthesia. Rees and Gray of Liverpool divided into three basic components involving narcosis, analgesia and relaxation. Lack of a relaxant, most intubations were done using inhalational technique which was associated with its own problems like laryngospasm and bronchospasm when intubation was attempted with inadequate depth. Further making the patient sufficiently deep to obtain intubating conditions led to haemodynamic disturbances because of higher concentration of inhalational agents that were used. A breakthrough was obtained in 1942 when Harrold Griffith introduced d-tubocurarine to the world. With this relaxant, jaw relaxation could easily be obtained to facilitate orotracheal intubation. This invention soon instigated R.R. Macintosh to invent the famous Macintosh laryngoscope in 1943.

In 1958, Christie and Churchill-Davidson described the use of a nerve stimulator to monitor neuromuscular block. However, it was not until the (TOF) Train

Of Four pattern of stimulation described in 1970 by Ali et al, that such equipment came into routine clinical use.

There has been many studies regarding which muscle is adequate indicator for intubating condition.

Day NS and Dretchen KL studied Characterization of Train of four responses in fast and slow muscle using , d- tubocurarine, pancuronium and vecuronium in 1983. They concluded that ,morphology of Neuro muscular junction is responsible for the observed difference in sensitivity of a given muscle to muscle relaxant.[21]

Smith CE, studied different effects of pancuronium on masseter and adductor pollicis muscles in humans in 1989. They said Adductor pollicis is made up of slow oxidative type of fibers which are more sensitive to non depolarizing muscle relaxant. They concluded that after pancuronium NMB is greater at the masseter and occurs sooner than at the adductor pollicis . This suggests that return of adductor pollicis function may not imply complete masseter muscle recovery.[12]

Donati F in 1990 , determined relationship among diaphragm, orbicularis oculi and adductor pollicis blockade. Train of four stimulation was applied to phrenic, facial and ulnar nerves in adult patients anesthetized with alfentanil – propofol – oxygen. Vecuronium 0.04 or 0.07mg/kg was used. Onset time was prolonged at adductor pollicis than at the diaphragm and orbicularis oculi onset time approached that of diaphragm. They concluded that orbicularis oculi response to facial stimulation reflects the extent of neuromuscular blockade of the diaphragm better than does the response of the adductor pollicis to ulnar nerve stimulation.[10]

Meistelman C in 1992 ,studied Rocuronium (ORG 9426) neuro muscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. They

used rocuronium in 0.25 and 0.5 mg/kg dose. Concluded that rocuronium onset and recovery are faster at the laryngeal adductor muscles, but blockade is less intense than at the adductor pollicis. These findings are similar to the observations made previously with vecuronium, except that rocuronium has a faster onset at both muscles. [11]

Friedrich K. Puhringer et al. in 1992 evaluated the endotracheal intubating conditions of Rocuronium bromide (ORG 9426) and Succinylcholine chloride in outpatient surgery. The study population consisted of 30 patients with 20 patients receiving Rocuronium bromide 0.6 mg/ kg and 10 patients receiving Succinylcholine chloride 1 mg/ kg. Anaesthesia was induced with propofol, alfentanil, followed by neuromuscular blocking drug. Sixty seconds after the administration of the muscle relaxant, the trachea was intubated and intubating conditions were assessed according to scale as Excellent ,Good, Poor and Inadequate. **T**hey concluded that the intubating conditions approximately 60 sec after the administration of Rocuronium bromide were satisfactory and similar to those observed after Succinylcholine chloride. The clinical duration of action associated with the intubating dose of Rocuronium bromide provides adequate muscle relaxation for the duration of most of surgical interventions in outpatient cases.

Dan Ungureanu and Jeanne Frossard in 1993 ,Studied to determine whether atracurium-induced neuromuscular block at the laryngeal adductor muscles could be predicted using visual assessment of Train of Four responses at either adductor pollicis or orbicularis oculi muscle. Train-of-four stimulation was applied to the ulnar, facial, and recurrent laryngeal nerves. Laryngeal response was measured as the pressure change in the tracheal tube cuff positioned between the vocal cords. The response at the adductor pollicis and orbicularis oculi was evaluated visually by two

observers using Train Of Four responses, who detected if and when block was complete. In patients receiving atracurium 0.5 mg/kg, laryngeal and orbicularis oculi responses were abolished faster than the adductor pollicis muscle. There was a significant correlation ($r = 0.94$; $P < 0.001$) between neuromuscular block onset time at the laryngeal adductor and orbicularis oculi muscles but not between laryngeal and thumb muscles. The authors conclude that, after injection of atracurium, laryngeal adductor and orbicularis oculi blocks have similar intensities and time courses. Thus, the orbicularis oculi is a better monitor of the onset of atracurium block at the vocal cords than the adductor pollicis. [13]

Donati F studied about Pharmacokinetic and pharmaco dynamic factors in clinical use of muscle relaxants in 1994 . They said faster onset of Neuro Muscular Block at OO compared to AP might be due to differences in circulation time and muscle blood flow. Muscles which are closer to central circulation like the Orbicularis Oculi or the diaphragm have relatively greater perfusion and tend to be paralyzed more rapidly than the more peripheral muscles like Adductor Pollicis. [22]

Bertrand Debaene and Andrer Lienhart in 1995 , monitored the onset of neuromuscular block at the orbicularis oculi, to predict good intubating conditions during atracurium – induced neuro muscular block. They concluded that orbicularis oculi monitoring can predict good intubating conditions earlier than Adductor pollicis monitoring when using 0.5 mg/kg but not 0.3mg/kg atracurium as good intubating condition may not be obtained because neither the vocal cords nor the diaphragm will be completely blocked after giving 0.3 mg/kg. [14]

Koscielniak Nielsen ZJ, Viby Mogensen J in 1996 , evaluated timing of tracheal intubation by monitoring the Orbicularis oculi, Adductor pollicis or using a

stopwatch. The most suitable time for tracheal intubation, following vecuronium 0.1 mg kg^{-1}, was estimated in 120 patients. The trachea was intubated at cessation of the visually observed response of the orbicularis oculi muscle to facial nerve stimulation , or cessation of responses at the adductor pollicis to ulnar nerve stimulation, or after waiting 3 min , or 4 min . Loss of response to train-of-four stimulation occurred significantly sooner in orbicularis oculi than in adductor pollicis($P = 0.021$). However, intubating conditions were poor in four patients (14%) in orbicularis oculi group, compared with none in adductor pollicis group and only in one patient where intubation was performed after waiting for 3 and 4 mins. Thus, contrary to expectations, the cessation of the response of the orbicularis oculi muscle did not guarantee good or even satisfactory intubating conditions. The results suggest that in fit adult patients it is as good to wait 3 min after injection of vecuronium 0.1 mg kg^{-1} before tracheal intubation, instead of using a nerve stimulator. [23]

Benot Plaud, Marc Laffon, in 1997 Compared visual estimation of onset of Neuro muscular blockade at both Aductor Pollicis and Orbicularis oculi in Children using Train Of Four. In the two groups, time from injection of vecuronium to complete neuromuscular blockade was shorter at the orbicularis oculi than at the adductor pollicis, ($P < 0.05$). Intubating conditions were excellent in all patients except one. where it was rated as good. Intubating conditions did not differ much between the two groups. They concluded that following administration of 0.15 mg · kg^{-1} vecuronium in children, monitoring of the OO can detect good intubating conditions 0.7 min earlier than with monitoring of the AP. [24]

G.Haller, in 1998 evaluated tracheal intubating conditions when intubation time is determined by the onset time of the neuromuscular block either of the adductor pollicis(AP) or of the Orbicularis oculi muscle (OO). Intubation condition was

excellent 95% in AP, excellent 65% in OO with poor 15% in OO. They concluded monitoring neuro muscular activity of the Adductor pollicis using Train Of Four(TOF) to determine the appropriate tracheal intubation time and conditions in patients paralyzed with rocuronium is more clinically relevant than monitoring the orbicularis oculi. [18]

Frederique Le Corre in 1999 conducted visual estimation of onset time at orbicularis oculi, after five muscle relaxant i.e Atracurium, Mivacurium, rocuronium, succinylcholine and vecuronium. They concluded that difference in onset time of muscle relaxants observed at adductor pollicis were also found at orbicularis oculi, Visual estimation of the response at the orbicularis oculi correctly predicted adequate intubating condition in more than 90% of cases for all the currently available muscle relaxant. [15]

Hemmerling TM in 2000, Did Simultaneous determination of Neuro Muscular Block at larynx, adductor pollicis, Orbicularis Oculi and corrugator supercilii muscles . They said Orbicularis oculi is made up of small, round and 89% fast twitch type 2 fibers, Adductor pollicis is made up of slow oxidative type fibers. They concluded onset time and times for the first twitch response to return to 25,75 and 90% at the adducting laryngeal muscles and the diaphragm were significantly ($p < 0.005$) shorter than at the adductor pollicis, corrugators supercilii or the orbicularis oculi muscles after using Mivacurium 0.2mg/kg. Onset and clinical duration of NMB at larynx and the diaphragm are shorter than in the peripheral muscles. Hence monitoring NMB in the diaphragm can successfully be used in all patients. [20]

Plaud B, Debaene B in 2001, compared 2 monitoring sites around the eye with adductor pollicis and the laryngeal adductor muscles . They concluded that

corrugator supercilii reflects blockade of laryngeal adductor muscles. Orbicularis oculi and adductor pollicis have similar sensitivities. They also said visual monitoring is a less objective method of measurement than the continuous monitoring and registration of the evoked mechanical or electromyographic response. [19]

Dr. Jacintha D'souza, Dr. Saroja V. Sharma in 2006, Monitored the onset of neuro muscular block for predicting intubating conditions , a randomized control trial between Orbicularis oculi and Adductor pollicis group using Visual assessment of Train of Four (Neuro muscular monitor) responses. They concluded that monitoring orbicularis oculi can predict excellent or good intubating conditions earlier than monitoring Adductor Pollicis. Intubating condition was similar between the two groups. [16]

H.J. Lee in 2009 did comparison of adductor pollicis , orbicularis oculi and corrugator supercilii as indicators of adequacy of muscle relaxation for tracheal intubation. Onset time in OO was shorter than in AP ($p < 0.001$), but was associated with poor intubating conditions. They concluded that after administration of Rocuronium, twitch monitoring at the orbicularis oculi allows a faster intubation but is associated with an acceptable incidence of inadequate intubating conditions. Excellent intubating conditions are observed most frequently with Adductor pollicis monitoring but with the longest delay before intubation is attempted. They have used TOF-Watch acceleromyograph , neuro muscular monitor for knowing ideal time to intubate the patient. [17]

Historical development

The term trachea is derived from Greek word meaning “Rough Vessel” Development of endotracheal intubation technique was stimulated by the need for safe anaesthesia during operations on head and neck. C.Kite of Gravesend described oral and nasal intubation for resuscitation of apparently drowned patients in 1788.

William McEwen of Glasgow first performed endotracheal intubation in 1880, as is known today. Franz Kuhn of Kassel (1866 – 1929) in 1901, extended the technique by using flexible metal tube introduced on a curved guide through the mouth. A year later he described nasotracheal intubation.

Alfred Kirstein (1863 – 1922) of Berlin and Gustav Killian (1860 – 1921) of Freiburg, the original bronchoscopist, pioneered direct laryngoscopy in 1895 and 1912 respectively.

A pilot balloon was described in 1893 by Victor Eisenmenger (1864 – 1932). Before the days of muscle relaxant blind nasal intubations was popular because it was quicker than oral intubation under direct vision and deep inhalation anaesthesia. The use of muscle relaxant to facilitate intubation was pioneered by Bourne.

The first laryngoscope prototype was introduced by Chevalier Jackson (1865 to 1958). It was later modified by Magill, Paluel. J. Flagg (1886 to 1970) of New York, Miller and Robert Macintosh of Oxford in 1897.

Neuro Muscular Junction[25]

Otto Loewi in 1921 identified Acetyl choline as chemical neurotransmitter. Gopfert and Schaefer in 1938 described the current concepts about neuro muscular transmission. They said stimulation of a motor nerve of a curarized muscle produced a transient electro negativity in the region of synaptic button.

Dale et al said acetyl choline was released at nerve terminal during activity and Cowen et al said that addition of acetylcholine to a bath of nerve muscle preparation causes a slow monophasic potential similar to that seen with nerve stimulation, served as the heralded start of our understanding of neuro muscular transmission in 1936.

Doyere in 1840 described the first vertebrate Neuro muscular junction. Liddel and Shreington described the term Motor unit in 1925. Current concepts of Neuro Muscular junction are attributated to Couteaux for his extensive work over 40 yrs.

Neuro Muscular Monitor[26]

In 1958, Christie and Churchill-Davidson described the use of a nerve stimulator to monitor neuromuscular block. However, it was not until the (TOF) Train Of Four pattern of stimulation described in 1970 by Ali et al, that such equipment came into routine clinical use.

Muscle relaxants

The arrow poison used for hunting by the native people of South America has been known for centuries. Benjamin Brodie(1783-1862) and Edward NathanielBrancroft(1772- 1842) showed that the poison paralyzed the respiratory muscles and that an animal given curare could be kept alive if ventilated. Claude

Bernad's study of effects of curare on neuromuscular transmission led to the conclusion that the site of action of curare is the neuromuscular junction.

Rocuronium bromide (ORG 9426) was introduced in 1994 in order to provide a very rapid relaxation for endotracheal intubation. It was synthesized from its parent molecule vecuronium bromide by various substitutions by Dr. T. Sleigh and Dr.Savage at Organon laboratory.

ANATOMY

The term airway refers to extra pulmonary air passage consisting of the nasal and oral cavity, pharynx, larynx, trachea and principle bronchi. The main function of the air way is conduction of air to and from the lung for gaseous exchange.

Larynx

Larynx is essentially a protective valve at the upper end of the respiratory passages; its development into an organ of speech is a much later affair.

The laryngeal cartilages

The principal cartilages are the thyroid, cricoid and the paired arytenoids, together with the epiglottis; in addition, there are the small corniculate and cuneiform cartilages.

The laryngeal ligaments

The ligaments of the larynx can be divided into the extrinsic and the intrinsic, which link together the laryngeal cartilages.

The extrinsic ligaments are as follows.

1. Thyrohyoid membrane,
2. Cricotracheal ligament,.
3. Cricothyroid ligament
4. Hyo-epiglottic ligament,

The intrinsic ligaments comprise the capsules of the tiny synovial joints between the arytenoid and cricoid, and between the thyroid and cricoid cartilages.

If the cavity of the larynx is inspected in a bisected specimen, two folds will be seen, the upper vestibular and the lower vocal fold (or the *false* and *true vocal cords*), between which is a slit-like recess termed the *sinus* of the larynx From the anterior part of the sinus, the *saccule* of the larynx ascends as a pouch between the vestibular fold and the inner surface of the thyroid cartilage.

The muscles of the larynx

The muscles of the larynx can be divided into the extrinsic group, which attach the larynx to its neighbors, and the intrinsic group, which are responsible for moving the cartilages of the larynx one against the other.

The **extrinsic muscles** of the larynx are the sternothyroid, thyrohyoid and the inferior constrictor of the pharynx. In addition, a few fibers of stylopharyngeus and palatopharyngeus reach forward to the posterior border of the thyroid cartilage.

Other muscles play an important part in movements of the larynx indirectly, via its close attachment, by ligaments and muscle, with the hyoid bone. These muscles help to elevate and depress the larynx; the indirect elevators are the mylohyoid,

stylohyoid and geniohyoid, and the indirect depressors are the sternohyoid and omohyoid.

The **intrinsic muscles** of the larynx have a threefold function: they open the cords in inspiration, they close the cords and the laryngeal inlet during deglutition, and they alter the tension of the cords during speech. They comprise the posterior and lateral cricoarytenoids, the interarytenoids and the aryepiglottic, the thyroarytenoid, the thyroepiglottic, the vocalis and the cricothyroid muscles.

The actions of the intrinsic laryngeal muscles can be summarized :

1. Abductors of the cords: posterior cricoarytenoids;
2. Adductors of the cords: lateral cricoarytenoids, interarytenoid;
3. Sphincters to vestibule: aryepiglottics, thyroepiglottics;
4. Regulators of cord tension: cricothyroids (tensors), thyroarytenoids (relaxors), vocalis (fine adjustment).

Blood supply

The *superior laryngeal artery* supplies the interior of the larynx.

The *inferior laryngeal artery*

Nerve supply

The nerve supply of the larynx is from the vagus via its superior and recurrent laryngeal branches.

1. The superior laryngeal nerve supplies the cricothyroid muscle ,sensory supply to the interior of the larynx as far down as the vocal cords; motor fibers to the interarytenoid muscle.

2. The internal laryngeal nerve.

3. The recurrent laryngeal nerve provides the motor supply to the intrinsic muscles of the larynx apart from cricothyroid, as well as the sensory supply to the laryngeal mucosa inferior to the vocal cords

TRACHEA

The trachea is a cartilaginous and membranous tube of about 10 to 11cm in length which extends from its attachment from the lower end of the cricoid cartilage at the level of the 6^{th} cervical vertebra to its termination at the bifurcation at the level of the upper border of T5 vertebra. It is kept constantly patent by the U shaped cartilage and have posterior wall that lies flat against the esophagus, which consist of muscle and connective tissue. The nerve supply of the trachea including the tracheal muscles are innervated by recurrent laryngeal nerve which also carry sensory fibers from the mucous membrane. Sympathetic supply is derived from the middle cervical ganglion and have connection with the recurrent laryngeal nerve.

Neuromuscular Anatomy And Physiology[27]

Neuromuscular Transmission

Neuromuscular transmission occurs by a simple mechanism. The nerve synthesizes acetylcholine and stores it in small, uniformly sized packages called vesicles. Stimulation of the nerve causes these vesicles to migrate to the surface of the nerve, rupture, and discharge acetylcholine into the cleft separating nerve from muscle. Acetyl Choline receptors (AChRs) in the end plate of the muscle respond by opening their channels for influx of sodium ions into the muscle to depolarize the muscle. The end-plate potential created is continued along the muscle membrane by the opening of sodium channels present throughout the muscle membrane to initiate a contraction. The acetylcholine immediately detaches from the receptor and is destroyed by the enzyme acetyl cholinesterase, which is also present in the cleft. Drugs, notably depolarizing relaxants or nicotine and carbachol (a synthetic analog of acetylcholine not destroyed by acetyl cholinesterase), can also act on these receptors to mimic the effect of acetylcholine and cause depolarization of the end plate. These drugs are therefore called agonists of the receptor because to a greater or lesser extent, they stimulate the receptor, at least initially. Nondepolarizing muscle relaxants (NDMRs) also act on the receptors, but they prevent acetylcholine from binding to the receptor and thus prevent depolarization by agonists. Because these nondepolarizers prevent the action of agonists (e.g., acetylcholine, carbachol, succinylcholine), they are referred to as antagonists of the Acetyl choline receptor(AChR). Reversal agents or antagonists of neuromuscular paralysis (e.g., neostigmine, prostigmine), inhibit acetyl cholinesterase and therefore impair the hydrolysis of acetylcholine. The increased accumulation of un degraded acetylcholine can compete with Nondepolarizing muscle relaxants effectively and thereby displace the latter from the

receptor (i.e., law of mass action) and antagonize the effects of Nondepolarizing muscle relaxants.

Morphology

The neuromuscular junction is specialized on the nerve side and on the muscle side to transmit and receive chemical messages. Each motor neuron runs without interruption from the ventral horn of the spinal cord or medulla to the neuromuscular junction as a large, myelinated axon (Fig. 1). As it approaches the muscle, it branches repeatedly to contact many muscle cells and gather them into a functional group known as a motor unit. The architecture of the nerve terminal is quite different from that of the rest of the axon. As the terminal reaches the muscle fiber, it loses its myelin, forms a spray of terminal branches against the muscle surface, and is covered by Schwann cells. This arrangement conforms to the architecture on the synaptic area of the muscle membrane. The nerve is separated from the surface of the muscle by a gap of approximately 20 nm, called the junctional or synaptic cleft. The nerve and muscle are held in tight alignment by protein filaments called basal lamina that span the cleft between the nerve and end plate. The muscle surface is heavily corrugated, with deep invaginations of the junctional cleft—the primary and secondary clefts—between the folds in the muscle membrane; thus, the end plate's total surface area is very large. The depths of the folds also vary between muscle types and species. Human neuromuscular junctions, relative to muscle size, are smaller than those of the mouse, although the junctions are located on muscle fibers that are much larger. Human junctions have longer junctional foldings and deeper gutters[29]. The functional significance of these folds is unclear. The shoulders of the folds are densely populated with Acetyl choline receptors (AChRs,) about 5 million of them in each junction.

