"A PROSPECTIVE, RANDOMIZED DOUBLE BLINDED COMPARATIVE STUDY OF THE EFFECT OF SEVOFLURANE ON INTUBATING CONDITIONS WITH ROCURONIUM IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMIES"

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE
MADRAS MEDICAL COLLEGE
CHENNAI- 600003

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CERTIFICATE

This is to certify that the dissertation titled **"A PROSPECTIVE, RANDOMIZED DOUBLE BLINDED COMPARATIVE STUDY OF THE EFFECT OF SEVOFLURANE ON INTUBATING CONDITIONS WITH ROCURONIUM IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMIES"** submitted by **DR.S.GAYATHIRI** in partial fulfillment for the award of the degree of **DOCTOR OF MEDICINE** in **ANAESTHESIOLOGY** by **THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY, CHENNAI** is a bonafide record of work done by her in the **INSTITUTE OF ANAESTHESIOLOGY& CRITICAL CARE**, Madras Medical College, during the academic year 2014 -2017.

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CERTIFICATE OF THE GUIDE

This is to certify that the dissertation titled," **A PROSPECTIVE, RANDOMIZED DOUBLE BLINDED COMPARATIVE STUDY OF THE EFFECT OF SEVOFLURANE ON INTUBATING CONDITIONS WITH ROCURONIUM IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMIES**" is a bonafide research work done by **DR.S.GAYATHIRI** in partial fulfilment of the requirement for the degree of **DOCTOR OF MEDICINE** in **ANESTHESIOLOGY.**

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DECLARATION

I, **S.GAYATHIRI**, hereby declare that the dissertation titled, **"A PROSPECTIVE, RANDOMIZED DOUBLE BLINDED COMPARATIVE STUDY OF THE EFFECT OF SEVOFLURANE ON INTUBATING CONDITIONS WITH ROCURONIUM IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMIES"** has been prepared by me under the guidance of **PROF.DR.SAMUEL PRABHAKARAN, MD, DA**, Professor of Anaesthesiology, **INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE, MADRAS MEDICAL COLLEGE, CHENNAI**, in partial fulfillment of the regulations for the award of the degree of **M.D (ANAESTHESIOLOGY)**, examination to be held in April 2017.

This study was conducted at **INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE, MADRAS MEDICAL COLLEGE, CHENNAI.**

I have not submitted this dissertation previously to any journal or any university for the award of any degree or diploma.

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CONTENTS

INTRODUCTION

1. INTRODUCTION

Neuroanaesthesia is a speciality which continues to develop and expand, where the knowledge and expertise of the anaesthetist may directly influence the patient's outcome. Evolution of neurosurgical practice is posed by new challenges for the anaesthetist with greater focus on functional recovery of the neurological status. The emphasis remains on the following factors.

- Maintainence of balanced Anaesthesia with hemodynamic stability
- Ensuring smooth induction and recovery
- Maintenance of adequate Cerebral perfusion pressure
- Avoiding rise in intra-cranial pressure
- Providing good operative condition
- Preservation of neurological status
- Rapid and high-quality recovery.
- Ensuring proper post-operative analgesia.

The goals of perioperative anaesthetic management for patients undergoing elective craniotomies are based on the following:

1. Keeping the intracranial pressure within normal range.

2. Recognising that cerebral autoregulation may be impaired.

3. Hemodynamically stable induction and maintenance of anaesthesia.

4. Minimal brain swelling to optimize surgical exposure**.**

Rapid and safe endotracheal intubation is of prime importance in the practice of general anaesthesia in neurosurgery. The ease with which intubation performed depends upon the degree of muscle relaxation, depth of anaesthesia and skill of the anaesthesiologist. Succinlycholine is still the drug of choice for rapid endotracheal intubation due to its rapid onset of action and good intubating conditions. However it falls short of ideal muscle relaxant due to its potentially hazardous adverse effects. Among the non- depolarizing muscle relaxants vecuronium and atracurium were presented as an attractive alternative to succinylcholine. However, neither of these agents had the onset time as short as needed for endotracheal intubation. The various methods like using higher bolous dose, priming principle, timing principle were used to reduce their onset

time, but, at the expense of increased duration of action or hazardous side effects. Therefore the quest for an ideal non-depolarizing agent for rapid endotracheal intubation continued until rocuronium was introduced into clinical practice.