Acetyl choline receptors (AChRs) are sparse in the depths between the folds. Instead, these deep areas contain sodium channels.

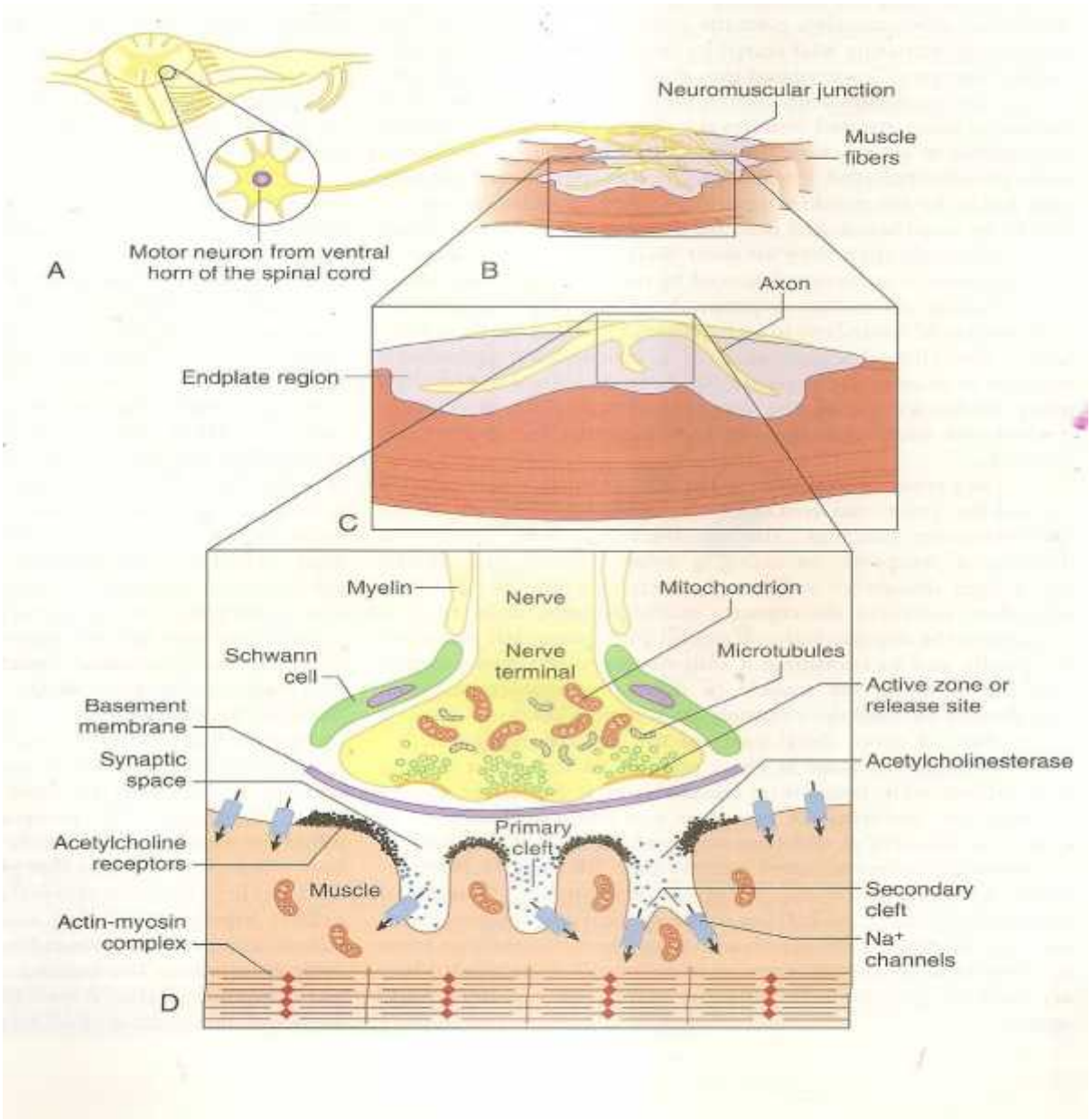


Figure 1:- Structure of the adult neuromuscular junction showing the three cells that constitute the synapse: the motor neuron (i.e., nerve terminal), muscle fiber, and Schwann cell. **A,** The motor nerve originates in the ventral horn of the spinal cord or brainstem. **B,** As the nerve approaches its muscle fibers and before attaching itself to the surface of the muscle fiber, the nerve divides into branches that innervate many individual muscle fibers. **C,** Each muscle receives only one synapse. The motor nerve loses its myelin and further subdivides into many presynaptic boutons to terminate on the surface of the muscle fiber. **D,** The nerve terminal, covered by a Schwann cell, has vesicles clustered about the membrane thickenings, which are the active zones, toward its synaptic side and mitochondria and microtubules toward its other side. A synaptic gutter or cleft made up of a primary and many secondary clefts separates the nerve from the muscle. The muscle surface is corrugated, and dense areas on the shoulders of each fold contain acetylcholine receptors. Sodium channels are present at the bottom of the clefts and throughout the muscle membrane. The acetylcholinesterase and proteins and proteoglycans that stabilize the neuromuscular junction are present in the synaptic clefts.

The trophic function of the nerve is vital for the development and maintenance of adequate neuromuscular function. Before birth, each muscle cell commonly has contacts with several nerves and has several neuromuscular junctions. At birth, all but one of the nerves retract, and a single end plate remains. Once formed, the nerve-muscle contact, especially the end plate, is durable. Even if the original nerve dies, the one replacing it innervates exactly the same region of the muscle. The nerve endings on fast muscles are larger and more complicated than those on slow muscles. The reason for this is unclear. These differences in the nerve endings on muscle surfaces may play a role in the difference in response of fast- and slow-twitch muscle fibers to muscle relaxants.

All the muscle cells in a unit are excited by a single neuron, stimulation of the nerve electrically or by an action potential originating from the ventral horn or by any agonist, including depolarizing relaxants (e.g., succinylcholine), causes all muscle cells in the motor unit to contract synchronously. Synchronous contraction of the cells in a motor unit is called *fasciculat.* Although most adult human muscles have only one neuromuscular junction per cell, an important exception is some of the cells in extraocular muscles. The extraocular muscles are “tonic” muscles, and unlike other mammalian striated muscles, they are multiply innervated, with several neuromuscular junctions strung along the surface of each muscle cell.[28] Quite in contrast to other muscles, even the adult ocular muscle contains mature and immature fetal receptor ,segregated into distinct synapses on different fibres. The ocular muscles contract and relax slowly rather than quickly as other striated muscles do; they can maintain a steady contraction, or contracture, the strength of which is proportional to the stimulus received.. These muscles are important to an anaesthesiologist because depolarizing relaxants instead of causing a brief contraction

followed by paralysis, they cause a long-lasting contracture response that pulls the eye against the orbit and could contribute to an increase in intraocular ocular pressure.

The perijunctional zone is the area of muscle immediately beyond the junctional area. It contains a mixture of receptors, including a smaller density of Acetly Choline Receptors (AChRs) and a high density of sodium channels. The admixture enhances the capacity of the perijunctional zone to respond to the depolarization (i.e., end-plate potential) produced by AChRs and to transduce it into the wave of depolarization that travels along the muscle to initiate muscle contraction. The density of sodium channels in the perijunctional area is richer than in more distal parts of the muscle membrane. The perijunctional zone is close enough to the nerve ending to be influenced by transmitter released from it. There can be variants (i.e., isoforms) of receptors and sodium channels, congenital abnormalities in the AChR or in the sodium and calcium channels (i.e., mutations) which can contribute to the differences in response to relaxants that are seen in patients with different pathologic conditions and ages.

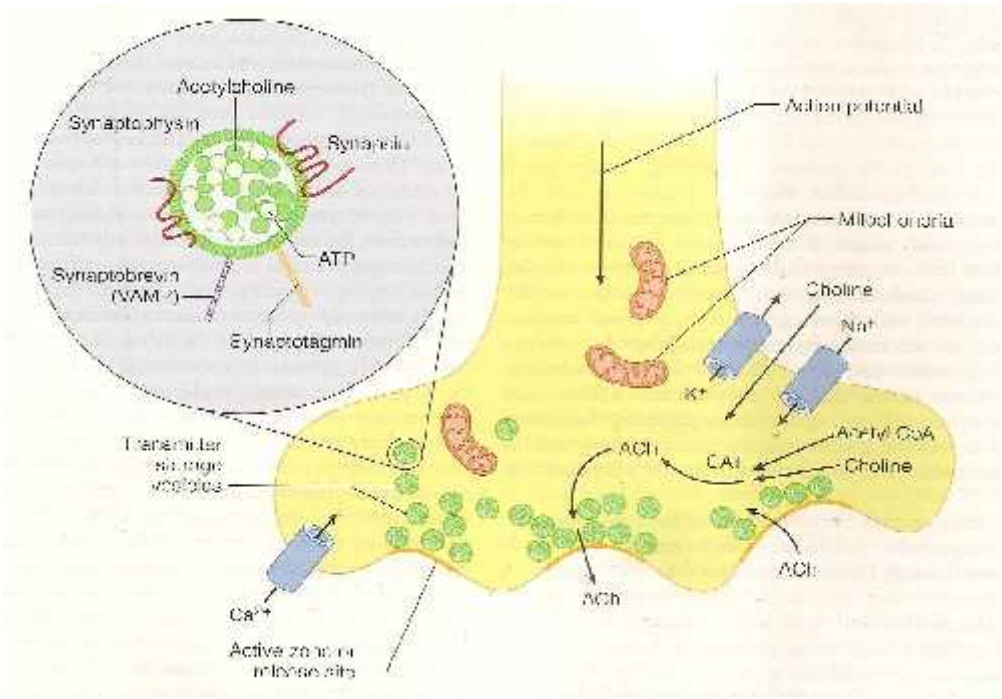


Figure 2 :- The working of a chemical synapse, the motor nerve ending, including some of the apparatus for synthesis of transmitter. The large intracellular structures are mitochondria. Acetylcholine (ACh), synthesized from choline and acetate by acetyl coenzyme A (acetyl CoA), is transported into coated vesicles, which are moved to release sites. A presynaptic action potential that triggers influx of calcium through specialized proteins (Ca^{2+} channels) causes the vesicles to fuse with the membrane and discharge transmitter. Membrane from the vesicle is retracted from the nerve membrane and recycled. Each vesicle can undergo various degrees of release of contents—from incomplete to complete. The transmitter is inactivated by diffusion, catabolism, or reuptake. The *inset* provides a magnified view of a synaptic vesicle. Quanta of ACh together with adenosine triphosphate (ATP) are stored in the vesicle and covered by vesicle membrane proteins. Synaptophysin is a glycoprotein component of the vesicle membrane. Synaptotagmin is the vesicle's calcium sensor. Phosphorylation of another membrane protein, synapsin, facilitates vesicular trafficking to the release site. Synaptobrevin (vesicle-associated membrane protein [VAMP]) is a SNARE protein involved in attaching the vesicle to the release site CAT, choline acetyltransferase.

Quantal Theory

The contents of nerve ending are not homogeneous. Vesicles are congregated (Fig – 1 & 2) towards the junctional surface, whereas microtubules, mitochondria, and other support structures are located toward the opposite side. The vesicles containing transmitter are ordered in repeating clusters alongside small, thickened, electron-dense patches of membrane referred to as active zones or release sites. This thickened area is a cross section of a band running across the width of the synaptic surface of the

nerve ending that is believed to be the structure to which vesicles attach (active zones) before they rupture into the junctional cleft. There are voltage-gated calcium channels—that allow calcium to enter the nerve and cause the release of vesicles. [29] The rapidity with which the neurotransmitter is released (200 µsec) suggests that voltage-gated calcium channels are close to the release sites.

There are small, spontaneous depolarizing potentials at neuromuscular junctions which have only one hundredth the amplitude of the evoked end-plate potential produced when the motor nerve is stimulated. They resemble the end-plate potential - called miniature end-plate potentials (MEPPs). They are unitary responses, produced by uniformly sized packages, or quanta, of transmitter released from the nerve (in the absence of stimulation). The stimulus-evoked end-plate potential is the additive depolarization produced by the synchronous discharge of quanta from several hundred vesicles. The action potential that is propagated to the nerve ending allows entry of calcium into the nerve through voltage-gated calcium channels, and this causes vesicles to migrate to the active zone, fuse with the neural membrane, and discharge their acetylcholine into the junctional cleft. Because the release sites are located immediately opposite the receptors on the postjunctional surface, little transmitter is wasted, and the response of the muscle is coupled directly with the signal from the nerve.

Alignment of the presynaptic receptor site is achieved by adhesion molecules or specific cell-surface proteins located on both sides of the synapse that grip each other across the synaptic cleft and hold the prejunctional and postjunctional synaptic apparatuses together. One such protein implicated in synapse adhesion is neurexin, which binds to neuroligins on the postsynaptic membrane. The amount of acetylcholine released by each nerve impulse is large, at least 200 quanta of about

5000 molecules each, and the number of AChRs activated by transmitter released by a nerve impulse is also large, about 500,000 molecules. The ions (mostly Na^+ and some Ca^{2+}) that flow through the channels of activated AChRs cause maximum depolarization of the end plate, which results in an end-plate potential that is greater than the threshold for stimulation of the muscle. The signal is carried by more molecules of transmitter than are needed, and they evoke a response that is greater than needed. At the same time, only a small fraction of the available vesicles and receptors or channels are used to send each signal. Consequently, transmission has a substantial margin of safety, and at the same time the system has substantial capacity in reserve.

Formation of Neurotransmitter at Motor Nerve Endings

The axon of the motor nerve carries electrical signals from the spinal cord to muscles and transforms the electrical signal into a chemical one. All the ion channels, enzymes, other proteins, macromolecules, and membrane components needed by the nerve ending to synthesize, store, and release acetylcholine and other trophic factors are made in the cell body and transmitted to the nerve ending by axonal transport[30] (Fig. 2). The simple molecules choline and acetate are obtained from the environment of the nerve ending, choline is transported from extracellular fluid to the cytoplasm and acetate in the form of acetyl coenzyme A from mitochondria. The enzyme choline acetyltransferase brings about the reaction of choline and acetate to form acetylcholine; the acetylcholine is stored in cytoplasm until it is transported into vesicles, which are in a better position for release.

Nerve Action Potential

During action potential, sodium from outside flows across the membrane, and the resulting depolarizing voltage opens calcium channels, which allows entry of calcium ions into the nerve and causes acetylcholine to be released. The number of quanta released by a stimulated nerve is greatly influenced by the concentration of ionized calcium in extracellular fluid. Doubling the extracellular calcium results in a 16-fold increase in the quantal content of an end-plate potential. The calcium current persists until the membrane potential is returned to normal by outward fluxes of potassium from inside the nerve cell. Along with calcium channels on the nerve terminal are potassium channels, including the voltage-gated and calcium-activated potassium channels, whose function is to limit entry of calcium into the nerve and therefore depolarization. The calcium current can be prolonged by potassium channel blockers (e.g., 4-aminopyridine, tetraethylammonium), which slow or prevent the efflux of potassium out of the nerve. The increase in quantal content produced in this way can reach astounding proportions. An effect of increasing calcium in the nerve ending is also seen clinically as the so-called post-tetanic potentiation, which occurs after a nerve of a patient paralyzed with an (NDMR) Non depolarizing muscle relaxant is stimulated at high, tetanic frequencies. Calcium enters the nerve with every stimulus, but because it cannot be excreted as quickly as the nerve is stimulated, it accumulates during the tetanic period. Because the nerve ending contains more than the normal amount of calcium for some time after the tetanus, a stimulus applied to the nerve during this time causes the release of more than the normal amount of acetylcholine. The abnormally large amount of acetylcholine antagonizes the relaxant and causes the characteristic increase in size of the twitch.

Calcium enters the nerve through specialized proteins called calcium channels. P channels and the slower L channels. P channels, responsible for normal release of transmitter, are located immediately adjacent to the active zones . They are voltage dependent and opened and closed by changes in membrane voltage caused by the nerve action potential. In addition to calcium channels, several forms of potassium channels are present in the nerve terminal, including voltage-gated and calcium-activated potassium channels. Potassium channels limit the duration of nerve terminal depolarization and hence entry of calcium and release of transmitter. Alterations in entry of calcium into the nerve ending can also alter release of transmitter. Higher than normal concentrations of bivalent inorganic cations (e.g., magnesium, cadmium, manganese) can also block entry of calcium through P channels and profoundly impair neuromuscular transmission. P channels, are not affected by calcium entry–blocking drugs such as verapamil, diltiazem, and nifedipine. These drugs have profound effects on the slower L channels present in the cardiovascular system. As a result, the L-type calcium channel blockers have no significant effect at therapeutic doses on the normal release of acetylcholine or on the strength of normal neuromuscular transmission.

Synaptic Vesicles and Recycling

There are two pools of vesicles that release acetylcholine, a readily releasable pool and a reserve pool, sometimes called VP2 and VP1, respectively. Vesicles in the former are smaller and limited to an area very close to the nerve membrane, where they are bound to the active zones. These vesicles release transmitter. Electron microscopic studies have demonstrated that the majority of synaptic vesicles (VP1) are sequestered in the reserve pool and tethered to the cytoskeleton in a filamentous

network composed mainly of actin, synapsin (an actin-binding protein), synaptotagmin, and spectrin.

Release occur when calcium ion enters the nerve through the P channels lined up on the sides of the active zones by SNARE proteins. The SNARE (soluble *N*-ethylmaleimide–sensitive attachment protein receptors) proteins are involved in fusion, docking, and release of acetylcholine at the active zone. Calcium needs to moves into vesicle and activate the proteins in the vesicle wall involved in a process known as docking.[31] The reactivated proteins seem to react with the nerve membrane to form a pore through which the vesicle discharges its acetylcholine into the junctional cleft. Some vesicles stay open briefly before retrieval and do not completely collapse into the surface membrane ("kiss and run"). Others stay open longer and probably do not collapse completely ("compensatory"). Still others collapse completely and are not retrieved until another stimulus is delivered ("stranded").

The larger reserve (VP1) vesicles, from their position deeper from the nerve ending and firmly tethered to the cytoskeleton by many proteins, including actin, synapsin (an actin-binding protein), synaptotagamin, and spectrin, may be moved to the readily releasable store to replace worn-out vesicles or to participate in transmission when the nerve is called on to work especially hard (e.g., when it is stimulated at very high frequencies or for a very long time). Under such strenuous circumstances, calcium may penetrate more deeply than normal into the nerve or may enter through L channels to activate calcium-dependent enzymes that break the synapsin links holding the vesicles to the cytoskeleton, thereby allowing the vesicles to be moved to the release sites. Repeated stimulation requires the nerve ending to replenish its store of vesicles filled with transmitter, a process known as *mobilization*.

The term is commonly applied to the aggregate of all steps involved in maintaining the nerve ending's capacity to release transmitter—everything from the acquisition of choline and the synthesis of acetate to the movement of filled vesicles to release sites. Uptake of choline and the activity of choline acetyltransferase, the enzyme that synthesizes acetylcholine, the rate-limiting steps.