Rocuronium bromide is 2morpholino 3-disacetyl 16 N-allyl pyrrolidino derivative of vecuronium. The works carried out by other workers in the past have shown that rocuronium has the onset time comparable to succinylcholine and it is free from side effects that are commonly seen with succinylcholine. Volatile anaesthetics are known to potentiate the effects of NDMRs. This study uses 1 MAC sevoflurane with rocuronium (at an intubating dose of 0.8 mg/kg) during induction in patients undergoing elective craniotomies and assessed the efficacy of sevoflurane with rocuronium in terms of reducing onset time for intubation, evaluating the intubating conditions and haemodynamic responses, so that it can be used for rapid sequence intubation.

AIM OF THE STUDY

2. AIMS AND OBJECTIVES

AIM:

The aim of the study is to compare the effect of sevoflurane on intubating conditions with rocuronium in patients undergoing elective craniotomies.

OBJECTIVES:

1. To comparatively evaluate the onset time of intubation using rocuronium vs rocuronium with 2% sevoflurane.

2. To compare the intubating conditions.

3. To study the haemodynamic responses during intubation

AIRWAY MANAGEMENT IN NEUROSURGERY

3. AIRWAY MANAGEMENT IN NEUROSURGERY:

Airway management plays a pivotal role in the acute management of neurosurgical patients. The primary neurological problem may pose difficulties on the techniques used for establishing an unobstructed airway. At the same time, inappropriate airway management may adversely affect the neurological outcome of the patient. A clear understanding of this interaction helps to determine the choice of appropriate airway maintenance technique in that patient.

Endotracheal intubation for elective craniotomies:

Surgical position and aggravation of intracranial hypertension are the two major considerations in the airway management for elective craniotomies.

Surgical position and airway:

Airway compromise may be expected in the positions used for neurosurgery.

- Flexion of the neck is generally required for approach to the lesions in infratentorial compartment and parietal region.

- Lateral position or park bench position is required for lesions in the lateral cerebellar and cerebellopontine angle.

- Prone position is commonly used for surgeries on the cerebellar and spinal lesions.

Hence the risk of kinking of the endotracheal tube or inadvertent extubation is common in all these positions. Flexion of the neck after intubation may lead to endobronchial migration of the endotracheal tube. In all these patients, position of the endotracheal tube and ventilation must be confirmed after surgical positioning.

There are reports of obstruction of a reinforced endotracheal tube through a valve-like mechanism caused by partial detachment of the inner coating from the embedded spiral of the tube. The detachment is most likely caused by the reuse of a single-use product after autoclaving. Continuous soaking of the tapes by saliva used for tracheal tube fixation increase the risk of self-extubation in these patients. Extensive oedema of the tongue and face requiring prolonged postoperative tracheal intubation has been reported following posterior fossa surgeries in sitting as well as lateral positions. The exact mechanism of the complication remains ill-understood. Pressure on endotracheal tube might be caused by the instruments used in anterior surgical approaches on the cervical spine.

An armored endotracheal tube prevents airway compromise in these situations. Postoperative airway oedema may occur following high cervical spine surgery or skull base surgery requiring extensive dissection.

Intracranial hypertension and airway management:

No specific measures other than those required for any routine endotracheal intubation are necessary in patients without evidence of raised ICP. In patients with evidence of raised ICP, acute exacerbation of intracranial hypertension should be avoided. A smooth and unhurried intubation is very essential. The dosage of the hypnotic used for induction should ensure adequate depth of anaesthesia at intubation. Profound muscle relaxation must be achieved with a non-deplorising muscle relaxant before intubation. An additional dose of thiopentone or propofol may be given just prior to intubation. Lignocaine in a dose of 1-2 mg/kg is administered intravenously to prevent a rise in ICP. Mild hyperventilation by mask before intubation and also after intubation may also help to reduce ICP. Hypercapnia at this stage may be meticulously avoided by continuous capnographic monitoring.

KEY ASPECTS OF INTUBATION IN NEUROSURGERY

- ensure adequate preoxygenation with 100% oxygen
- target an ETCO2 that correlates to a PaCO2 of 35-40 mmHg
- control hypertension prior to intubation using a rapid acting, antihypertensive agent
  - which include labetolol or esmolol
  - nicardipine and clavidipine

  treat for intracranial hypertension
  - if raised ICP is present, consider osmotherapy (e.g. hypertonic saline bolus or mannitol)
  - provide adequate analgesia
  - keep the head in neutral position and avoid neck constrictions (e.g. remove c-spine collar)

prevent the reflex sympathetic response to intubation using non-pharmacological measures

- best possible intubator
- ear-to-sternal notch postioning
- head up 30-45 degrees
- gentle laryngoscopy and ensure first pass success
- e.g. use video laryngoscopy for glottic exposure

prevent reflex sympathetic response to intubation using pharmacological measures

- use fentanyl at the dose of 3-7 mcg/kg IV as a cardiostable sympatholytic agent; may lead to respiratory depression, chest rigidity. Allow at least 3 minutes for onset prior to performing laryngoscopy.

- Remifentanil at the dose of 1-3 mcg/kg IV is an alternative to fentanyl; it has got a rapid onset of action and is rapidly titratable.

- Lignocaine at the dose of 1.5 mg/kg IV is an alternative option for sympatholysis, but may cause hypotension

- topical lignocaine (e.g. 5 ml of 4% lidocaine spray) effectively attenuates the cardiovascular responses to intubation

- esmolol 1.5-2 mg/kg IV could be used as a sympatholytic agent.

Induction agent

- propofol or thiopentone; adjust the dose to avoid hypotension
- ketamine, though no longer considered contra-indicated in most patients with raised ICP, indirect sympathetic effects may increase blood pressure
- etomidate

Neuromuscular blocker

- rocuronium (0.8- 1.2 mg/kg) IV is the agent of choice; rapid onset, does not increase ICP
- suxamethonium may increase ICP and fasciculations may cause increased oxygen consumption; avoid in patients with hyperkalaemia

Post-intubation

- adjust respiratory rate to a target ETCO2 35mmHg
- target SaO2 95% (avoid hypoxia)
- use minimum possible PEEP to avoid hypoxia,

PHYSIOLOGICAL RESPONSES TO INTUBATION

4. PHYSIOLOGICAL RESPONSES TO TRACHEAL INTUBATION

The goal of endotracheal intubation is to provide a secure and definitive airway. Unfortunately, laryngoscopy and intubation results in a cascade of physiological and pathophysiological reflex responses. These responses are initiated by the stimulation of the afferent receptors in the posterior pharynx supplied by the glossopharyngeal(X1) and vagus (X) nerves. The central nervous system (CNS), cardiovascular system, and respiratory system all respond to these stimuli, and the resultant physiologic manifestations may affect the patients' outcome. Stimulation of the autonomic nervous system results in increases in the heart rate and blood pressure, and stimulation of the upper and lower respiratory tract results in increases in airway resistance and hence it is mandatory to attenuate these responses in a compromised patient.

CENTRAL NERVOUS SYSTEM RESPONSE:

The central nervous system responds to airway manipulation by increasing the cerebral metabolic oxygen demand ($CMRO_2$) and cerebral blood flow (CBF). If the intracranial compliance is decreased, the increase in CBF may increase the intracranial pressure further. This response is important in situations when there is loss of autoregulation

such that blood flow to the brain, or regions of the brain, becomes pressure-passive (ie, increases in blood pressure result in increases in ICP).'

CARDIOVASULAR RESPONSE:

Laryngoscopy and intubation stimulates protective reflexes and leads to cardiovascular and respiratory system responses mediated by the sympathetic nervous system. In children, this process is believed to be a "monosynaptic reflex" promoting vagal stimulation of the SA node, which in turn results in bradycardia. In adults, a "polysynaptic event" occurs whereby impulses travel afferently via the glossopharyngeal and vagus nerves to the brain stem and spinal cord. An efferent sympathetic response results in norepinephrine release from the adrenergic nerve terminals, epinephrine release from the adrenal glands, and activation of renin–angiotensin system leading to tachycardia, hypertension and cardiac dysrthymias. These responses are short lived but catastrophic in patients with myocardial ischemia, intracerebral or aortic aneurysms, major vessel dissection, or major vascular injuries. Hypertension also leads to significant increases in ICP if autoregulation has been lost.