Process of Exocytosis

During an action potential and calcium influx, neurotransmitter is released. Vesicle releases its contents - process is called *exocytosis*. The SNAREs include the synaptic-vesicle protein synaptobrevin and the plasmalemma-associated proteins syntaxin and synaptosome-associated protein of 25 kd (SNAP-25). The current model of protein-mediated membrane fusion in exocytosis is as follows. Syntaxin and SNAP-25 are complexes attached to the plasma membrane. After initial contact, the synaptobrevin on the vesicle forms a ternary complex with syntaxin and SNAP-25. Synaptotagmin is the protein on the vesicular membrane that acts as a calcium sensor, localizes the synaptic vesicles to synaptic zones rich in calcium channels, and stabilizes the vesicles in the docked state. Assembly of the ternary complex forces the vesicle close to the underlying nerve terminal membrane (i.e., the active zone), and the vesicle is then ready for release (Fig. 3). An action potential in the nerve terminal allows the entry of calcium. The close proximity of release sites, calcium channels, and synaptic vesicles and use of the calcium sensor lead to a burst of release of new transmitter synchronous with the stimulus. The vesicle can release part or all of its contents, some of which can be recycled to form new vesicles as described previously (kiss and run, etc.).[32]

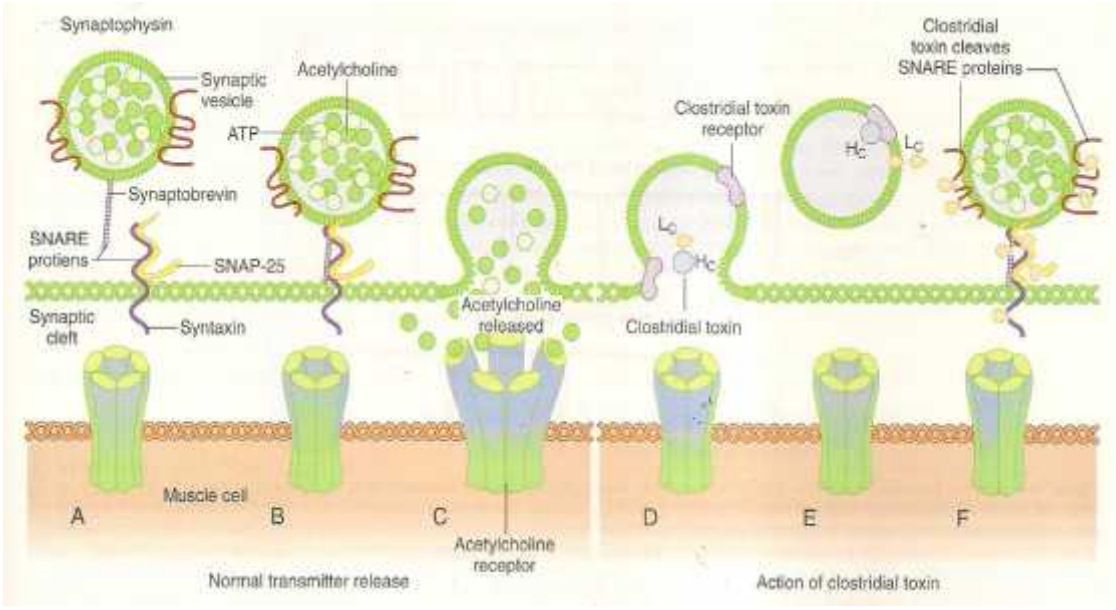


Figure 3:- Model of protein-mediated membrane fusion and exocytosis. **A,** Release of acetylcholine from vesicles is mediated by a series of proteins collectively called SNARE proteins. Synaptotagmin is the neuronal calcium receptor that detects entry of calcium. Synaptobrevin (i.e., vesicle-associated membrane protein [VAMP]) is a filament-like protein on the vesicle. **B,** During depolarization and entry of calcium, synaptobrevin on the vesicle unfolds and forms a ternary complex with syntaxin/SNAP-25. This process is facilitated by phosphorylation of synapsin, also present on the vesicle membrane. **C,** Assembly of the ternary complex forces the vesicle in close apposition to the nerve membrane at the active zone with release of its contents, acetylcholine. The fusion is disassembled, and the vesicle is recycled. Clostridial toxins, including tetanus and botulinum, inhibit the release of acetylcholine and cause paralysis of muscles. The toxin consists of a light (L_c) and heavy (H_c) chain. **D,** The first stage in intoxication is interaction of the toxin with a thus far unidentified receptor. **E,** This is followed by internalization of the toxin within the vesicle and release of the light chain from the vesicle. The liberated L_c cleaves a variety of SNARE proteins, depending on the type of toxin released, thereby preventing assembly of the fusion complex and thus blocking release of acetylcholine.

Acetylcholinesterase

The acetylcholine released from the nerve diffuses across the junctional cleft and reacts with specialized receptor proteins in the end plate to initiate muscle contraction. Transmitter molecules that do not react immediately with a receptor or those released after binding to the receptor are destroyed almost instantly by acetyl cholinesterase in the junctional cleft. Acetyl cholinesterase at the junction is the asymmetric or A12-form protein made in the muscle, under the end plate. Acetyl cholinesterase is a type B carboxylesterase enzyme. There is a smaller concentration of it in the extrajunctional area. The enzyme is secreted from the muscle but remains attached to it by thin stalks of collagen fastened to the basement membrane. Most of

the molecules of acetylcholine released from the nerve initially pass between the enzymes to reach the postjunctional receptors, but as they are released from the receptors, they invariably encounter acetyl cholinesterase and are destroyed. Under normal circumstances, a molecule of acetylcholine reacts with only one receptor before it is hydrolyzed. Acetylcholine is a potent messenger, but its actions are very short lived because it is destroyed in less than 1 millisecond after it is released.

Postjunctional Acetylcholine Receptors

Three isoforms of postjunctional nicotinic AChRs exist, a junctional or mature receptor, an extrajunctional or immature (fetal) receptor, and the most recently described neuronal α7 receptor.

AChRs are synthesized in muscle cells and are anchored to the end-plate membrane by a special 43-kd protein known as rapsyn. This cytoplasmic protein is associated with the AChR in a 1:1 ratio. The receptors, formed of five subunit proteins, are arranged like the staves of a barrel into a cylindrical receptor with a central pore for ion channeling. The key features are sketched in Figure 4. The receptor protein has a molecular mass of about 250,000 daltons. Each receptor has five subunits. The mature receptor consists of α, β, δ, and ε and the fetal (immature, extrajunctional) receptor, α, β, δ, and γ; there are two subunits of α and one of each of the others. The neuronal α7 AChR consists of five α7-subunits. Each of all receptor subunits consists of approximately 400 to 500 amino acids. The receptor-protein complex passes entirely through the membrane and protrudes beyond the extracellular surface of the membrane and into the cytoplasm. The binding site for acetylcholine is on each of the α-subunits, and these are the sites of competition between receptor agonists and antagonists. Agonists and antagonists are attracted to the binding site,

and either may occupy the site, which is located near cysteine residues (unique to the α-chain) at amino acid positions 192-193 of the α-subunit.

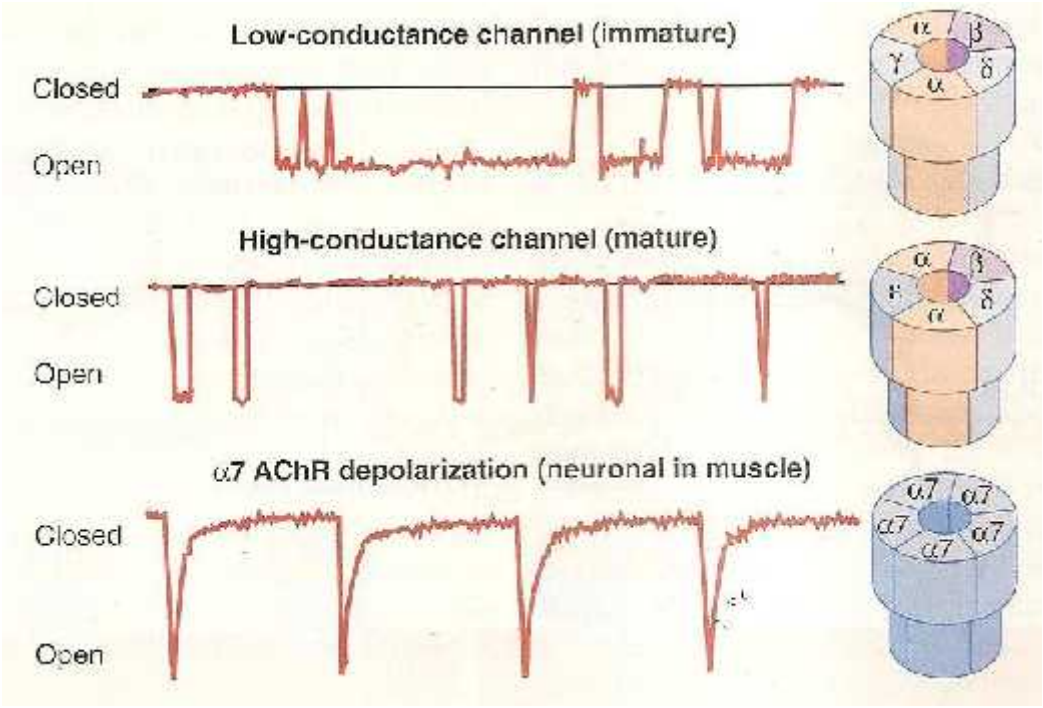


Figure 4 :- Sketch of acetylcholine receptor (AChR) channels (*right*) and tracings of cell-patch records of receptor channel openings (*left*). The mature, or junctional, receptor consists of two α-subunits and one each of β-, δ-, and ε-subunits. The immature, extrajunctional or fetal, form consists of two α- and one each of β, δ, and γ-subunits. The latter is thus called the γ-subunit receptor. Recently, a neuronal receptor consisting of five α7-subunits has been described in muscle. All the subunits are arranged around the central cation channel. The immature isoform containing the γ-subunit has long open times and low-amplitude channel currents. The mature isoform containing the ε-subunit has shorter open times and high-amplitude channel currents during depolarization. Substitution of the ε-subunit for the γ-subunit gives rise to the fast-gated, high-conductance channel type. As expected, application of acetylcholine to the α7 AchR also results in a fast, rapidly decaying inward current. All these depolarizing events are insensitive to treatment with atropine but sensitive to treatment with α-bungarotoxin or muscle relaxants, which block the flow of current.

Basic Electrophysiology of Neurotransmission

Figure 5. illustrates the results of the classic depolarizing action of acetylcholine on end-plate receptors. Normally, the pore of the channel is closed by approximation of the cylinders (i.e., subunits). When an agonist occupies both α-subunit sites, the protein molecule undergoes a conformational change in which a channel is formed in the center through which ions can flow along a concentration

gradient. When the channel is open, sodium and calcium flow from the outside of the cell to the inside and potassium flows from the inside to the outside. The channel in the tube is large enough to accommodate many cations but it excludes anions (e.g., chloride). The current carried by the ions depolarizes the adjacent membrane. The net current is depolarizing and creates the end-plate potential that stimulates the muscle to contract.

The pulse stops when the channel closes and one or both agonist molecules detach from the receptor. The current that passes through each open channel is minuscule, only a few picoamperes (about 10^4 ions/msec). However, each burst of acetylcholine from the nerve normally opens about 500,000 channels simultaneously, and the total current is more than adequate to produce depolarization of the end plate and contraction of muscle. Opening of a channel causes conversion of chemical signals from a nerve to flow of current to end-plate potentials, thereby leading to muscle contraction. End-plate potential is the summation of many all-or-nothing events occurring simultaneously at myriad ion channels. It is these tiny events that are affected by drugs.

Both α-subunits must be occupied simultaneously by agonist; if only one of them is occupied, the channel remains closed (see Fig. 5). This is the basis for prevention of depolarization by antagonists. NDMRs typified by tubocurarine act by binding to either or both α-subunits and thus preventing acetylcholine from binding and opening the channel. This interaction between agonists and antagonists is competitive, and the outcome—transmission or block—depends on the relative concentrations and binding characteristics of the drugs involved.

Individual channels are also capable of a wide variety of conformations. They may open for a longer or shorter time than normal, open or close more gradually than usual, open briefly and repeatedly (i.e., chatter), or pass fewer or more ions per opening than they usually do. Their function is also influenced by drugs, changes in fluidity of the membrane, temperature, electrolyte balance in the milieu, and other physical and chemical factors. Receptor channels are dynamic structures that are capable of a wide variety of interactions with drugs and of entering a wide variety of current-passing states. All these influences on channel activity are ultimately reflected in the strength or weakness of neuromuscular transmission and the contraction of a muscle.

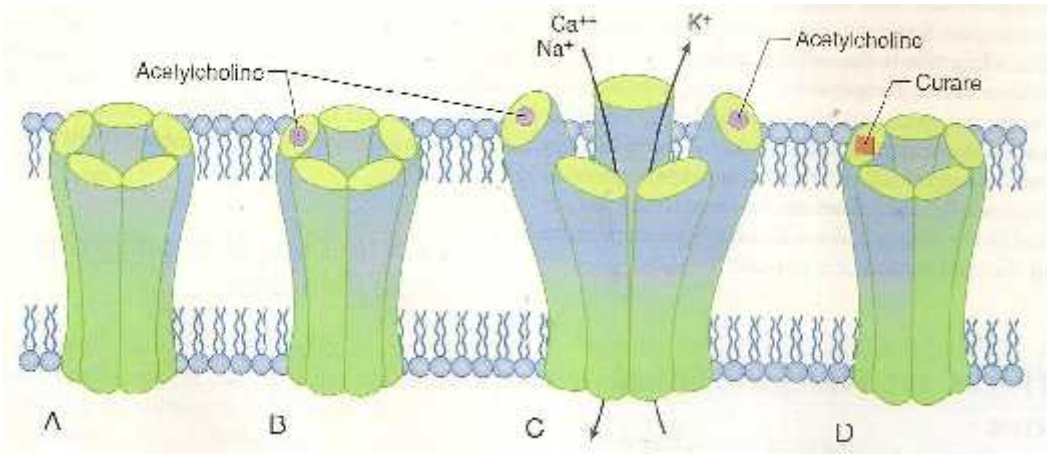


Figure 5 :- Actions of acetylcholine or curare on end-plate receptors. **A,** The ion channel is inactive and does not open in the absence of acetylcholine. **B,** Even binding of one acetylcholine molecule (*filled circle*) to one of two binding sites does not open the channel. **C,** When acetylcholine binds to the recognition sites of both α-subunits simultaneously (*filled circles*), a conformation change is triggered that opens the channel and allows ions to flow across the membrane. **D,** Action of antagonists such as curare (*filled square*). Acetylcholine is in competition with tubocurarine for the receptor's recognition site but may also react with acetylcholinesterase. Tubocurarine is a prototypical nondepolarizing muscle relaxant. Inhibiting the enzyme increases the lifetime of acetylcholine and the probability that it will react with a receptor. When one of the two binding (recognition) sites is occupied by curare, the receptor will not open, even if the other binding site is occupied by acetylcholine.

Pre synaptic acetyl choline receptors

They have been demonstrated pharmacologically and by molecular biology techniques., but their form and functions are not completely understood when

compared with those in the post synaptic area. A clue to differences between presynaptic and postsynaptic nicotinic acetylcholine receptors was the finding that presynaptic receptors can bind beta bungarotoxin only, while postsynaptic receptors bind to alpha – bungoratoxin. Additional clues to differences between pre and post synaptic nicotinic actyl choline receptors is the response of these receptors to different nicotinic actylcholine receptor agonists and antagonists.

The nicotinic receptor on the presynaptic surface of the nerve senses transmitter in the cleft and, by means of a positive and negative feedback system, causes the released of more transmitter. This positive feedback is also complemented by a negative feedback system that senses when the concentration of transmitter in the synaptic cleft has increased appropriately and shuts down the release system. It is believed that tetanic fade and train of four fade during Neuro muscular block due to non depolarizing NMB arise from inhibition of presynaptic cholinergic autoreceptors at the motor nerve endings. The neuronal nAcHR subtype on the nerve terminal that causes fade has been identified as alpha3beta2. Quite in contrast, suxamethonium does not inhibit the presynaptic alpha3beta2 nicotinic autoreceptor at clinically relevant concentrations. This may be reason for the typical lack of train of four fade during suxamethonium induced neuro muscular block.

Classic Actions of Nondepolarizing Muscle Relaxants

All (NDMR) Non depolarizing muscle relaxants impair or block neurotransmission by competitively preventing the binding of acetylcholine to its receptor. Fig 5 shows a system exposed to acetylcholine and tubocurarine. One receptor has attracted two acetylcholine molecules and opened its channel, where current will flow to depolarize that segment of membrane. Another has attracted one

tubocurarine molecule; its channel will not open, and no current will flow, even if one acetylcholine molecule binds to the other site. The third receptor has acetylcholine on one α-subunit and nothing on the other. What will happen depends on which of the molecules binds. If acetylcholine binds, the channel will open and the membrane will be depolarized; if tubocurarine binds, the channel will stay closed and the membrane will not be depolarized. At other times, one or two tubocurarine molecules may attach to the receptor, in which case the receptor is not available to agonists; no current flow is recorded. In the presence of moderate concentrations of tubocurarine, the amount of current flowing through the entire end plate at any instant is reduced from normal, which results in a smaller end-plate potential and, if carried far enough, a block in neurotransmission or production of neuromuscular paralysis.

Acetyl cholinesterase destroys acetylcholine and removes it from competition for a receptor, so tubocurarine has a better chance of inhibiting transmission. If, however, an inhibitor of acetyl cholinesterase such as neostigmine is added, the cholinesterase cannot destroy acetylcholine. The concentration of agonist in the cleft remains high, and this high concentration shifts the competition between acetylcholine and tubocurarine in favor of the former, thereby improving the chance of two acetylcholine molecules binding to a receptor even though tubocurarine is still in the environment. Cholinesterase inhibitors overcome the neuromuscular paralysis produced by NDMRs by this mechanism. The channel opens only when acetylcholine attaches to both recognition sites. Mathematically, if the concentration of tubocurarine is doubled, the concentration of acetylcholine must be increased fourfold if acetylcholine is to remain competitive. Paralysis produced by high concentrations of antagonist is more difficult to reverse than that produced by low concentrations. After large doses of NDMRs, cholinesterase inhibitors may be ineffective until the

concentration of relaxant in the perijunctional area decreases to a lower level by redistribution or elimination of the drug.

Classic Actions of Depolarizing Muscle Relaxants

Depolarizing relaxants, simulate the effect of acetylcholine and can therefore be considered agonists despite the fact that they block neurotransmission. Succinylcholine or decamethonium can bind to the receptor, open the channel, pass current, and depolarize the end plate. These agonists, similar to acetylcholine, attach only briefly; each opening of a channel is of very short duration, 1 millisecond or less. The response to acetylcholine, however, is over in milliseconds because of its rapid degradation by acetylcholinesterase, and the end plate resets to its resting state long before another nerve impulse arrives. In contrast, the depolarizing relaxants characteristically have a biphasic action on muscle—an initial contraction, followed by relaxation lasting minutes to hours. Because they are not susceptible to hydrolysis by acetylcholinesterase, the depolarizing relaxants are not eliminated from the junctional cleft until after they are eliminated from plasma. Because relaxant molecules are not cleared from the cleft quickly, they react repeatedly with receptors, attaching to one almost immediately after separating from another, thereby repeatedly depolarizing the end plate and opening channels.

The quick shift from excitation of muscle contraction to blockade of transmission by depolarizing relaxants occurs because the end plate is continuously depolarized. This comes about as a result of juxtaposition of the edge of the end plate with the muscle membrane—a different kind of ion channel, the sodium channel, that does not respond to chemicals but opens when exposed to a transmembrane voltage change. The sodium channel is also a cylindrical transmembrane protein through

which sodium ions can flow. Two parts of its structure act as gates that allow or stop the flow of sodium ions. Both gates must be open if sodium is to flow through the channel; closing of either cuts off the flow. Because these two gates act sequentially, a sodium channel has three functional conformational states and can move progressively from one state to another.

When the sodium channel is in its resting state, the lower gate (i.e., the time-dependent or inactivation gate) is open, but the upper gate (i.e., the voltage-dependent gate) is closed, and sodium ions cannot pass. When the molecule is subjected to a sudden change in voltage by depolarization of the adjacent membrane, the top gate opens, and because the bottom (time-dependent) gate is still open, sodium flows through the channel. The voltage-dependent gate stays open as long as the molecule is experiencing a depolarizing influence from the membrane around it; it will not close until the depolarization disappears. However, shortly after the voltage-dependent gate opens, the bottom gate closes and again cuts off the flow of ions. It cannot open again until the voltage-dependent gate closes. When depolarization of the end plate stops, the voltage-dependent gate closes, the time-dependent gate opens, and the sodium channel returns to its resting state. This whole process is short lived when depolarization occurs with acetylcholine. The initial response of a depolarizing muscle relaxant resembles that of acetylcholine, but because the relaxant is not hydrolyzed rapidly, depolarization of the end plate is not brief

Depolarization of the end plate by the depolarizing relaxant initially causes the voltage gate in adjacent sodium channels to open, thereby producing a wave of depolarization that sweeps along the muscle and generates a muscle contraction. Shortly after the voltage-dependent gate opens, the time-dependent inactivation gate closes. Because the relaxant is not removed from the cleft, the end plate continues to

be depolarized. Because the sodium channels immediately adjacent to the end plate are influenced by depolarization of the end plate, their voltage-dependent gates stay open and their inactivation gates stay closed. Since sodium cannot flow through a channel that has a closed inactivation gate, the perijunctional muscle membrane does not depolarize. When the flow of ions through sodium channels in the perijunctional zone stops because of closure of the inactivation gates, the channels downstream (beyond the perijunctional zone) are freed of depolarizing influence. In effect, the perijunctional zone becomes a buffer that shields the rest of the muscle from events at the end plate. Consequently, the muscle membrane is separated into three zones: the end plate, which is depolarized by succinylcholine; the perijunctional muscle membrane, in which the sodium channels are frozen in an inactivated state; and the rest of the muscle membrane, in which the sodium channels are in the resting state. Because a burst of acetylcholine from the nerve cannot overcome the inactivated sodium channels in the perijunctional zone, neuromuscular transmission is blocked. This phenomenon is also called *accommodation*. During accommodation, when the synapse is inexcitable through the nerve (transmitter), direct electrical stimulation of muscle causes muscle contraction because the sodium channels beyond the junctional area are in the resting excitable state.

The extraocular muscles contain tonic muscle, which is multiply innervated and chemically excitable along most of its surface. Despite its innervation, the ocular muscles express both mature and fetal receptors. Accommodation does not occur, and these muscles can undergo a sustained contracture in the presence of succinylcholine. The tension thus developed forces the eye against the orbit and accounts for part of the increase in intraocular pressure produced by depolarizing relaxants. There is also evidence that the extraocular muscles contain a special type of receptor that does not

become desensitized during the continued presence of acetylcholine or other agonists. Whether it is the immature γ-subunit AChR or the α7 AChR that plays a role in this resistance to desensitization in the ocular muscles is unknown.

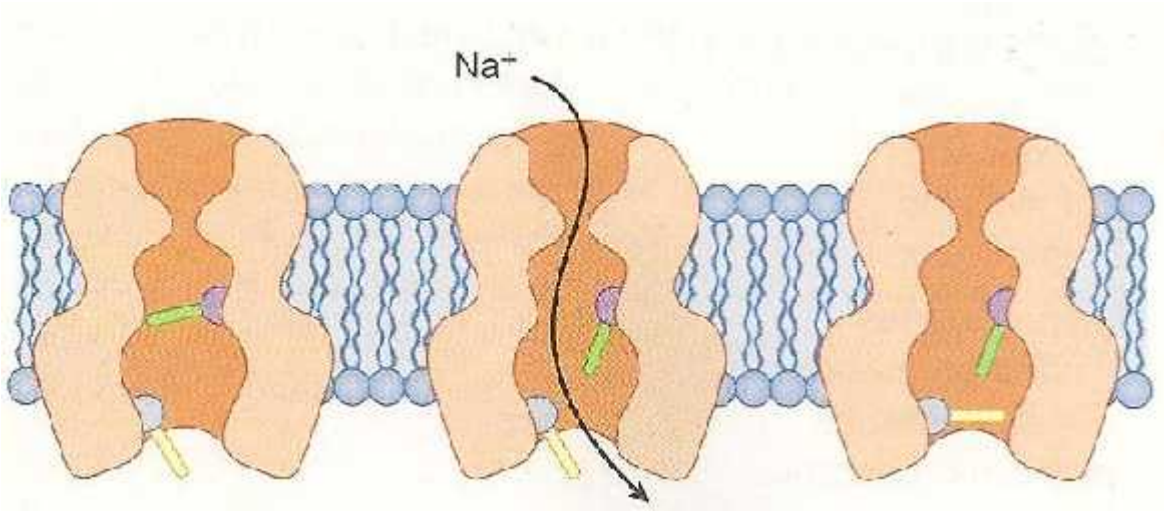


Figure 6 :- Sketch of a sodium channel. The *bars* represent parts of the molecule that act as gates. The *upper bar* is voltage dependent; the *lower bar* is time dependent. The left side of the drawing represents the resting state. Once activated by a change in voltage, the molecule and its gates progress as illustrated (left to right).

Phase II Block

A phase II block is a complex phenomenon that occurs slowly at junctions continuously exposed to depolarizing agents. The junction is depolarized by the initial application of a depolarizing relaxant, but then the membrane potential gradually recovers toward normal, even though the junction is still exposed to drug. Neuromuscular transmission usually remains blocked throughout the exposure. Several factors are involved. The repeated opening of channels allows a continuous efflux of potassium and influx of sodium, and the resulting abnormal electrolyte balance distorts the function of the junctional membrane. Calcium entering the muscle through the opened channels can cause disruption of receptors and the sub–end-plate elements themselves. The activity of the sodium-potassium adenosine triphosphatase pump in the membrane increases with increasing intracellular sodium and, by

pumping sodium out of the cell and potassium into it, works to restore the ionic balance and membrane potential toward normal. As long as the depolarizing drug is present, the receptor channels remain open and ion flux through them remains high.

Mechanism of Antagonism

The Non Depolarizing Muscle relaxants block neuromuscular transmission predominantly by competitive antagonism of acetylcholine at the postjunctional receptor. The most straightforward way to overcome their effects is to increase the competitive position of acetylcholine. Two factors are important, the first of which is the concentration of acetylcholine. Increasing the number of molecules of acetylcholine in the junctional cleft changes the agonist-to-antagonist ratio and increases the probability that agonist molecules will occupy recognition sites of the receptor. It also increases the probability that an unoccupied receptor will become occupied. Normally, only about 500,000 of the 5 million available receptors are activated by a single nerve impulse, and a large number of receptors are in “reserve” and could be occupied by an agonist. The second factor important to the competitive position of acetylcholine is the length of time that acetylcholine is in the cleft. Acetylcholine must wait for the antagonist to dissociate spontaneously before it can compete for the freed site. NDMRs bind to the receptor for slightly less than 1 millisecond, which is longer than the normal lifetime of acetylcholine. The destruction of acetylcholine normally takes place so quickly that most of it is destroyed before any significant number of antagonist molecules have dissociated from the receptor. Prolonging the time during which acetylcholine is in the junction allows time for the available acetylcholine to bind to receptor when the antagonist dissociates from the receptors. Three classes of drugs, potassium channel–blocking

drugs, acetylcholinesterase inhibitors, and γ-cyclodextrin derivatives, can be used clinically to reverse nondepolarizer-induced paralysis.

Neuro Muscular monitoring

Muscle relaxants are employed in anaesthesia to provide muscle relaxation and/or abolish patient movement. Numerous studies have documented enormous variation in patients' responses to muscle relaxants. Disease states and perioperative medications can also modify the responses of these medications . The depth of neuromuscular block (NMB) should be monitored when muscle relaxants are used to avoid drug overdosage or underdosage and residual NMB during recovery.

Equipment

Monitoring the magnitude of NMB is accomplished by delivering an electrical stimulus near a peripheral motor nerve and evaluating the evoked response of the muscle(s) innervated by that nerve.

Stimulator

Desirable features include compactness, light weight, and simplicity. Most are battery-operated with a means to check the battery status. A stimulator may be in a module in a multi parameter monitor. The ability to deliver information to an automated record should be considered when choosing a stimulator.

Current

Current, not voltage, is the determining factor in nerve stimulation. The force of muscle contraction is proportional to the number of activated muscle fibers. If a motor nerve is stimulated with sufficient current, all of the muscle fibers supplied by

that nerve will contract. The current required for this is called the maximal current. In the clinical setting, stimuli of greater than maximal (supramaximal) intensity are used to ensure that maximal stimulation is delivered if resistance increases. In the majority of patients, a current of 30 milliamperes (mA) will produce a supramaximal response when the ulnar nerve is stimulated. When the posterior tibial nerve is stimulated, higher currents are needed. A supramaximal current is generally 2.5 to 3 times higher than the lowest current capable of eliciting an evoked response (threshold current) [33.] Higher currents may be needed in patients with edema or diabetes. Much lower currents (5 to 8 mA) are needed when needle electrodes are used.

A submaximal current may be better for awake patients or for those recovering from anesthesia, because patient discomfort increases with the intensity of the stimulating current . Use of a submaximal current may result in more reliable detection of residual NMB when visual or tactile monitoring is used . A submaximal current is not reliable for general NMB monitoring.

Frequency

The frequency of stimuli is usually expressed in Hertz (Hz), which is cycles/second. One Hz is one cycle/ second, and 0.1 Hz is equal to 1 stimulus every 10 seconds. With a nondepolarizing block, increased stimulus frequency will shorten the onset time and prolong the duration of action [34,35.]

Waveform

The stimulus waveform should be rectangular (square wave) and monophasic. Biphasic waves may produce repetitive stimulation, which can lead to underestimation of the depth of NMB present.

Duration

The duration should be 300 µs or less. If the duration of the pulse is over 0.5 msec, a second action potential may be triggered.

Stimulation Patterns

Single Twitch

Single-twitch (T_1) stimuli are usually delivered at a frequency of 0.1 or 1 Hz. A frequency greater than every 10 seconds is associated with a progressively diminished response and could result in overestimating the NMB.

The control response strength is noted (Fig.7). The strengths of subsequent twitches are then compared with the control and expressed as a percentage of the control (single-pulse or -twitch depression, T_1%, T1%, T_1:T_c). With both a nondepolarizing and a depolarizing block, there will be progressive depression of the response as the block develops. A decrease in temperature will also cause a reduced response .

The single stimulus is useful in establishing a supramaximal stimulus and for identifying when conditions satisfactory for intubation have been achieved. It can be used (in conjunction with a tetanic stimulus) to monitor deep levels of NMB (the post-tetanic count).

There are several disadvantages associated with using single twitch. There needs to be a control. It cannot distinguish between a depolarizing and nondepolarizing block. Most importantly, the response's return to control level does not guarantee that full recovery from NMB has occurred.

Train-of-four

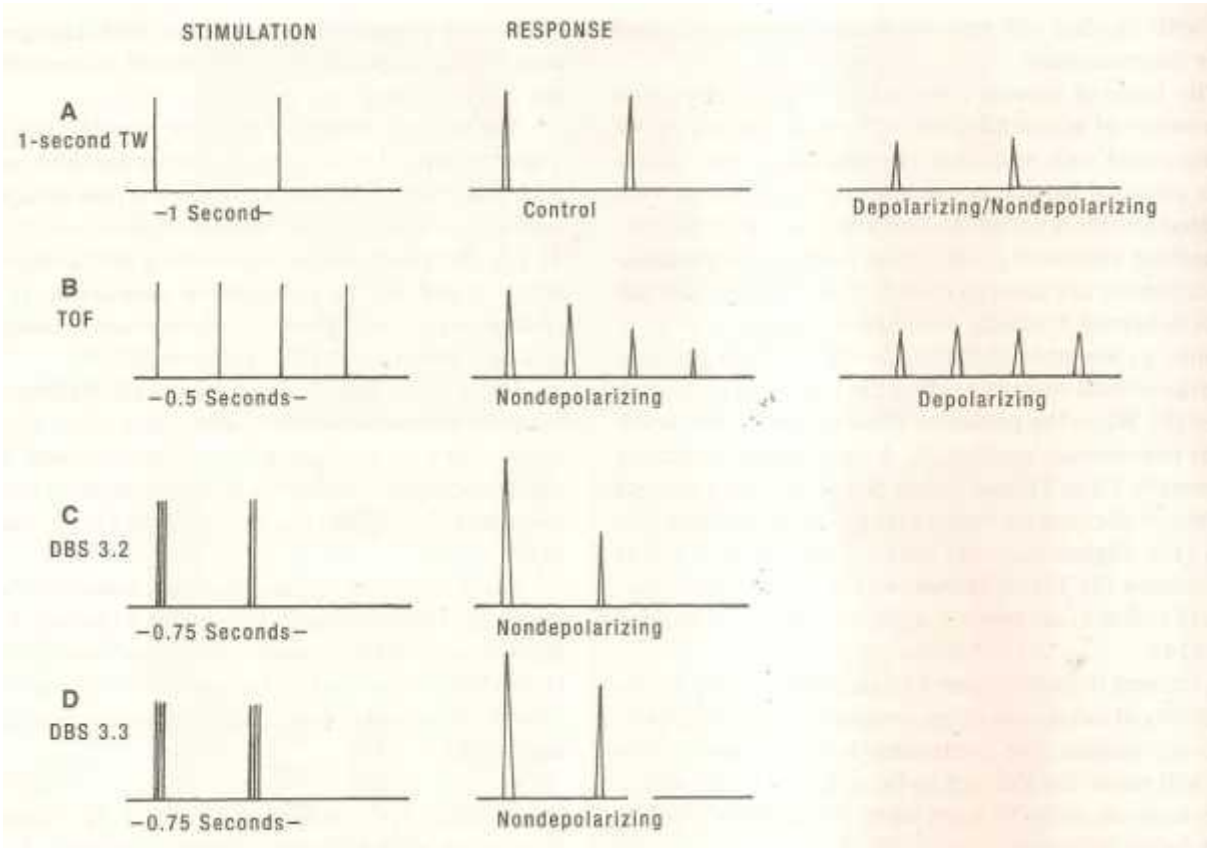
Train-of-four (TOF, T_4, T_4/T_1) consists of four single pulses of equal intensity delivered at intervals of 0.5 seconds (2 Hz) (Fig. 7). TOF should not be repeated more frequently than every 10 to 12 seconds[36]. Many modern stimulators do not allow the TOF to be repeated more often. Use of TOF every 10 seconds will result in a shorter onset time for NMB than if it is used every 20 seconds [35,37.]

With the control response (before any relaxant has been given), all four responses are the same. The pattern seen with a depolarizing block differs from that of a nondepolarizing block With a partial depolarizing block, there is an equal depression of all four twitches. With a nondepolarizing block, there is progressive depression of height with each twitch (fade). As the block is deepened, the fourth twitch will be eliminated first, then the third, and so on (Fig. 7). Counting the number of twitches (train-of-four-count or TOFC) permits quantitative assessment of a nondepolarizing block. With recovery or reversal of a nondepolarizing block, the TOFC increases until there are four responses, then fade decreases.

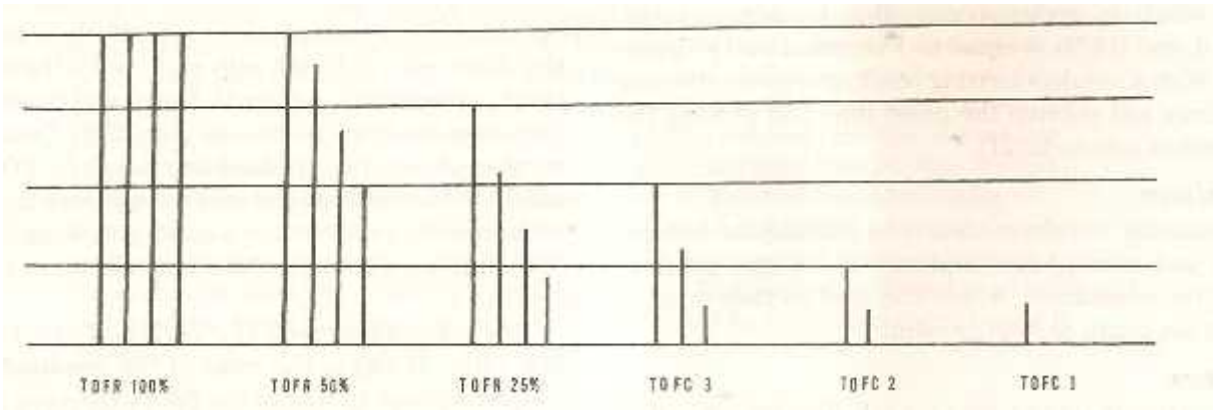
The TOF pattern has several advantages. It is a more sensitive indicator of residual NMB than the single twitch. A control is not necessary. It can distinguish between a depolarizing and a nondepolarizing block and is of value in detecting and following the development of a phase II block following succinylcholine administration.

The main disadvantage of TOF is its poor performance at both extremes of NMB, deep relaxation or near complete recovery . Tactile or visual observation of the TOFR is of little value above a ratio of 0.4–0.5.

Figure 7 :-



Patterns of stimulation and response. A: Single-stimulus stimulation at 1 Hz (1 stimulus/second). The height of the control twitches are noted. With either a depolarizing or a nondepolarizing block, twitch height is decreased. B: Train-of-four stimulation. Four successive single stimuli are delivered with 0.5-second intervals. With a nondepolarizing block, there will be progressive depression of the response with each stimulus (fade). With a depolarizing block, the responses will be depressed equally. C, D: Double-burst stimulation. Three stimuli are delivered at 50 Hz, followed 0.75 seconds later by two or three similar stimuli. There will be depression of the response to the second burst with a nondepolarizing block. Note the increased height of the response to the first burst compared with that seen with TOF stimulation. TW, time weight TOF, train of four; DBS, double-burst stimulation.



Onset and progressive deepening of nondepolarizing block using train-of-four stimulation. When there is no NMB present, all four responses are equal. With onset of the block, there is progressive depression of twitch height with each twitch (fade). As the block progresses, the last twitch is lost and the TOFC is less than 4. TOFR, train-of-four ratio; TOFC, train-of-four count.

Tetanus

Tetanus is a rapidly repeated (e.g., 50, 100 or even 200 Hz) stimulus. In the absence of NMB, this causes sustained contraction of the stimulated muscles. With a depolarizing block, the response will be depressed in amplitude but sustained. With a nondepolarizing block, the response is depressed in amplitude and the contraction is not sustained (fade or decrement). With profound NMB, there is no response. Fade after 50 Hz tetanic stimulation is a more sensitive index of NMB than single twitch but not sufficiently sensitive to be used for assessing adequate recovery . Studies differ on the significance of fade after 100 Hz.

The most commonly used frequency is 50 Hz, because it stresses the neuromuscular junction to the same extent as a maximal voluntary effort. Fade may not be seen at lower frequencies when a significant nondepolarizing block is present. Use of 100 Hz allows more sensitivity in evaluating residual paralysis and is more useful in monitoring profound NMB .

The duration of the tetanic stimulus is important because it affects fade. The standard duration is 5 seconds. Tetanic stimulation should not be repeated more often than every 2 minutes .

Post-tetanic facilitation (potentiation, PTF) is a temporary increase in response to stimulation following a tetanic stimulus. It is seen with a nondepolarizing, but not a depolarizing, block. It is maximal at around 3 seconds and lasts up to 2 minutes.

When the NMB is so profound that there is no response to single twitch or TOF stimulation, it may be possible to estimate NMB by using the post-tetanic count (PTC). This is performed by administering a tetanic stimulus of 50 Hz for 5 seconds.

After a 3-second pause, single-twitch stimuli are applied at 1 Hz, and the number of (post-tetanic) responses is counted. The number of twitches elicited increases as the depth of NMB decreases. The time to appearance of the first twitch in a TOF is inversely related to the number of post-tetanic twitches present. An even deeper block can be monitored by counting the number of responses following 100-Hz tetanus.

A significant disadvantage of tetanic stimulation is that it is very painful and should be avoided in the conscious patient.

Double-burst Stimulation

Double-burst stimulation (DBS, minitetanus) consists of two short sequences of 50 Hz tetanic stimuli separated by 750 msec. The two most commonly used are $DBS_{3,3}$ and $DBS_{3,2}$. $DBS_{3,3}$ consists of three 0.2-msec impulses at 50 Hz, followed 750 msec later by an identical burst (Fig. 22). $DBS_{3,2}$ consists of three impulses followed by two such impulses 750 msec later. Another permutation of DBS is $DBS_{3,3}$ 80-40, which is three stimuli at 80 Hz followed 750 msec later by three stimuli at 40 Hz. A modified DBS consisting of first two stimuli of 0.3 ms duration at 50 Hz and then two stimuli of 0.2 ms duration at 50 Hz has also been used.

The primary use of DBS has been to detect residual NMB. Studies show that fade (response to the second burst weaker than that to the first) is more readily detected with DBS than TOF using visual or tactile monitoring. It also has been used for intraoperative assessment of NMB DBS and TOF have a close relationship over a wide range of NMB. [36,38,39] Another use of DBS is to assess deep block, since the first twitch in double burst can be detected at deeper block levels than the first twitch in TOF.

DBS causes more discomfort to the awake patient than TOF stimulation but less than tetanic stimulation . It can be used at submaximal currents. This causes less discomfort in the awake patient and, in most cases, is more reliable than testing with supramaximal stimuli .

DBS should not be repeated at intervals of less than 12 seconds. Caution should be used when switching between double-burst and TOF stimulation. Up to 92 seconds may be required before the responses are stabilized.

Electrodes

Stimulation is achieved by placing two electrodes along a nerve and passing a current through them. Stimulation can be carried out either transcutaneously using surface electrodes or per cutaneously with needle electrodes.