RESPIRATORY SYSTEM RESPONSE:

The respiratory system responds in three important ways to laryngoscopy and intubation:

1. activation of upper airway reflexes leading to laryngospasm

2. bronchospasm

3. Coughing.

Laryngospasm is a forceful involuntary spasm of the laryngeal muscles, produces difficulty in intubation as well as ventilation. Persistent and life-threatening laryngospasm is treated with CPAP with 100% oxygen, intravenous lignocaine (1.5 mg/kg), and even if persistent, neuromuscular block with suxamethonium at 10% of the intubating dose. Negative intrathoracic pressure created by inspiratory attempts against a closed glottis (laryngospasm) may result in negative pressure pulmonary edema (NPPE).

DRUGS TO BLUNT INTUBATION RESPONSE:

Various drugs and techniques have been used for attenuating the stress response to laryngoscopy and intubation, which include opioids, benzodiazepines, beta blockers, calcium channel blockers, vasodilators, alpha-2 agonists etc...

OPIOIDS:

Fentanyl:

Fentanyl acts at opioid receptors and predominantly acts on μ receptors. Fentanyl causes haemodynamic stability during perioperative period by its action on the cardiovascular and autonomic regulatory areas. It decreases the sympathetic tone and increases the parasympathetic tone.

Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. It attenuates the response at 2μg/kg IV given before laryngoscopy and intubation. Optimal time of administration is 5 minutes before laryngoscopy and intubation

Low dose fentanyl was employed because a large dose might lead to chest wall rigidity, bradycardia, nausea and vomiting. Large doses may also cause postop respiratory depression; especially in surgeries with short duration(<1hr)

Sufentanil and alfentanil at dose of 15 to 30mcg/kg possess a more rapid onset and shorter duration of action than fentanyl, making these agents as pharmacologic adjuncts against the hemodynamic responses of intubation. Alfentanil has the fastest onset of action of all the opioids.

BETA BLOCKERS:

Esmolol is the only beta-blocker that could be used to prevent intubation response because it is beta-1 selective, possesses a rapid onset, and it has an ultrashort duration of action. Its onset of action is within seconds, and its elimination half-life is 9 minutes. It is used at a dose of 1 mg/kg administered as a simple bolus 2 minutes before laryngoscopy and intubation.

SODIUM CHANNEL BLOCKER:

Lignocaine blocks the Na+ channels in the cell membranes of the heart and reduces the rate of the rise of the action potential and the conduction velocity in the atrial, ventricular musculature and His purkinji system. Intravenous lignocaine blunts the rises in pulse, blood pressure, intracranial and intraocular pressure. The possible mechanism include a direct myocardial depressant effect, a peripheral vasodilating effect and finally an effect on synaptic transmission. A dose of prophylactic

lidocaine at dose of 1.5 mg/kg given intravenously 3 minutes before intubation is optimal.

Wang et al, reported most optimal time of administration of intravenous lidocaine to attenuate the increase of intraocular pressure seemed to be the space between 1-3 minutes before laryngoscopy and tracheal intubation.

Other ways of administering lignocaine to blunt intubation response include topical anaesthesia of oropharynx (viscous lignocaine), laryngotracheal instillation of lignocaine just prior to laryngoscopy and intubation. Topical lidocaine (e.g..,4% lignocaine spray) effectively reduces the cardiac responses to the laryngoscopy and intubation.

CALCIUM CHANNEL ANTAGONIST:

NICARDIPINE:

Nicardipine is a water soluble, dihydropyridine calcium channel antagonist with predominant vasodilatory action, used to attenuate the reflex increase in systolic BP, diastolic BP and MAP. It selectively acts on L- TYPE calcium channels in vascular smooth muscle. It can be administered orally and by intravenous route. It has got a rapid onset and offset of action. It is used at doses of 0.02 to 0.03mg/kg.

ALPHA AGONISTS: Alpha-2 agonists like clonidine and dexmedetomidine have been used recently for attenuation of sympathoadrenal stimulation caused by tracheal intubation and surgery.

CLONIDINE:

Clonidine, α2 adrenergic receptor agonist, has been studied as a premedication in a dose of 1-3 μg kg^{-1} due to its beneficial effect on the hyperdynamic response to endotracheal intubation. The hemodynamic effects of clonidine are both peripheral and central.

- Peripheral stimulation of subendothelial receptors causes vasoconstriction and on peripheral sympathetic nervous system nerve endings inhibit release of norepinephrine.