Types

- Surface Electrodes
- Metal Electrodes
- Needle Electrodes

Polarity

Stimulators produce a direct current by using one negative and one positive electrode. The polarity of the outlet sockets should be indicated on the stimulator. Usually, the positive electrode is red, and the negative is black. Maximal effect is achieved when the negative electrode is placed directly over the most superficial part of the nerve being stimulated. [40] The positive electrode should be placed along the course of the nerve, usually proximally to avoid direct muscle stimulation. If the

polarity is unknown, the connections can be reversed to determine which arrangement evokes the greater response.

Methods for Evaluating Evoked Responses

Visual

Visual assessment can be used to count the number of responses present with a TOF stimulus, to determine the PTC, and to detect the presence of fade with TOF or DBS. Posttetanic facilitation can also be assessed. Studies have shown that it is difficult to determine the TOFR accurately or to compare a single-twitch height to its control visually. Visually recognizing fade with TOF stimulation may be easier with submaximal currents.[41.] Visually assessing fade with 100-Hz tetanic stimulation appears to be fairly accurate when evaluating residual paralysis. For visual assessment, the observer should be at an angle of 90 degrees to the motion.

Tactile

Tactile evaluation is accomplished by placing the evaluator's fingertips lightly over the muscle to be stimulated and feeling the strength of contraction . It is more sensitive than visual monitoring for assessing NMB using TOF [42.] It can be used to evaluate the presence or absence of responses and/or fade with train-of-four, double burst, and tetanic stimulation. The PTC can be determined. If there is a response to all four stimuli with TOF stimulation, the TOFR can be estimated. However, it is difficult for even trained observers to detect TOF fade manually unless the TOF ratio is below 40%. Detecting fade tactilely is somewhat easier with DBS but cannot be depended on to detect residual paralysis. Detection is better when the evaluator uses the dominant hand of the patient .

Mechanomyography

The mechanomyogram (MMG) utilizes a force-displacement transducer, such as a strain gauge, attached to a finger or other part of the body that can be restrained by a preload and will move when stimulated. The transducer converts the contractile force into an electrical signal, which is amplified and displayed on a monitor screen or recorded on a chart. Single-twitch height, response to tetanic stimulation, and the T_4 ratio can be accurately measured by using an MMG.

Disadvantage - devices are cumbersome and difficult to set up for stable and accurate measurements. Proper transducer orientation, isometric conditions, and application of a stable preload are required, maintenance of muscle temperature. Mechanomyography is rarely used clinically but is regarded as the gold standard for scientific measurement of neuromuscular response [43.]

Acceleromyography

With acceleromyography (ACG, AMG), a thin piezoelectric transducer or a small aluminum rod with electrodes on both sides is fixed to the moving part(Fig. 8). When the part moves, a voltage which is proportional to the acceleration of the moving part is generated. This method requires unrestricted movement of the muscle being stimulated. An elastic preload can be applied to return the moving part to its original position.

ACG can be used to assess NMB at the hand with the patient's arm tucked at the side as long as the thumb can move freely. A protective device can be used to allow thumb motion while protecting the hand and forearm .

Most studies show a fairly close relationship between TOFRs measured by ACG and the MMG [44,45,46] or electromyography (EMG) [47,48], although the results are not interchangeable. Some studies show poor correlation. In awake patients, the results are affected by extra movements to which the thumb may be subjected, leading to poor repeatability.

Accelerometry is easy and convenient to use, relative inexpensive, and can be interfaced with a computer. It does not require a preload. It gives more accurate results than visual or tactile evaluation [49,50].

Train Of Four (TOF – Guard) Acceleromyograph (Organon-Teknika, Belgium)

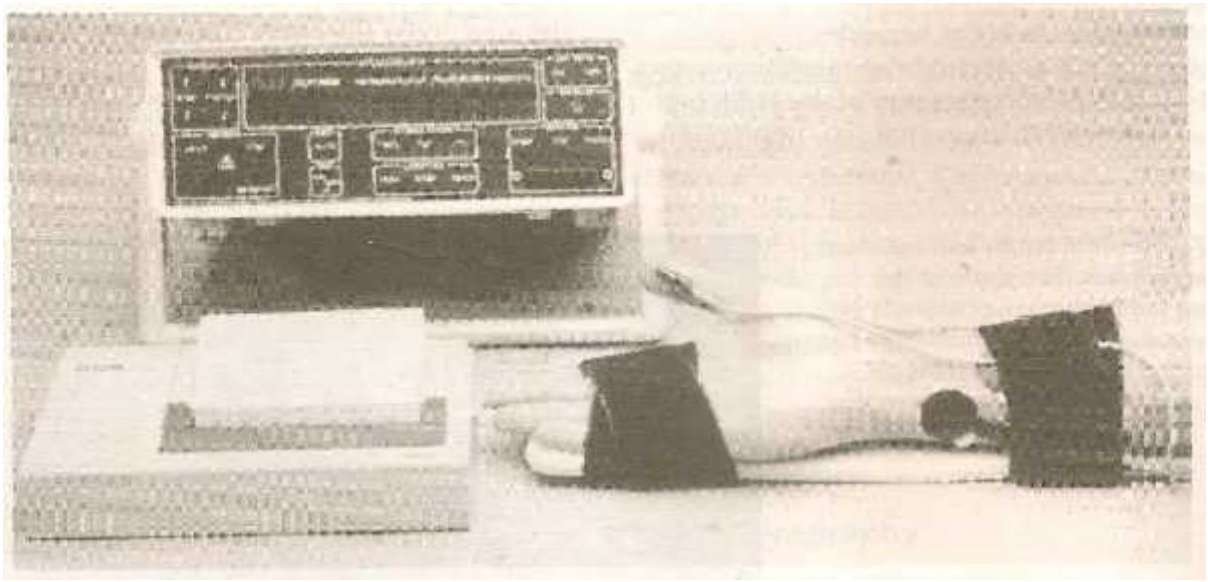


Figure 8a:- Accelerography. The piezoelectric wafer is attached to the moving part—-in this case, the thumb. When the thumb moves, an electrical signal proportional to the acceleration is produced. The monitor allows determination of single-twitch depression, TOF count or ratio and/or the PTC. Responses can be displayed by using the printer.

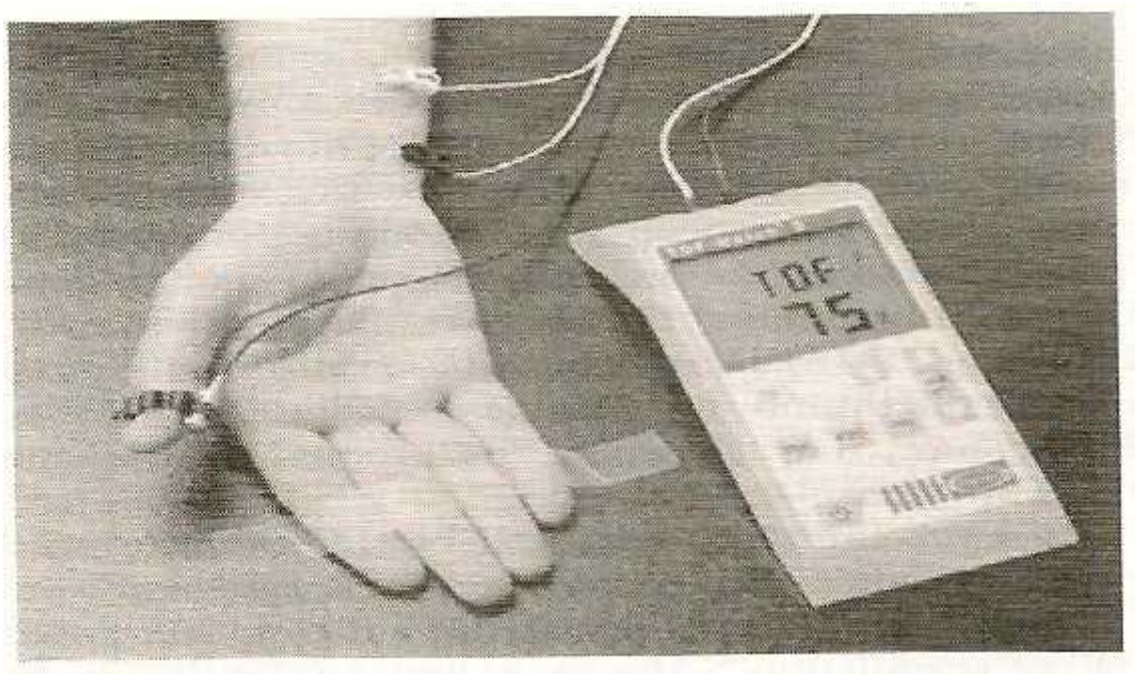


Figure 8 b:- TOF-Watch (Organon, part of Schering-Plough, Corp.). This neuromuscular transmission monitor is based on measurement of acceleration with a piezoelectric transducer. [51] [52] Note that the transducer is fastened to the thumb and the stimulating electrodes. On the display of the TOF-Watch, the train-of-four (TOF) ratio is given in percentage.

Kinemyography

Kinemyography (KMG) utilizes a bending sensor that is placed between the thumb and forefinger . The core of the sensor is a piezoelectric material . Movement is determined by the change in shape of the material when it is bent by adductor pollicis muscle contraction. When the piezoelectric material changes shape, the electrical charge in the material is redistributed, and this leads to an electron flow to balance the charges. This flow is measured as a potential change that is proportional to the amount of distortion. The hand need not be immobilized since the position and direction of the thumb do not affect the measurement as long as the thumb is able to move freely. This device is in a module that can be added to a multipurpose monitor . The results of the neuromuscular testing are displayed on the monitor screen. This technology can measure TOF, double burst, and single twitch. KMG has been compared with mechanomyography . There was agreement as to the time to intubation and recovery, but KMG lagged behind the MMG in determining recovery from NMB.

Piezoelectric Film

This method uses a disposable piezoelectric film . This is placed so that it spans a movable joint . Muscle movement from evoked stimulation bends the film and generates a voltage that is proportional to the amount of bending. It has been used on the thumb, fifth digit, and the great toe . It can be used with the patient's hands tucked at his or her sides. This method is not as accurate as mechanomyography or EMG but may predict recovery of the TOFR better than visual or tactile evaluation .

Electromyography

Electromyography (EMG) is the process of recording the electrical activity of a muscle . When a motor nerve is stimulated, a biphasic action potential is generated in each of the muscle cells it supplies, unless some degree of NMB exists. The sum of a number of these action potentials can be sensed by using electrodes placed over the muscle being stimulated. Five electrodes are used. Two stimulating electrodes are placed over the nerve to be stimulated. Three electrodes, two receiving (sensing, recording) and one ground, are used for recording. The best signal is usually obtained by placing the active receiving electrode over the belly of the muscle with the indifferent (reference) electrode over the tendon insertion site. The ground electrode, whose function is to decrease stimulation artifacts, is placed between the stimulating and recording electrodes. Best results will be seen when the electrodes have been in contact with the skin for at least 15 minutes (cure time) before calibration. Careful skin preparation will help to give good results. Movement artifact can be minimized by fixation or by applying a constant preload to the muscle being recorded .

EMG of the larynx can be accomplished by using either a specialized tracheal tube with incorporated wire electrodes or a superficial electrode attached circularly around the tube and placed between the vocal cords [51].

The evoked EMG signal is filtered, rectified, amplified, and then displayed and/or recorded at a much slower speed. Measurements may be made of peak-to-peak amplitude of the major deflection. The sum of the amplitudes of the major positive and negative deflections, or the area under the curve (integrated EMG), can be measured .

An electromyography machine automatically determines the supramaximal stimulus, establishes a control response, stimulates at a selected interval, measures the response, and compares it with the control. Available features include an alarm to warn when the single pulse response exceeds a chosen value and a printer to provide a permanent record. Most have alarms for functioning errors, loose connections, increased skin resistance, absence of supramaximal stimulation, and the like. Most show the electromyography waveform and automatically adjust the gain so that it occupies the full scale.

With a nondepolarizing NMB, the action potential amplitude is decreased, and there is fade with TOF. Frequently, the amplitude does not return to 100% of control with recovery, although the TOFR will equal approximately 100%. Different hand positions may affect the results.

Advantages over mechanomyography - Less immobilization, does not require bulky apparatus , hand and arm do not need to be extended or put on a board . It can be used to monitor muscles not available to the MMG such as the diaphragm and the laryngeal muscles[20.] It can be used to assess motor nerve block induced by regional anesthesia .

Disadvantages to electromyography - sensitive to electrical interference, response may vary according to muscle, equipment is expensive. Skin preparation and electrode placement must be done carefully. Since the site is not immobilized, changes in the relative position of the recording electrodes cause variation in electromyography response. Temperature plays an important role in the response amplitude with amplitude increasing with decreasing muscle temperature .

Phonomyography

Phonomyography (acoustic myography or monitoring) relies on the fact that when a muscle contracts, low-frequency sounds are emitted. These acoustic waves propagate to the skin, generating waves that can be recorded by a small piezoelectric microphone. The signal amplitude has been shown to be proportional to the degree of muscle contraction.

This method has been used to measure responses in the hand muscles when the microphone is tightly secured to the thenar mass to monitor the adductor pollicis muscle, or to the groove between the first and second metacarpal bone to monitor the first dorsal interosseus muscle . The corrugator supercilii muscle can be monitored by placing the microphone above the medial portion of the eyebrow. The muscles of the larynx can be monitored by placing the sensor in the vestibular fold just lateral to the vocal cords . Studies comparing phonomyography, ACG, and mechanomyography by using hand and corrugator supercilii muscles show some agreement, although the results are not interchangeable [52,53].

The phonomyogram is easy to use and can be used on a number of different muscles. It provides a stable baseline with relatively few disturbances from artifacts . Data can be transferred to an automated anesthesia record.

Since this method monitors low frequency sounds, artifacts are possible. Vessel pulsations can cause small waves in the baseline. Electrosurgery units may cause interference. The microphone may come off the skin.

Choice of Monitoring Site

Ulnar Nerve

The ulnar nerve is most commonly used, and the adductor pollicis (thumb) muscle is most commonly monitored. Because this muscle is on the side of the arm opposite the site of stimulation, there is little direct muscle stimulation. However, residual NMB may be easier to detect tactilely by using the index finger.

The ulnar nerve can be stimulated at the elbow, wrist, or hand . Stimulation at the wrist will produce thumb adduction and finger flexion. Stimulation at the elbow produces hand adduction as well. If an mechanomyography or electromyogram is used for measuring the response, the stimulating electrodes should be placed at the wrist to limit hand motion.

At the wrist, the two electrodes should be placed along the medial aspect of the distal forearm, approximately 2 cm proximal to the proximal wrist skin crease with the negative electrode distal [54] (Fig. 9). Ulnar nerve is superficial. Alternately, the positive electrode may be placed on the dorsal side of the wrist (Fig. 9). At the elbow, the electrodes should be placed over the sulcus of the medial epicondyle of the humerus (Fig. 9). Caution must be exercised to ensure that the electrodes do not cause ulnar nerve compression. The electrodes may also be placed on the hand with the negative electrode on the palm between the base of the thumb and the second finger and the positive electrode in the same position on the dorsal side of the hand .

When electromyography monitoring is used, the recording electrodes can be placed over the hypothenar, thenar, or dorsal interosseous muscle. The electrical resistance of the palm skin may vary because of sweat production and may be increased in manual workers . The dorsum of the hand is less affected than the palm

in both respects, so the dorsal interosseous muscle may be preferred. To record the reaction of the dorsal interosseous muscle, the active receiving electrode is placed in the web between the index finger and the thumb and the other electrode at the base of the second finger . Surface electrodes are simple to fix here, easy to maintain in position, and seldom are disturbed by hand movements . For the hypothenar electromyography, both electrodes are placed on the palmar side over the hypothenar eminence or the active electrode is placed on the hypothenar eminence and the other below the second line on the ring finger or at the base of the dorsum of the fifth finger. If the thenar muscle electromyography is recorded, electrodes are placed on the thenar eminence and the proximal phalanx of the middle or index finger or the lateral side of the base of the thumb .Abduction of the thumb with a constant pretension will bring the muscles closer to the skin and minimize movement .

For tactile assessment, the thumb should be held in slight abduction and the observer's fingertips placed over the distal phalanx in the direction of movement. Preloading the thumb with a rubber band may improve visual assessment. It should be noted that the adductor pollicis is sometimes supplied by the median nerve. When monitoring the adductor pollicis muscle, it is important to realize that the onset and duration of NMB at the larynx and the diaphragm are shorter than at the peripheral muscles[13,20,43].

Placement of Electrodes for Ulnar nerve stimulation along with TOF –Guard

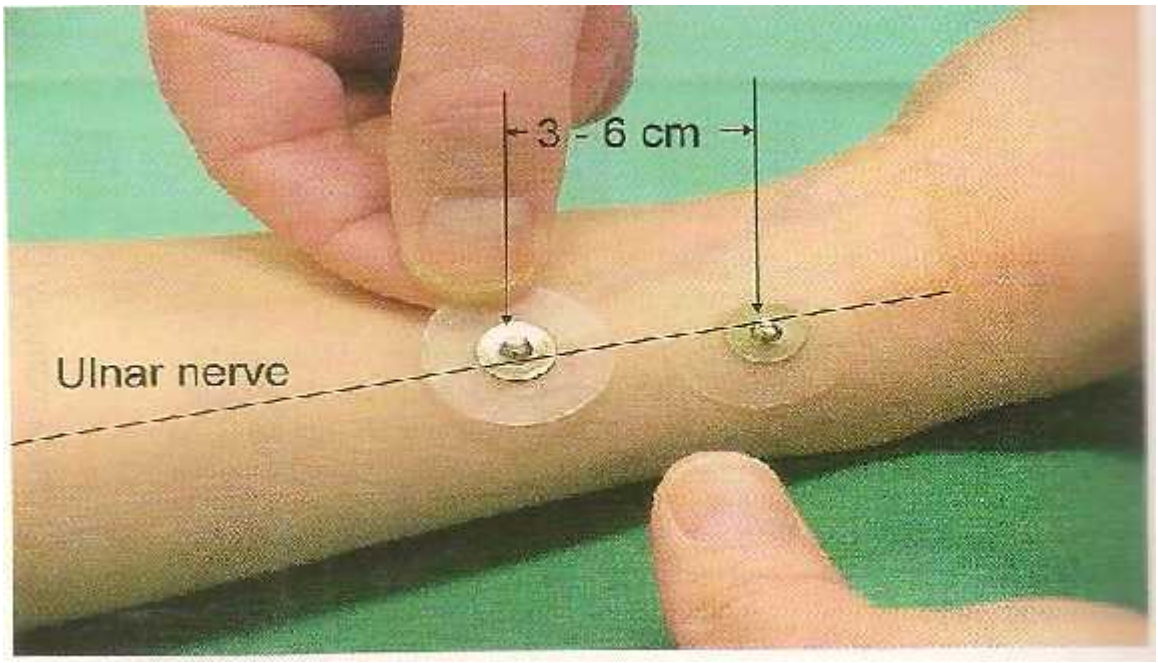


Figure 9 a :-Stimulating electrodes with the appropriate contact area in the correct position over the ulnar nerve of the left forearm.

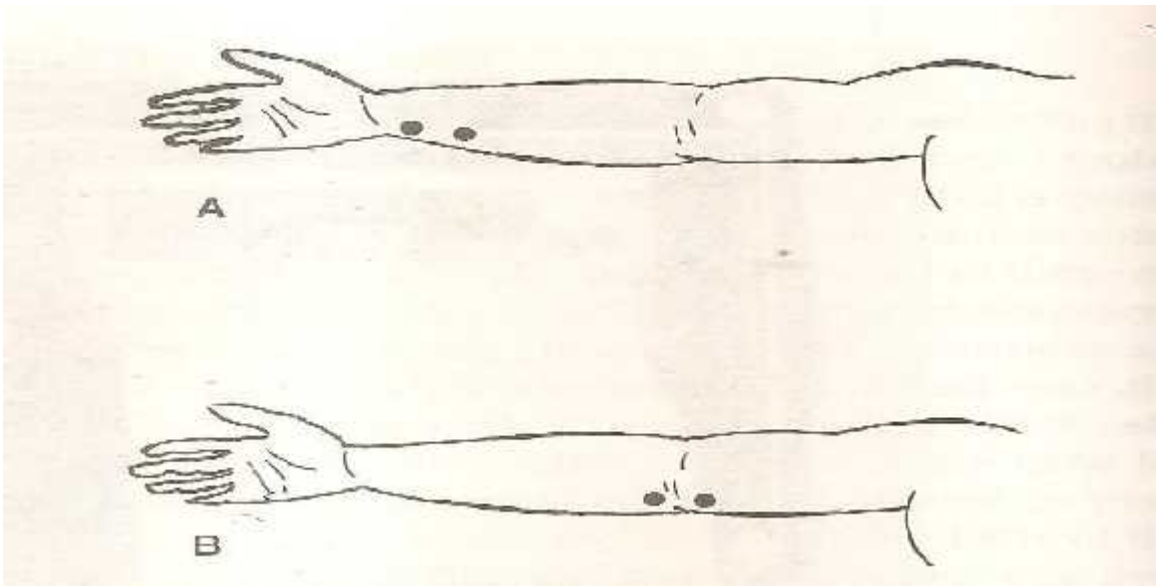


Figure 9 b:-Placement of electrodes for ulnar nerve stimulation. A: The electrodes are placed along the ulnar aspect of the distal forearm. B: The electrodes are placed over the sulcus of the medial epicondyle of the humerus.

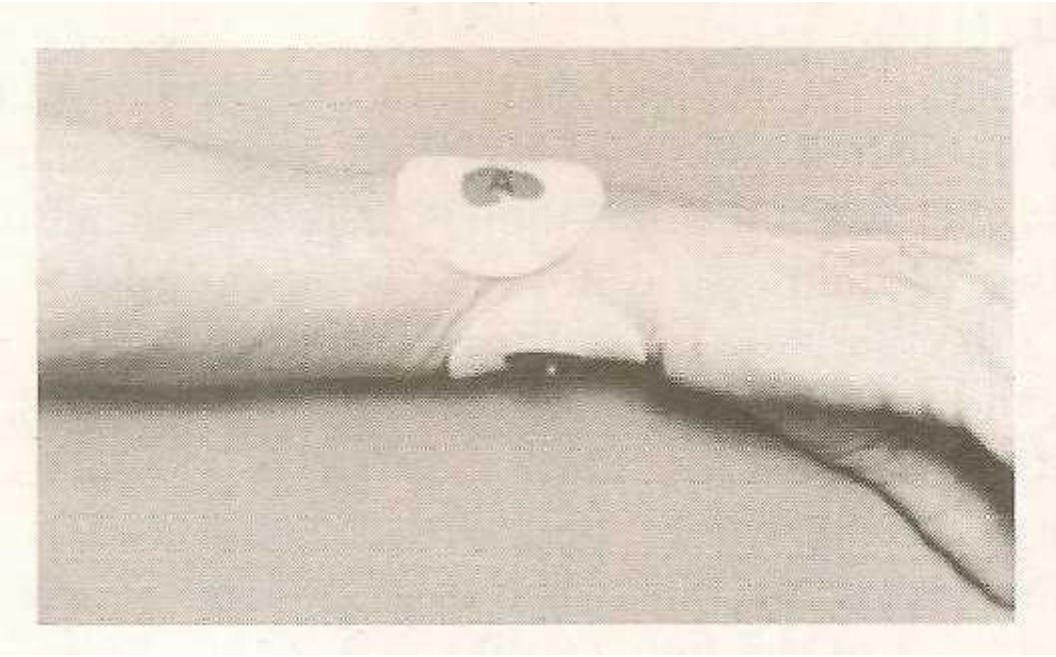


Figure 9 c:- Alternate placement of electrodes for ulnar nerve stimulation. The negative electrode is placed along the ulnar aspect of the ventral side of the wrist. The positive electrode is placed on the dorsal side.

Facial Nerve

The facial nerve, which enervates the muscles around the eye, is one of the easier muscles to stimulate and observe. It is most useful for detecting the onset of relaxation in the muscles in the jaw, larynx, and diaphragm. ACG can be used with the facial nerve [55,56].

Several different electrode configurations have been used for stimulating the facial nerve:

- The negative electrode is placed just anterior to the inferior part of the ear lobe, and the other electrode is placed just posterior or inferior to the lobe (Fig. 10). Stimulation at this site will make it more likely that muscle contractions are the result of nerve stimulation rather than direct muscle stimulation.

- One electrode is placed lateral to and below the lateral canthus of the eye, and the other electrode is placed anterior to the earlobe [57] or 2 cm lateral to and above the lateral canthus. This placement may result in direct muscle stimulation. If one of these configurations is used, low currents (20–30 mA) should be used [51].

The facial muscles are relatively resistant to NMB drugs [56,58]. Therefore, managing NMB by stimulating the facial nerve will result in greater relaxation than from stimulating a limb nerve if equivalent responses are used. The facial nerve should not be used to assess recovery from NMB because the responses may show complete recovery while significant NMB is still present [55,57].

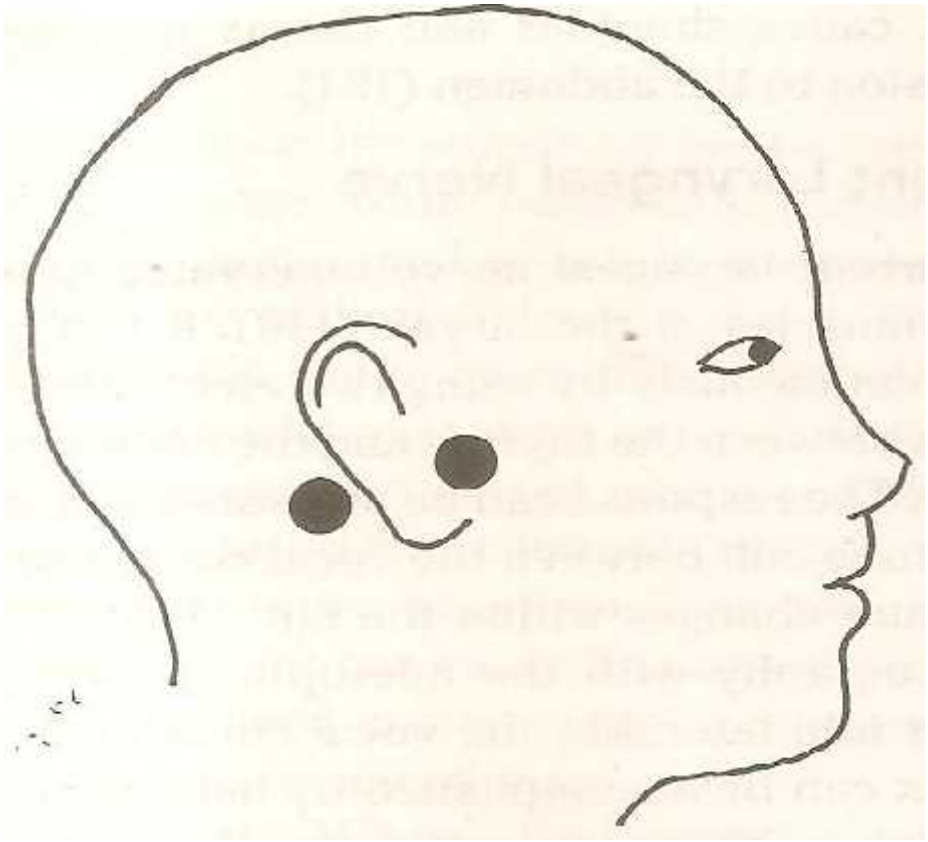
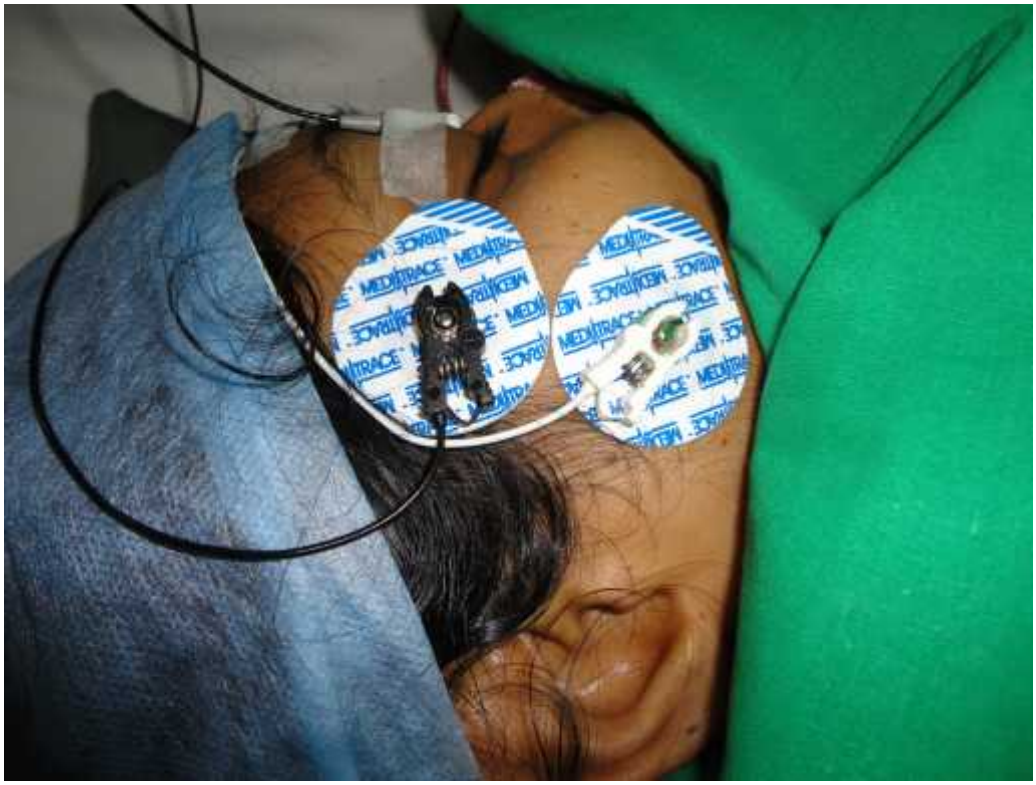


Figure 10:- Electrode placement for stimulating the facial nerve. The negative electrode is placed anterior to the earlobe. The positive electrode is placed posterior or inferior to the earlobe.

Placement of Electrodes for facial nerve stimulation



Other nerves that can be used are :-

1. Peroneal Nerve
2. Muscular Branch of the Femoral Nerve
3. Mandibular Nerve
4. Spinal Accessory Nerve
5. Recurrent Laryngeal Nerve
6. Median nerve
7. Posterior Tibial nerve
8. Tibial nerve

Uses

Intubation

Recommended that single twitch at 0.1 Hz be used and that the clinician wait until a response is barely perceptible before attempting laryngoscopy and intubation. More rapid stimulation may accelerate the onset of block at the stimulated site . Double burst has been used as an indicator of optimal conditions for tracheal intubation [59].

Electroconvulsive Therapy

A common error in electroconvulsive therapy is delivering the electrical stimulus prematurely. It is recommended that a single stimulus be applied at 1 Hz to the posterior tibial nerve . When there is complete abolition of response, the electroconvulsive therapy should be applied.

Maintenance

During maintenance, the stimulator can be used to titrate the relaxant dosage to the needs of the operative procedure so both under- and overdosage are avoided. It is important to correlate the reaction to nerve stimulation with the patient's clinical condition because there may be a discrepancy between the degree of relaxation of the monitored muscles and that of the muscles at the site of surgery.

TOF is commonly regarded as the most useful pattern for monitoring NMB during maintenance. Supramaximal currents are traditionally used. The goal for most cases in which abdominal muscle relaxation is required should be to maintain at least one response to TOF stimulation in a peripheral nerve.[60] If no response is present, further administration of relaxants is not indicated. If two responses are present, abdominal relaxation may be adequate using balanced anesthesia . Presence of three twitches is usually associated with adequate relaxation if a volatile anesthetic agent is used. Deeper levels of NMB may be required for upper abdominal or chest surgery or if diaphragmatic paralysis is needed. If the facial muscles are used, at least one twitch should be added to the mentioned recommendations.

Muscle relaxants are sometimes administered in cases such as eye surgery or laser surgery on the vocal cords to guarantee that movement does not occur. To ensure total diaphragmatic paralysis, the NMB should be so intense that there is no response to post-tetanic stimulation (i.e., the PTC is 0). One approach is to give a bolus of a short-acting muscle relaxant when the PTC is 1. Alternatively, the twitch response at a resistant muscle such as the orbicularis oculi may be monitored and a dose of relaxant given as soon as there is any response.

Recovery and Reversal

At the end of a procedure, a stimulator allows the anesthesia provider to determine whether or not the block is reversible and adjust the dose of reversal agent, if required, to the patient's requirements . Numerous studies have shown that some patients entering the postanesthesia care unit have an unacceptable level of block. A nerve stimulator may detect residual NMB, which could lead to life-threatening complications. The probability of detecting fade by using the index finger is greater than if the thumb or great toe is used [61.]

As recovery progresses, the responses to TOF will progressively appear, then fade will disappear. The ease of reversing a nondepolarizing block is inversely related to the degree of block at the time of reversal [62]. If the first twitch (T_1) is present, it can be estimated how quickly the block can be reversed. The time depends on the relaxant that has been used. It is best to use a peripheral muscle to monitor recovery, because its complete recovery would indicate that residual muscular weakness contributing to problems with airway patency or respiration is unlikely [51,63].

In the past, many investigators thought that a TOFR of 0.7 was adequate . However, a normal response to hypoxemia, protection from pulmonary complications, and absence of heaviness of the eyelids, visual disturbances, difficulty swallowing, or patient anxiety may require a higher ratio. Most investigators now recommend that the TOFR at the adductor pollicis be at least 90% measured by mechanomyography before extubation[64]. This is probably most reliably accomplished by using ACG and achieving a TOFR at least 90% of the baseline [46,49,50]. If electromyography monitoring is being used, residual anesthetic effects usually prevent the return of T_1 to the preanesthetic reference level, but the TOFR should exceed 90% .

Residual NMB cannot be reliably detected by using TOF stimulation if visual and/or tactile monitoring is used . Detection may be somewhat better when using DBS[37,41]. Both may be more reliable at detecting fade at lower currents .

Clinical criteria in an awake patient have been used to ascertain whether the return of muscle strength is adequate. These include the ability to

- open the eyes for 5 seconds and not experience diplopia,
- sustain tongue protrusion,
- sustain head lift for at least 5 seconds,
- sustain hand grip,
- sustain leg lifting in children,
- cough effectively, and
- swallow.

A more sensitive test may be the ability to resist removing a tongue blade from clenched teeth . Clinical criteria in an asleep patient include an adequate tidal volume and an inspiratory force of at least 25 cm H_2O negative pressure. Subjecting the patient to negative inspiratory pressure can cause pulmonary edema. These clinical criteria do not exclude clinically significant residual paralysis.

Long-term Muscle Relaxant Infusions

Long-term muscle relaxants infusions are sometimes used in critical care areas. NMB monitoring should be used to avoid over dosage .

Nerve Location

A peripheral nerve stimulator may be used to locate nerves for regional block. The current needed is far below that needed for monitoring NMB. Stimulators with different current outputs for both functions are available.

Hazards

- Burns
- Nerve Damage
- Complications associated with needle electrodes include infection, bleeding, and pain.
- Pain
- Electrical Interference : The use of a nerve stimulator may cause changes in the ECG tracing or interfere with an implanted pacemaker.
- Incorrect Information : With some stimulators, when the batteries are low, only three pulses are generated during TOF stimulation . This could lead to incorrect interpretation of the degree of NMB.

Pharmacology of Rocuronium

Structure of Rocuronium

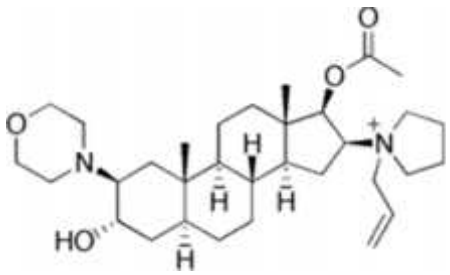


Figure 11 :- (2β,3α,5α,16β,17β)-17-(acetyloxy)-16-(1-allylpyrrolidinium-1-yl)-3-hydroxy-2-morpholin-4-ylandrostane

Rocuronium bromide (ORG 9426) was introduced in 1994 in order to provide a very rapid relaxation for endotracheal intubation. It was synthesized from its parent molecule vecuronium bromide by various substitutions by Dr. T. Sleigh and Dr.Savage at Organon laboratory.

Rocuronium is a newer amino-steroid based neuro muscular blocking agent with shorter onset of action and intermediate duration of action. Rocuronium is the 2-Morpholino, 3- desacetyl, 16 –N- allyl pyrrolidino derivative of vecuronium. It differs from vecuronium at 3 positions on the steroid nucleus and the absence of acetylcholine like fragment that is found in the steroid nucleus of vecuronium in the A-ring. The replacement of methyl group attached to the quaternary nitrogen of vecuronium by an allyl group and the absence of the acetylcholine like fragment in the A-ring may be partly responsible for the decrease in potency seen with rocuronium. It possesses tertiary nitrogen at the A-ring end of the molecule. Replacement of acetate group attached to the A-ring by a hydroxyl group makes it possible to present Rocuronium as a stable solution.

Rocuronium Vial

Pharmacokinetics

Rocuronium is taken up into the liver by a carrier medicated active transport system. Rocuronium is largely excreted unchanged in the bile (upto 50% in 2 hrs). Deacetylation of rocuronium does not occur and the metabolite 17 – desacetyl rocuronium has not been detected in significant quantity. In patients with liver disease there is increase in the volume of distribution and may result in prolonged duration of action. Renal excretion of rocuronium may be more than 30% in 24 hrs and in patients with renal failure, Rocuronium may produce longer duration of action.

Pharmacodynamics

Mechanism of action : Rocuronium being amino steroid based neuro muscular blocking agent has a post junctional effect and high degree of selectivity for receptors at the neuro muscular junction. Muscle paralysis is produced by competitive antagonism of nicotinic cholinergic receptors of skeletal muscle. Its potency is about 10 – 15% of vecuronium. Rocuronium antagonises acetylcholine receptors. Therefore it is likely that it competes with acetylcholine at its binding site. The tetanic fade phenomenon is observed with rocuronium indicating activity not only at post synaptic but also at presynaptic nicotinic receptors. Activity is terminated by gradual dissociation from the receptor shifting the agonist/antagonist equilibrium in favour of acetylcholine.

Dosage, onset and duration of action : Rocuronium has a rapid onset of neuro muscular block, presumably due to its relatively low potency. This ensures the presence of more relaxant molecules in the blood stream and results in large concentration gradient towards biophase. It has been assumed that this is the main rate

limiting step overriding individual differences in affinity constant for the receptors. Intubating dose of Rocuronium is 0.6 mg/kg.

Table 1 : Doses of Rocuronium for intubating and maintenance of neuro muscular blockade.[65]

	Dosage mg/kg	**Clinical duration (min)**
ED95	0.3 – 0.4	
Intubation at 60–90 seconds	0.6 – 1.0	35 – 75
Maintenance	0.1 – 0.15	15 – 25
Infusion	8 – 12 microg/kg/min	

Onset of action of rocuronium is shorter when compared other nondepolarising muscle relaxant. When the dose of rocuronium is increased, onset of action decreases further.

Table 2 : Onset and clinical duration of action of different doses of Rocuronium [66]

Onset	**Dose of Rocuronium**		
	0.6 mg/kg	0.9mg/kg	1.2mg/kg
Mean	89	75	55
Standard Deviation	33	28	14
Range	48 – 156	48 – 144	36 – 84

Duration	Dose of Rocuronium		
	0.6 mg/kg	0.9mg/kg	1.2mg/kg
Mean	37	53	73
Standard Deviation	15	21	32
Range	23-75	25-88	38-150

Variables : Onset = The time interval between the completion of injection of neuro muscular block and time to maximal depression of T1.

Duration = The time interval between the completion of injection of Neuro Muscular Block and time to recovery of 25% of control.

Rocuronium and continuous infusion

Rocuronium can be used for continuous infusion. The infusion rate depends on the anesthetic technique and age of the patient. It can be used at a rate of 8 – 12microg/kg/min. [67]

Recovery

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

T**able 3** : Recovery profile of different doses of Rocuronium

	Rocuronium 0.6 mg/kg	Rocuronium 0.9 mg/kg	Rocuronium 1.2 mg/kg
Mean (minutes)	14	22	24
Standard Deviation	8	14	11
Range	6 – 27	8 – 29	11 – 43

Recovery index = The time from T25 to T75% of recovery.