- Central action is by stimulating the α2 adrenergic inhibitory neurons in the vasomotor center of medulla. As a result, there is a decrease in the sympathetic nervous system outflow from central nervous system to peripheral tissues. Decreased sympathetic nervous system activity is manifested as peripheral vasodilatation and decrease in systemic blood pressure, HR, and cardiac output.

DEXMEDETOMIDINE:

Dexmedetomidine is a highly selective, α_2 receptor agonist having eight times high affinity and α_2 selectivity compared to clonidine and has a shorter duration of action than clonidine. It provides anxiolysis, co-operative sedation and analgesia without respiratory depression. The mechanism of action of dexmedetomidine differs from clonidine as it possesses selective alpha $_2$ -adrenoceptor agonism, especially for the 2A subtype of this receptor, which causes it to be a more effective sedative and analgesic agent than clonidine.

The hemodynamic effects of dexmedetomidine result from peripheral and central mechanism. Alpha $_2$ -adrenoreceptor agonists show a biphasic, dose-dependent, blood pressure effect. At low doses the dominant action of α_2 -adrenoreceptor agonist activation is a reduction in sympathetic tone, mediated by a reduction of norepinephrine release at the neuroeffector junction, and an inhibition of neurotransmission in sympathetic nerves. The net effect of dexmedetomidine is a significant reduction in the circulating catecholamines with a slight decrease in blood pressure and a modest reduction in heart rate.

Other drugs to blunt intubation response include vasodilators like hydralazine, sodium nitroprusside, nitroglycerine, deepening the inhalational anaesthetic..

Non-Pharmacologic Methods to Blunt Reflex Response include:

- Limiting the time of laryngoscopy and atraumatic laryngoscopy.
- Leaving the patient in upright position until the last possible moment, then intubate in 20 degrees head-up position.
- No-touch intubation with video-laryngoscopy by the best intubator.

INTUBATING CONDITIONS

5. INTUBATING CONDITIONS

Various scores have been used to grade the intubating conditions

Tracheal intubation was graded according to

- position of vocal cords,
- Coughing
- Ease of laryngoscopy
- Jaw relaxation
- Movement of limbs.

SCORE	1	2	3	4
Jaw relaxation	complete	Slight tone	stiff	Rigid
Laryngoscopy	Easy	Fair	difficult	Impossible
Position of vocal cords	Open	Moving	closing	Closed
Coughing	None	Slight	moderate	Severe
Limb movement	None	Slight	moderate	Severe

This is a modification of the scoring system described by Helbo-Hansen, Ravlo, and Trap Anderson. One attempt was allowed at laryngoscopy and assessment of all variables was made from this attempt.

Intubating conditions were judged as acceptable when all the scores were 2 or less. If any of the scores were 3/4 for any of the five variables. Intubating conditions were classified unfavourable.

COOPER SCORING SYSTEM:

Intubating conditions can also be assessed and graded using cooper scoring system.

Jaw relaxation	**Vocal cords**	**Response to intubation**	**score**
Poor (impossible)	Closed	Severe coughing /bucking	0
Minimal (difficult)	Closing	Mild cough	1
Moderate (fair)	Moving	Slight diaphragmatic movements	2
Good (easy)	Open	None	3

Intubating conditions		Intubating score
1.excellent	→	8 and 9
2. good	→	6 and 7
3. fair	→	3-5
4. poor	→	0-2

GCRP GUIDELINES:

VARIABLE	CLINICALLY ACCEPTABLE		CLINICALLY NOT ACCEPTABLE
	EXCELLENT	**GOOD**	**POOR**
1.LARYNGOSCOPY a.Jaw relaxation b.Resistance to laryngoscopy	 Relaxed None	 Not fully relaxed Slight	 Poor relaxation Active
2.VOCAL CORDS a.position b.movement	 Abducted none	 intermediate moving	 closed closing
RESISTANCE TO TUBE INSERTAION OR CUFF INFLATION a. Movement of limbs b. coughing	 None None	 Slight Slight	 Vigorous Sustained

INTUBATING CONDITIONS;

Excellent→all qualities are excellent.

Good →all qualities are good or excellent.