As for other nondepolarizing agents the onset of action of rocuronium is more rapid at the diaphragm and adductor laryngeal muscles than at the adductor pollicis[51] probably a result of a greater blood flow to centrally located muscles. Laryngeal adductor muscles are important in anesthesia because they close the vocal cords and insufficient relaxation prevents easy passage of the tracheal tube. Laryngeal adductor muscles are resistant to the effect of rocuronium, and the plasma concentration required for equivalent blockade is greater at the larynx than at the adductor pollicis. The same is true of the diaphragm, which is resistant to the effect of rocuronium and other neuromuscular blocking agents. Recovery is faster at the diaphragm and larynx than at the adductor pollicis.[51]

Rocuronium and Cardiovascular effects

Rocuronium is typically devoid of cardio vascular effects. Circulatory effects or release of histamine do not occur after rapid IV administration of even large doses of rocuronium. The structural feature for this difference is the absence of Acetyl

choline like character of A – ring substitution, which decreases the action on cardiac muscarinic receptors.

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

Rocuronium and age

In neonates and infants, the volume of distribution of rocuronium is increased and the plasma clearance is diminished. This result in longer elimination half life. IN children, the volume of distribution is unchanged but clearance is increased, resulting in shorter half life of rocuronium. In the elderly volume of distribution of rocuronium is unaltered or slightly reduced and clearance is diminished. This result in similar or slightly longer half life compared to adults.[68]

Rocuronium and Anaphylaxis

Single release of rocuronium on to the worldwide market, concern has been expressed about its propensity to cause anaphylaxis. Rose M, Fisher M identified 24 patients who met clinical and laboratory (intramedal, mast cell tryptase and morphine radio immunoassay) criteria for anaphylaxis to rocuronium. Data from intradermal testing suggested that rocuronium is intermediate in its propensity to cause allergy in known relaxant reactors compared with low risk agents (e.g Pancuronium, vecuronium) and higher risk agents (e.g Alcuronium, succinyl choline). Baillard C et al reported two cases of documented anaphylaxis.[69]

MATERIALS AND METHODS

SOURCE OF DATA : KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, NEHRU NAGAR, BELGAUM -10

Sample size :

Total sample size = 40 Patients in each group (Total of 80)

Using the formula

$$N = \frac{2 (Z\alpha + Z\beta)^2 \; P(1-P)}{(P_0 - P_1)^2}$$

$\alpha = 0.05$, $\beta = 0.1$, Power = 90%

$P_0 = 95\%$, $P_1 = 65\%$, $P = 80\%$

$Z\alpha = 1.96$, $Z\beta = 1.28$

$$P = \frac{P_0 + P_1}{2}$$

Inclusion Criteria

1. ASA physical status I or II
2. Age between 18 to 60 yrs.
3. Elective surgeries

Exclusion Criteria

1. Pts having CVS , hepatic renal or neurological disease or was receiving any drug known or suspected of interfering with neuro muscular function

2. Anticipated abnormal airway

3. Suspected allergy to neuromuscular blocking agents.

4. Addiction, obesity, pregnancy.

Study design: Randomized Clinical Trial. Duration Of study (Data Collection)= 6 months

Methodology:

After obtaining written informed consent, patients were randomly divided into two groups of each, Group OO (Orbicularis Oculi) and Group AP (Adductor Pollicis) using computer generated randomization table. In the operating room, patients were attached to pulse oximeter, ECG, non invasive blood pressure monitor and Neuro Muscular monitor -Train of Four (TOF – Guard) acceleromyograph monitor.

Patient was pre-oxygenated with 100% oxygen for 3 mins using face mask. Anaesthesia induced with Inj Thiopentone 5mg/kg and Inj Fentanyl 2 microg/kg I.V. IPPV was given using face mask with 100% oxygen until tracheal intubation. After induction , surface electrodes were applied over the ulnar nerve at wrist and facial nerve ,near orbit i.e anterior to ear lobe and connected to respective TOF(Train Of Four) Guard acceleromyograph monitor. Neuro Muscular monitoring done using Train Of Four(TOF) GUARD acceleromyograph (Organon-Teknika, Belgium) . Both nerves were stimulated with Train of Four (TOF) stimulation (a series of four twitches in 2 sec, 2 Hz frequency, each 0.2ms long) every 15 secs after loss of the eyelash reflex. Current intensity of 20mamps for facial nerve and 50 mamps for ulnar nerve were used. The evoked responses at thumb and around the orbit were recorded using (Train of four) TOF - GUARD acceleromyograph.

Patients in each group were given Inj Rocuronium 0.6mg/kg injected over 10secs. Onset of neuro muscular block was defined as the interval between the administration of rocuronium injection and complete disappearance of all four TOF responses. Intubation was performed when all four TOF responses from OO muscle was abolished in OO group. In Group AP intubation was performed when AP was completely blocked, i.e all four TOF responses from AP muscle was disappeared, selection of muscle group was randomly done. Intubation was performed by an independent Anaesthesiologist within 10secs , who was blinded about patient grouping and the time course of NMB, not involved in Anaesthesia technique and was unaware about NMB agent's dose and observations. Intubation conditions were graded using scoring scale described by Kreig et al. This scale distributes intubating conditions into four classes : excellent, good, poor and inadequate.

Table 4

Points	**1**	**2**	**3**	**4**
Vocal Cords	Open	Moving	Closing	Closed
Coughing	None	With Diaphragm	Clear	Severe
Laryngoscopy	Easy	Fair	Difficult	Impossible
Total Score	3-4	5-7	8-10	11-12
Intubating Conditions	Excellent (Class 1)	Good (Class 2)	Poor (Class 3)	Inadequate (Class 4)

Intubating Condition =

Statistical Analysis

Sample size was calculated as Total = 80 (40 in each group) with 90% power with Alpha error = 0.05, B error = 0.1, Z alpha = 1.96, Z beta = 1.28. Results expressed as mean +/- Standard deviation. Results of Intubating condition expressed as frequency %. Paired student t – test was used to compare the onset time at Orbicularis Oculi and Adductor Pollicis muscle within each group. Chi square test with Yate's correction and / or Fisher Exact test was used to compare intubating condition between the two groups. Probability values < 0.05 are considered significant

RESULTS

Demographic data were similar between the two groups. There were no important differences with respect to patient characteristics between the two groups studied. (Refer Table 5, 6, 7 & 8) (Figure :- 12, 13, 14 & 15)

Onset time was shorter at OO (Orbicularis oculi muscle) than at the AP (Adductor pollicis) muscle in both group i.e 80.2 +/- 26.21 seconds in OO muscle Vs 162.4 +/- 37.80 seconds in AP muscle for OO group in which intubation was done when Orbicularis oculi muscle was blocked and 79.9 +/- 19.03 seconds in OO muscle Vs 156.7 +/- 29.21 seconds in AP muscle for AP group in which intubation was done when AP muscle was blocked (P = <0.001) (Table – 9, Figure – 17) . The onset time at the same muscle did not differ significantly between the two groups. (Figure – 16). In group OO complete blockade was achieved 82.2 +/- 22.27 seconds earlier at Orbicularis Oculi muscle than at Adductor Pollicis muscle. Similarly in Group AP, Orbicularis Oculi muscle was blocked 76.8 +/- 21.26 seconds earlier than at Adductor Pollicis muscle.

Intubating condition after Inj. Rocuronium 0.6 mg/kg in the Adductor Pollicis group (AP Group) (Excellent – 87.5%, Good – 12.5%, Poor – 0%) were significantly better than in the Orbicularis Oculi group (OO Group) (Excellent – 27.5%, Good – 45%, Poor – 27.5%) → P = <0.001. (Table :- 10, Figure :- 18)

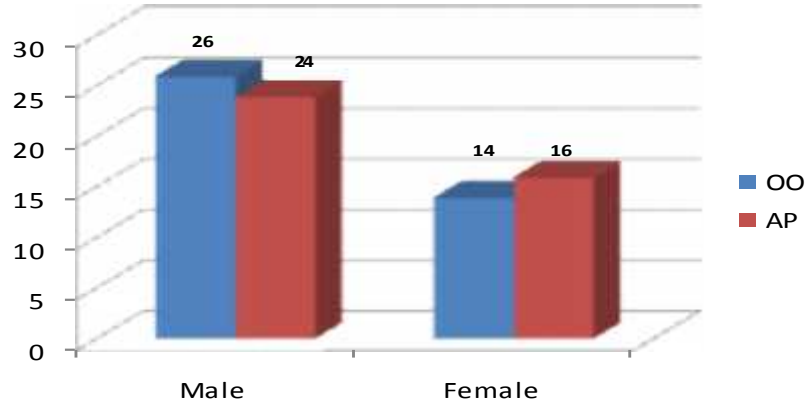
Measured onset time was longest in The AP group, however, all patients had Good to Excellent intubating condition. At the OO group, onset time was shortest, however 27.5% patients had poor intubating condition. No patients in both group had inadequate intubating condition.

Sex Distribution (Table – 5)

	Male	**Female**	**Total**
OO Group	26 (65%)	14 (35%)	40
AP Group	24 (60%)	16 (14%)	40

Chi Square = 0.213 P = 0.644

Figure12:-

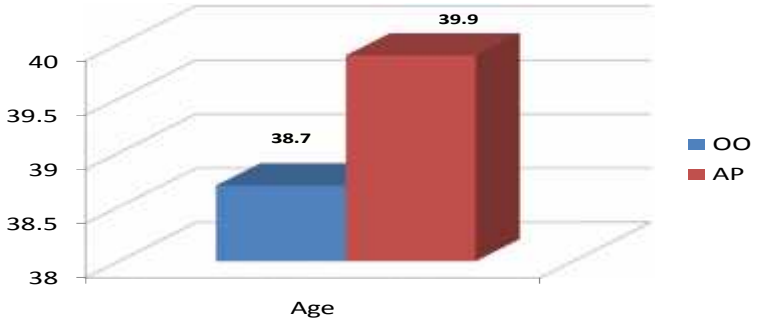


Age Distribution (Table – 6)

	Mean	**Standard Deviation**
OO Group	38.7 Years	13.11
AP Group	39.9 Years	14.26

t = 0.383, P = 0.702

Figure :- 13

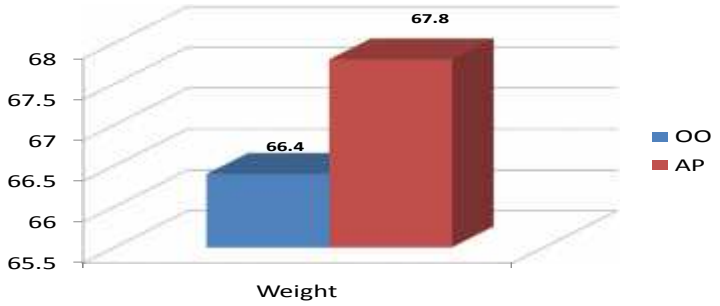


Weight Distribution (Table – 7)

	Mean	**Standard Deviation**
OO Group	66.4 Kilograms	7.80
AP Group	67.8 Kilograms	7.28

t = 0.859 , P = 0.393

Figure :- 14

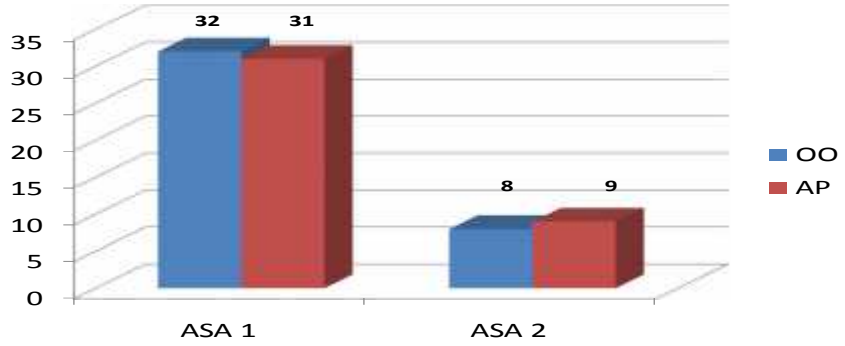


ASA Classification (Table – 8)

	ASA 1	**ASA 2**	**Total**
OO Group	32 (80%)	8 (20%)	40
AP Group	31 (77.5%)	9 (22.5%)	40

Chi Square = 0.075 , P = 0.785

Figure :- 15



Comparison of onset time between the two muscles (Table – 9)

Group	Onset Time	Mean Time +/- S.D (Seconds)	Significance
OO Group	Onset at OO Muscle Onset at AP Muscle	80.2 +/- 26.21 162.4 +/ - 37.80	t = 23.322 P = 0.000 (< 0.001)
AP Group	Onset at OO Muscle Onset at AP Muscle	79.9 +/- 19.03 156.7 +/- 29.21	t = 22.865 P = 0.000 (< 0.001)

Figure :- 16

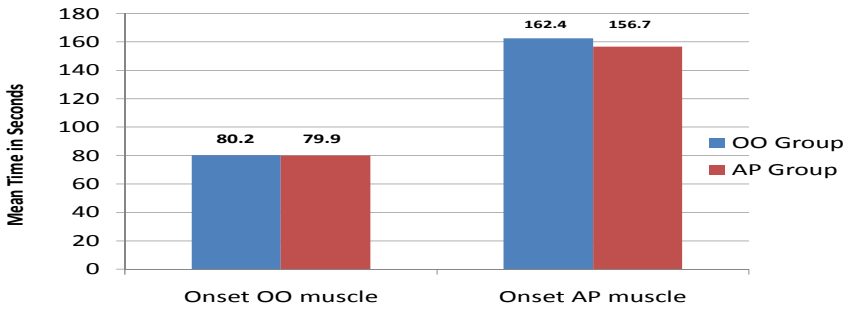
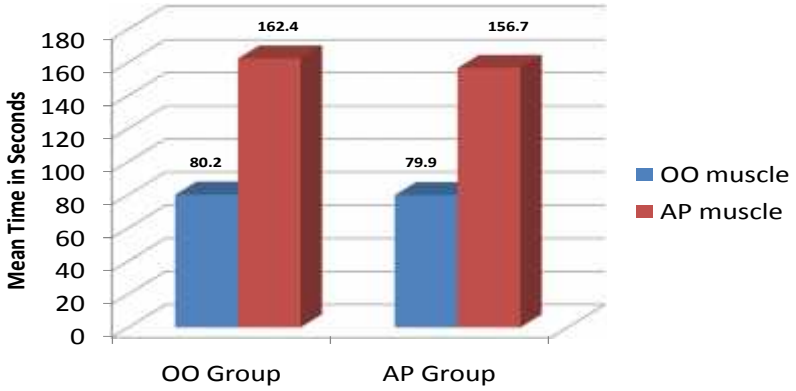


Figure :- 17



Comparison of intubating condition between two groups (Table -10)

Excellent Intubating condition

	Excellent	**Good**	**Poor**	**Inadequate**	**Total**
OO Group	11 (27.5%)	18 (45%)	11 (27.5%)	0	40
AP group	35 (87.5%)	5 (12.5%)	0	0	40

Chi square = 30.870 p = 0.000 (<0.001)

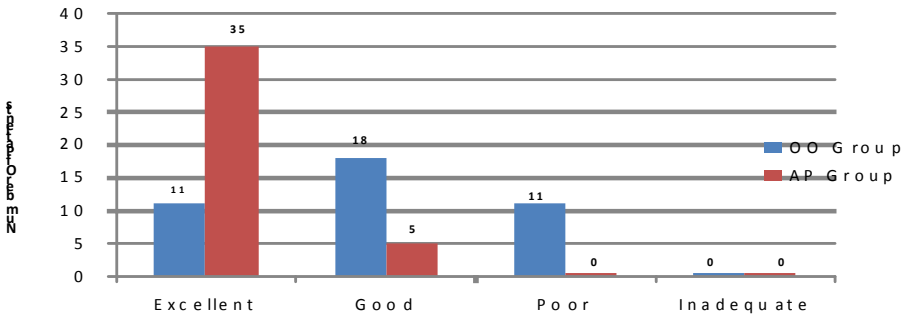
Excellent + Good Intubating condition

	Excellent + Good	Poor	Inadequate	Total
OO Group	**29 (72.5%)**	**11 (27.5%)**	**0**	**40**
AP Group	**40 (100%)**	**0**	**0**	**40**

Fisher Exact test P = 0.000 (< 0.001)

Chi square with Yate's correction = 10.540 P =0.000 (< 0.001)

Figure :- 18



DISCUSSION

This study demonstrates , which of the two muscles between Adductor Pollicis and Orbicularis Oculi monitoring, following Rocuronium 0.6mg/kg induced neuromuscular block will predict the presence of adequate tracheal intubating condition.

For onset of action , monitoring at the eye muscles correlates better with onset and degree of neuro muscular block at the larynx.[2]

In a randomized clinical trial done by Haller et al, patients receiving thiopentone and fentanyl , onset time after administration of a dose of 0.9mg/kg of Rocuronium at the OO was shorter (110 secs) than that at the AP (144 secs). However excellent intubating condition were observed significantly more with AP (95%) compared to OO group (65%)[18] . Cessation of response of the OO muscle did not guarantee satisfactory intubating condition.

In our study excellent intubating condition after Inj. Rocuronium 0.6mg/kg was 87.5% in Adductor Pollicis (AP) and 27.5% in Orbicularis Oculi (OO), which was similar to the study conducted by Haller et al as mentioned above. In group OO 27.5% of patients had poor intubating condition with bucking and coughing which can be associated with an increased risk of laryngeal trauma and post operative sore throat[70]. Four patients of OO group observed cessation of response in < 50 seconds after Inj Rocuronium 0.6mg/kg, showed severe coughing and bucking during tracheal intubation.

The sensitivities of Orbicularis Oculi were different, with comparable maximum effects with that of the laryngeal adductor muscles.[19] But in my study after 0.6mg/kg

dose of Rocuronium rapidly produced a complete block at the OO, where as laryngeal and diaphragm blocks were still incomplete.

This study confirms the findings of previous studies showing that complete relaxation of the Orbicularis Oculi precedes complete relaxation of the laryngeal muscles and diaphragm. Using Orbicularis Oculi relaxation as a guide to adequacy of relaxation for intubation will thus result in an unacceptable incidence of inadequate intubating condition and cannot be recommended.

In another randomized study , done to compare Adductor Pollicis , Orbicularis Oculi and Corrugator Supercilii as indicators of adequacy of muscle relaxation for tracheal intubation using Remifentanil 0.5micro gram /kg/min for 2 min followed by Propofol 2 to 2.5mg/kg and Using TOF –watch (Train of Four) acceleromyograph to guide onset time for Intubation after giving two doses of Rocuronium 0.6mg/kg and 1.0 mg/kg.[17] They concluded that Orbicularis oculi had faster intubation time but associated with inadequate intubating condition.(Excellent being 32%, good 62% and poor 6%) as against Adductor pollicis (Excellent 87% and good 13%). In my study excellent intubating condition is in Adductor Pollicis, is been 87.5% close value as this study, but after a long delay as compared to Orbicularis oculi. This does contradict[19] previous study, which says Orbicularis Oculi is more resistant in terms of maximum blockade and its sensitivity is similar to that of laryngeal adductor muscles.[12]

The faster onset of Neuro muscular blockade at Orbicularis Oculi compared to Adductor Pollicis might be due to differences in circulation time and muscle blood flow.[10,73]. Muscles which are closer to the central circulation like Orbicularis Oculi or

diaphragm have relatively greater perfusion and tend to be paralyzed more rapidly than the peripheral muscles like Adductor Pollicis.[16].

Neuro muscular blocking drugs affect small, rapidly moving skeletal muscles before those of abdomen. Onset of neuro muscular blockade after administration of non depolarizing muscle relaxant is more rapid but less intense at laryngeal muscles than peripheral muscle like adductor pollicis muscle. The sparing effects of Non depolarizing muscle relaxant at laryngeal muscles may be due to role of skeletal muscle fiber types. Muscles involved in closure of glottis have fast contraction times, where as adductor pollicis is composed mainly of slow fibers. The density of acetyl choline receptors is greater in fast than in slow contraction fibers. It is likely that more receptors need to be occupied to block a fast muscle than a slow muscle. More rapid onset at vocal cords than at adductor pollicis suggests more rapid equilibration between plasma concentration and those at the airway muscles when compared with adductor pollicis muscle.[74]

Factors that determine the sensitivity to neuro muscular blocking drugs of a given muscle or group of muscles are poorly understood. It may depend on type of fibers [12,75] that make of a muscle because the morphology of neuro muscular junction is different whether the muscle fiber is classified as red (slow), intermediate or white (fast) [12,76]. It has been suggested that slow fibers are more sensitive to NDMR although this not been constant finding. [12,75&77] Orbicularis oculi is made up of small, round and 89% fast twitch type 2 fibres.[20] Adductor Pollicis is made up of slow oxidative type of fibers.[12,78].