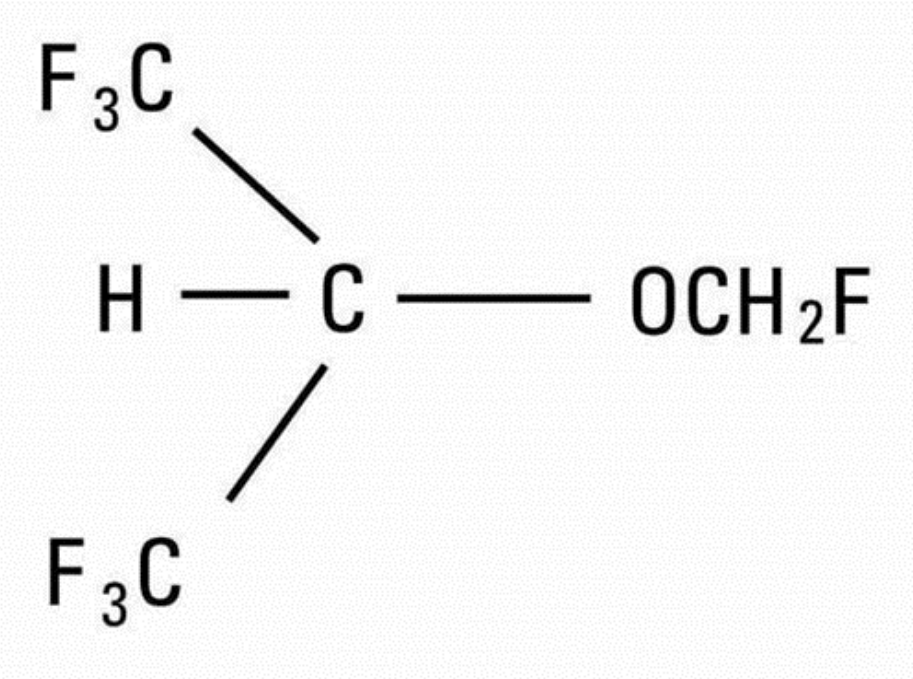
Poor → any quality is poor

PHARMACOLOGY OF SEVOFLURANE

6. PHARMACOLOGY OF SEVOFLURANE

Sevoflurane is a halogenated inhalational agent, which is non-flammable and pleasant smelling. The first reports of this agent appeared in the early 1970's.

STRUCTURE



It is 1, 1, 1, 3, 3 –Hexafluromethoxypropane. Sevoflurane does not contain an asymmetric carbon atom and therefore does not exist as optical isomers. In this aspect it is unique amongst currently available inhaled anaesthetics.

PHYSICAL PROPERTIES:

Molecular weight	:	200.05
Boiling point at 760mm hg	:	58.6 °c
Specific gravity at 20 °c	:	1.520 – 1.525
Vapour pressure at 200 °c	:	157
Blood/ gas partition co-efficient	:	0.63 – 0.69

The blood gas partition co-efficient is substantially lower than other agents. It is not irritant to the upper airways and produces bronchodilatation and causes the least degree of airway irritation among currently available volatile anaesthetics and so suitable for gaseous induction. It is stable without additives for over years at 45 °c in amber bottles with polyethylene- lined caps.

THE MINIMUM ALVEOLAR CONCENTRATION AND THE EFFECT OF AGE ON THE MAC OF SEVOFLURANE:

The minimum alveolar concentration (MAC) is defined as the partial pressure (alveolar concentration at 1 atm) that produces immobility in 50% of patients exposed to noxious supramaximal stimuli. Since the definition of MAC incorporates the condition of a barometric

pressure of one atmosphere, the value of MAC also does not change with changes in barometric pressure. MAC is also used as an index of comparision of potency between two anaethetic agents. The higher the MAC, the lower is the potency.

METABOLISM

About 3-5% of absorbed sevoflurane undergoes oxidative metabolism by cytochrome P-450 enzymes to form organic and inorganic fluoride metabolic. [In addition, sevoflurane is degraded by strong bases present in the absorbents to potentially toxic compounds].the resulting metabolites include inorganic fluorides and hexo fluro iso propranol. The chemical structure is such that it cannot undergo metabolism to an acyl halide that could result in formation of trifluroacetylated liver proteins. So it does not stimulate the formation of anti fluoro acetylated protein antibodies leading to hepatotoxicity. Despite higher peak plasma fluoride concentrations compared with enflurane, prolonged sevoflurane anaesthesia does not impair renal concentrating function. This is because intrarenal production of inorganic fluoride is a more important factor for nephrotoxicity than hepatic production. Methoxyflurane and enflurane undergoes greater intrarenal metabolism to fluoride than sevoflurane which undergoes greater hepatic metabolism.