Based on above Orbicularis oculi has to be better indicator for intubation earlier than adductor pollicis. My study results has been similar to other studies which have shown orbicularis oculi is not a adequate indicator for intubation.[17,18,19&23]

Circulatory factors determine the distribution of NMB agents from site of injection to different muscles. Thus muscle perfusion and consequently onset of NMB, may be affected by haemodynamic effects of I.V anaesthetic agents.[79] Many factors including depth of anesthesia, determine adequate intubating condition. Autonomic and arousal responses to laryngoscopy and tracheal intubation was blunted by optimizing the combination of hypnotics and analgesia drugs during induction.[80] No patients had recall and no dangerous tachycardia or hypertension was observed. Inhalation agents were avoided because of there possible interaction with rocuronium.[67]

Most of the previous studies have used visual estimation of complete neuro muscular block by evaluating area around the eye. Owing to the fact that all studies used visual estimation of the onset of NMB , a subjective element renders the comparison between these studies difficult. Visual monitoring is a less objective method of measurement than continuous monitoring and registration of the evoked mechanical or electromyographic response. Neuromuscluar responses to rocuronium by acceleromyography recorded at the OO and AP are similar sensitive.[19] Therefore acceleromyography (TOF – Guard) to detect neuro muscular response in OO and AP was chosen.

One limitation was that, other muscles of the face may be activated by facial nerve stimulation or by direct muscle stimulation and there by interfere with the response measured during contraction of the Orbicularis Oculi. To minimize this direct muscle stimulation , chose to position the stimulating electrodes in such a way as to lessen the direct activation of the OO and to use 20mA of current intensity for stimulation of the facial nerve.[55,81]

CONCLUSION

In this Randomized Comparative Clinical trial between Orbicularis Oculi and Adductor Pollicis as indicators of adequacy of muscle relaxation for tracheal intubation following Rocuronium induced Neuromuscular Block, conclude that even though orbicularis oculi has early onset of neuro muscular block as compared to adductor pollicis, it is associated with significantly inadequate intubating condition as compared to adductor pollicis i.e 27.5% poor condition. Adductor pollicis has 87.5% excellent intubating condition as compared to Orbicularis Oculi which has 27.5% excellent intubating condition. After Rocuronium administration , orbicularis oculi does not have sensitivity similar to laryngeal adductor muscles. Neuro muscular activity of the Adductor Pollicis using Train of Four (TOF Guard) to determine the appropriate tracheal intubation time and conditions in patients paralyzed with Rocuronium is more clinically relevant than monitoring the Orbicularis Oculi muscle. Optimum intubating condition can prevent post operative sore throat, hoarseness of voice and laryngeal trauma. Monitoring the response of Orbicularis Oculi will reflect the time of onset but not the level of Neuro Muscular Block at the airway musculature. While monitoring peripheral muscles, i.e Adductor Pollicis will underestimate the rate of onset of Neuro Muscular Block, but will adequately estimate the degree of neuro muscular blockade in the airway musculature.

SUMMARY

There has been discrepancies between Orbicularis Oculi and Adductor Pollicis muscles as to which muscle is an ideal indicator for predicting adequate intubating condition. Orbicularis Oculi exhibits similar features with respect to time course of neuromuscular blockade and sensitivity to muscle relaxants like the laryngeal adductor muscle. Hence studies have quoted that monitoring Orbicularis Oculi could predict adequate intubating condition. Other studies have argued saying that Adductor Pollicis is a better indicator for predicting adequate intubating condition.

Hence this study was undertaken to see which muscle among the two is an adequate indicator.

Eighty patients undergoing General Anaesthesia for various surgeries were studied by dividing into two groups of forty each i.e Orbicularis Oculi and Adductor Pollicis group. Train Of Four (TOF – Guard) acceleromyograph, Neuro muscular monitor was used to estimate the onset of neuromuscular block at Orbicularis Oculi and Adductor Pollicis muscle. Intubating condition was graded using the scale given by Krigh et al.

Patients were randomized into two groups to receive Rocuronium at a dose of 0.6mg/kg during Inj Thiopentone – Fentanyl anaesthesia. Tracheal intubation was performed after maximal neuromuscular block at the Adductor Pollicis (thumb) muscle and Orbicularis Oculi (eyelid) muscle. Onset time and Intubating conditions were assessed.

Onset time was significantly shorter in Orbicularis Oculi muscle group than Adductor Pollicis muscle group, but adequate intubating condition was significantly

seen in Adductor Pollicis group, as patients in Orbicularis Oculi muscle group had poor intubating conditions.

In conclusion monitoring neuro muscular activity of the Adductor Pollicis using Train Of Four (TOF – Guard) acceleromyograph, Neuro muscular monitor to determine the appropriate tracheal intubation time and conditions in patients paralyzed with Rocuronium is more clinically relevant than monitoring the Orbicularis Oculi muscle.

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INFORMED CONSENT FORM

Mr/Mrs/Miss. _____ we are requesting you to enroll yourself in study titled **"Comparison between Adductor Pollicis and Orbicularis Oculi as indicators of adequacy of muscle relaxation for tracheal intubation following Rocuronium induced Neuromuscular Block" - Randomized Comparative Clinical trial at KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE,** conducted by Dr. XXXXX, Post Graduate in M.D. Anaesthesiology under the guidance of Dr. XXXXXX., Professor, Department of Anaesthesiology, J.N. Medical College, Belgaum under KLE university, Belgaum.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to compare Adductor Pollicis and Orbicularis Oculi as indicators for adequacy of muscle relaxation for tracheal intubation after administration of Rocuronium.

Procedure Involved :

If you agree to enroll yourself in my study, I will ask your present past and family history. Then you will be clinically examined in detail and routine

investigations like Haemoglobin will be done. After giving General Anaesthesia with I.V induction agents and Muscle relaxation with rocuronium , you will be connected to Neuro muscular monitor – TOF Guard which will provide current intensity of 20 to 50 mamps to assess onset of neuro muscular blockade at 2 muscles i.e Adductor pollicis and Orbicularis oculi. Then you will be intubated using endotracheal tube to compare adequate intubating conditions between Adductor Pollicis and Orbicularis Oculi.

Risks and Benefits :

There is no risk involved with use of Neuro muscular monitor i.e Train Of Four (TOF) Guard acceleromyograph. Rarely Rocuronium may be associated with allergy or sometimes patient may have delayed recovery**.** Benefits are ,Complications like Laryngeal trauma and sore throat can be minimized under excellent to good intubating condition.

Voluntary Participation / Withdrawal :

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.S hospital.

Alternatives :

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality :

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except :

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results :

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation :

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation :

In the event of injury related to the study, treatment will be made available through KLES Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr.XXXXXX , at Department of Anaesthesiology, KLES Hospital & MRC or by Ph. No : 0831 - 2473777.

Questions :

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr.XXXXXX, Department of Anaesthesiology, KLES Hospital and MRC, Ph No. 0831-2473777. For any information about the study during the study or after that may be collected from Dr. XXXXXXX, Professor, Department of Anaesthesiology, KLES Hospital & MRC, Belgaum Ph: 0831-2473777.

If you have any queries about your rights as a study subject, you may call Principal and Chairman, J. N. Medical College Institutional Ethical Committee for Human Subjects Research, Ph. 0831-2473777 at J.N. Medical College, Belgaum.

Consent for participation in research trial

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject : _____ Date :

Witness Name : _____ Signature : _____ Date :

Investigator Name: _____ Signature : _____ Date :

Place : _____

PROFORMA

"Comparison between Adductor Pollicis and Orbicularis Oculi as indicators of adequacy of muscle relaxation for tracheal intubation following Rocuronium induced Neuromuscular Block" - Randomized Comparative Clinical trial at KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE.

Name & Address of the patient : _____

_____

Age of the Patient : _____ Years Sex : _____ IP. No. _____

Anaesthesiologist : _____ Surgeon : _____

PREANAESTHETIC EVALUATION :

Chief Complaints :

Past History :

1. History of Hypertension, Diabetes Mellitus, G.E reflux, Addiction.
2. History of drug intake eg. Aminoglycosides,,Local Anesthetics, cardiac anti dysrhythmic drugs like lidocaine, quinidine. Diuretics like Furosemide, Azathioprine, Lithium, Phenytoin,Cyclosporine, Ephidrine and esmolol.
3. History of cardiac, pulmonary diseases, renal disease, hepatic disease and neurological diseases.
4. History of allergy to Neuro muscular drugs, Thermal (Burn injury), Paresis or hemiplegia..

Family History

General Physical Examination :

Weight : Temperature : Pallor : Height :

Cyanosis : Pedal Edema : Clubbing :

Pulse : B.P : RR :

M.P Grading

Thyro mental distance Mouth opening

TMJ examination

SYSTEMIC EXAMINATION :

Respiratory System : Cardiovascular System :

Central Nervous system: Per Abdomen :

Air way assessment : Spine assessment :

INVESTIGATIONS :

Diagnosis :

Proposed Surgery :

Inclusion Criteria :

1. ASA physical status I and II
2. Age between 18 to 60 yrs.
3. Elective surgeries

Exclusion Criteria

1. Pts having CVS , hepatic renal or neurological disease or was receiving any drug known or suspected of interfering with neuro muscular function
2. Anticipated abnormal airway
3. Suspected allergy to neuromuscular blocking agents.
4. Addiction, obesity, pregnancy and Gastro Esophageal reflux.

Methodology:

After obtaining written informed consent, patients will be randomly divided into two groups of each, Group OO (Orbicularis Oculi) and Group AP (Adductor Pollicis) using computer generated randomization table. In the operating room, patients will be attached to pulse oximeter, ECG (Lead 2), and non invasive blood pressure monitor .Neuro Muscular monitoring will be done using TOF GUARD in which surface electrodes will be applied over the area of ulnar nerve at the wrist and on the temporal branch of facial nerve near the orbit i.e Anterior to the ear lobe. All nerves will be stimulated with Train of Four (TOF) stimulation (a series of four twitches in 2 s, 2 Hz frequency, each 0.2ms long) every 15 secs after loss of the

eyelash reflex. Current intensity of 20mamps for facial nerve and 50 mamps for ulnar nerve will be used. The evoked responses at thumb and around the orbit will be measured by TOF - GUARD acceleromyograph (Organon-Teknika, Belgium)

Pt will be pre-oxygenated with 100% oxygen for 3 mins using face mask. Anaesthesia induced with Inj Thiopentone 5mg/kg and Inj Fentanyl 2 microg/kg I.V. IPPV will be given using face mask with 100% oxygen until tracheal intubation. After induction , surface electrodes will be applied over the ulnar nerve at wrist and facial nerve ,near orbit i.e anterior to ear lobe and connected to respective TOF Guard acceleromyograph monitor. Supra maximal current of 20mamps to facial nerve and 50 mamps to ulnar nerve will be applied simultaneously and responses recorded. Patients in each group will be given Inj Rocuronium 0.6mg/kg injected over 10secs. Onset of neuro muscular block will be defined as the interval between the administration of rocuronium injection and complete disappearance of all four TOF responses. Intubation will be performed when all four TOF responses from OO is abolished in OO group. In Group AP intubation will be performed when AP will be completely blocked, selection of muscle group being made at random. Intubation will be performed by an independent Anaesthesiologist within 10secs , who will be blinded about pt grouping and the time course of NMB, not involved in Anesthesia technique and is unaware about NMB agent's dose and observations. Intubation conditions will be graded using scoring scale described by Kreig et al. This scale distributes intubating conditions into four classes : excellent, good, poor and inadequate.

Observations :

Group	**Onset time**	**IN seconds**
	Onset OO	
	Onset AP	

Intubating conditions is graded according to scoring scale given by Kreig et al as following:-

Points	**1**	**2**	**3**	**4**
Vocal Cords	Open	Moving	Closing	Closed
Coughing	None	With Diaphragm	Clear	Severe
Laryngoscopy	Easy	Fair	Difficult	Impossible
Total Score	3-4	5-7	8-10	11-12
Class	1	2	3	4
Intubating Conditions	Excellent	Good	Poor	Inadequate

Intubating Condition =

Orbicularis Oculi Group								
Name	I.P no	Age	Sex	Weight (Kgs)	ASA	Onset time at O.O (secs)	Onset time at A.P (secs)	Intubating Score
Shivappa	366309	41	Male	65	1	90	135	5
Shekar	367768	33	Male	75	1	90	150	7
Madev Gowda	364006	25	Male	60	1	105	165	8
Tahir	364024	22	Male	70	1	60	120	6
Jagdish	365206	58	Male	68	2	90	165	4
Janaki	365766	56	Female	58	1	150	240	4
Kashinath	365894	42	Male	70	1	45	90	9
Shabbir	365738	32	Male	70	1	75	135	9
Jagadish	365444	35	Male	62	1	60	135	9
Jayashree	360555	37	Female	55	1	45	120	6
Anita	360185	21	Female	57	1	90	150	6
Shantawwa	363280	55	Female	67	1	90	135	4
Vimla J.B	358947	40	Female	58	1	60	165	4
Jyotiba	362507	46	Female	75	1	45	120	6
Jannawa	3571147	52	Female	55	2	45	120	7
Chetan Patil	355987	18	Male	50	1	90	150	8
Sushila	357211	44	Female	58	1	60	120	7
Soni Chowdhary	357680	35	Female	75	1	75	150	4
Ramesh	357811	34	Male	60	1	60	135	6
Babu SomeshKar	357943	23	Male	50	1	60	135	4
Jagadish	358842	46	Male	74	1	105	150	6
Rajaram	358911	41	Male	70	1	30	105	8
Bassamma	353410	55	Male	75	2	120	210	7
Prashanth	354328	28	Male	80	1	75	180	8
Siddan Gowda	350782	53	Male	71	1	90	195	7
Basavantappa Gujjal	351471	26	Male	68	1	45	150	8
Venkatesh Yallappa	350735	60	Male	76	2	75	195	7
Sridhar	347817	18	Male	64	1	45	135	8
Kamala	348737	55	Female	68	2	90	195	6
Channappa	349248	18	Male	62	1	105	210	8
Anand	350016	45	Male	62	2	90	195	8
Vandana Shah	349598	48	Female	77	1	105	210	7

Shiva Kumar	350190	20	Male	67	1	120	225	7
Maruti	350932	44	Male	77	1	105	210	5
Shashidhar	350719	55	Male	66	2	60	120	4
Akkathai Magdum	332237	60	Female	63	2	120	225	4
Pushpa	333022	40	Female	71	1	75	195	3
Mahesha	334545	25	Male	77	1	90	195	3
Ravi sethi	350876	34	Male	69	1	90	180	7
Sushma	347657	29	Female	60	1	90	180	7
Adductor Pollicis Group								
Sharada	368043	42	Female	70	1	45	135	4
Shankarappa	368043	58	Male	71	1	90	165	4
Appanna	366413	57	Male	80	2	90	180	4
Shrikanth	366738	60	Male	74	2	75	180	4
Mallikarjun	367167	56	Male	65	1	90	210	4
Vijay	368783	23	Male	64	1	75	150	6
Dhanraj	366437	24	Male	80	1	105	195	3
Abdul Shaikh	36669	31	Male	73	1	90	195	4
Shivappa	366360	25	Male	67	1	105	180	3
Chinnawwa	366369	60	Female	63	2	90	180	4
Mahesh	367130	53	Male	71	2	60	150	4
Shreesha	367039	24	Male	58	1	60	120	4
Anil	366385	31	Male	72	1	45	90	7
Supriya	367154	36	Female	68	1	45	105	4
Prakash	363761	40	Male	73	1	60	120	3
Tapanna	365356	32	Male	58	1	90	150	4
Asha	365673	18	Female	50	1	90	135	4
Ashok	365414	37	male	83	1	105	165	7
Mahadev	366636	42	Male	77	1	90	150	5
Bagawwa	366495	51	Female	65	1	105	180	3
Santosh	366793	18	Male	66	1	60	150	4
Janaki	361323	50	Female	69	2	105	120	7
Shantawwa	361999	35	Female	60	1	75	135	3
Sanjay	363443	27	Male	66	1	60	150	4
Channava Gowda	356820	54	Male	71	1	60	90	4

Shanta Bai	355881	60	Female	67	2	90	180	4
Shamshad	357745	40	Female	63	1	90	165	4
Swathi	358131	30	Female	62	1	60	150	3
Mallesh Kumarswamy	358271	22	Male	67	1	90	150	3
Laxmi Bai	355785	60	Female	64	2	90	165	4
Mahesh	352157	21	Male	66	1	105	180	4
Ravi	348112	24	Male	69	1	75	180	3
Yashodha	348176	59	Female	72	2	90	195	4
Laxman	349689	49	Male	64	1	45	120	4
Krishna Nigappa	350065	52	Male	76	1	75	165	3
Shashi Kala	350342	40	Female	65	1	90	180	3
Bhagyashree	350915	18	Female	50	1	75	165	3
Parasappa	350721	55	Male	78	2	105	195	3
Afrana	331206	34	Female	62	1	60	135	4
Shaikh Bala Saheb	332885	48	Female	74	1	90	165	3

Intubating Condition	Type of Surgery
Good	PCNL
Good	Cranioplasty
Poor	V.P Shunt
Excellent	ORIF for fracture Humerus
Excellent	Discetomy L3 - L4
Excellent	V.P Shunt
Poor	ORIF for Leforts Fracture
Poor	Fusion of L1 fracture
Poor	Fusion of D12 Fracture
Good	Excission of Fibroadenoma Breast
Good	Laprotomy for mass abdomen
Excellent	Open Cholesystectomy
Excellent	Skin Grafting for operated MRM breast
Good	Mesh repair for inscissional hernia
Good	Total Thyroidectomy for Papillary CA thyroid
Poor	Pistows Procedure for CA Pancreas
Good	ORIF for Leforts Fracture
Excellent	Excission of Fibroadenoma Breast
Good	Partial Nephrectomy
Excellent	Palate repair
Good	Cysto Gastrostomy + Cholecystectomy
Poor	Laminectomy L4 - L5
Good	Thoracoscopy + Sternotomy for neck abscess
Poor	ORIF for nasal bone fracture
Good	ORIF for fracture Humerus
Poor	Urethroplasty for urethral stricture
Good	Discetomy L3 - L4
Poor	Skin Grafting for operated Both bone fracture
Good	Choleystectomy
Poor	Skin grafting for superfecial burns on LL
Poor	Whipple procedure
Good	Urethrolithotomy

Good	SSG
Good	Hernia repair of umbalius
Excellent	decompression and fixation of Koch's spine
Excellent	B/L TKR
Excellent	ORIF for fracture Humerus
Excellent	Laproscopic Appendicetomy
Good	Laminectomy L4 - L5
Good	Fibroadenoma excission
Excellent	Laminectomy L4 -L5
Excellent	Disectomy c3 - c4
Excellent	ORIF fracture humerus
Excellent	Craniotomy
Excellent	Cranioplasty
Good	ORIF for Leforts Fracture
Excellent	ORIF for fracture tibia
Excellent	Partial nephrectomy
Excellent	ORIF for fracture humerus
Excellent	Oesophagectomy
Excellent	PCNL
Excellent	Septo rhinoplasty
Good	V.P Shunt
Excellent	Trans sphenoidal excission of pitutatry adenoma
Excellent	ORIF for Leforts Fracture
Excellent	ORIF for Leforts Fracture
Excellent	V.P Shunt
Good	Laminectomy and decompression for osteoclastoma
Good	Laminectomy L4 -L5
Excellent	Laminectomy L2 -L5
Excellent	Laminectomy for traumatic L4 -L5 PIVD
Good	Lap Appendicetomy
Excellent	Lap rectopexy
Excellent	LapAppendicectomy
Excellent	Lap Appendicetomy

Excellent	Posterior Instrumentation for Koch's Spine
Excellent	Laproscopic hernia repair
Excellent	Laproscopic Cholesystectomy
Excellent	Sural nerve flap graft
Excellent	Debridment and grafting of raw are left fore arm
Excellent	Septo rhinoplasty
Excellent	SSG and debridment of superfecial burns
Excellent	Decompression and fixation of D11 - D12 koch's spine
Excellent	Gastrectomy for ca Stomach
Excellent	Burr Hole
Excellent	Right Nephrectomy
Excellent	Palate Repair
Excellent	C3 - C4 fusion
Excellent	Craniotomy for aneurysm of right MCA
Excellent	ORIF for both bobe fracture upper limb