PHARMACODYNAMICS

CENTRAL NERVOUS SYSTEM EFFECTS

- 1. Electro encephalogram: sevoflurane in concentration of <0.4 MAC increases frequency and voltage on EEG. Above 0.4 MAC, the cerebral metabolic oxygen requirements(CMRO2) is decreased which produces decreased frequency on EEG. At 1 MAC, the frequency of EEG decreases and maximum voltage occurs. Burst suppression occurs at 1.5 and 2 MAC, electrical silence predominates.

- Evoked potentials: sevoflurane causes dose related decrease in amplitude and increase in latency of cortical component of somatosensory, visual and auditory evoked potentials.

- Cerebral blood flow: all volatile anaesthetics during normocapnia and in concentrations of 0.6 MAC produce cerebral vasodilation, decreased cerebral vascular resistance and dose dependent increase in CBF despite concominant decrease in CMRO2. This increase in CBF is greatest with halothane and least with sevoflurane. Sevoflurane is only a mild cerebral vasodilator with little impairment of autoregulation. Reactivity

of the cerebral circulation to co2 is preserved or enhanced. By decreasing the CMRO2 and thereby co2 production sevoflurane opposes any increase in cerebral blood flow.

- Cerebral metabolic oxygen requirements: sevoflurane in concentrations above 0.4 MAC decreases the CMRO2 in a dose dependent manner. When the EEG becomes isoelectric, an additional increase in the concentration of the volatile anaesthetic does not produce further decrease in CMRO2.

- Cerebral protection: animal studies have demonstrated the neuroprotective effects of sevoflurane. In humans undergoing carotid endarterectomy, the CBF at which ischaemic changes appear on EEG is lower during sevoflurane than other volatile anaesthetics. Unchanged CBF and decreased cerebral metabolic oxygen requirements during sevoflurane induced controlled hypotension for cerebral aneurysms clipping indicate that global oxygen supply-demand is favourably altered in patients anaesthetised with sevoflurane.

- Intracranial pressure: sevoflurane perse produces mild cerebral vasodilation in normocapnic patients. Sevoflurane enhances the reactivity of cerebral circulation to changes in arterial partial

pressure of carbondioxide. So hyperventilation of lungs to decrease the paco2 to about 25mmHg produces cerebral vasoconstriction and thus decreases the ICP. But below paco2 0f 20mmHg, there is no further decrease in ICP and metabolic signs of cerebral ischemia occurs.

CARDIOVASCULAR EFFECTS:

Sevoflurane produces minor decrease in cardiac contractility and cardiac output. There is a moderate decrease in systemic vascular resistance and so the mean arterial pressure. The decrease in MAP is not accompanied by any changes in the heart rate. Renal and hepatic blood flow are very well maintained with sevoflurane. Studies on the use of sevoflurane in patients with pheochromocytoma indicate that it does not sensitize the myocardium to the effects of catecholamines. Unlike isoflurane, sevoflurane do not produce coronary artery vasodilation that could lead to coronary steal syndrome.

RESPIRATORY EFFECTS:

Although all potent inhaled anaesthetics are ventilatory depressants and sevoflurane is no exception to this, it has been suggested that this propyl ether causes less increase in the respiratory rate with a large tidal

volume and longer inspiratory and expiratory times. Thus the cardiorespiratory profile of sevoflurane proves to be the most benign of all halogenated anaesthetics. Sevoflurane is non-irritant to the upper airways and does not increase airway resistance and so is suitable for inhalational induction. After tracheal intubation, in patients without bronchial asthma, sevoflurane decreases airway resistance as much or more than isoflurane or halothane.

HEPATIC EFFECTS:

Unlike other volatile anaesthetics, hepatic blood flow is well maintained during administration of sevoflurane. Maintanence of hepatic oxygen delivery relative to demand during exposure to sevoflurane is uniquely important in view of the evidence that hepatocytic hypoxia is a significant mechanism in the multifactorial etiology of postoperative hepatic dysfunction. Current evidence indicates that neither sevoflurane nor its degradation products produce hepatic injury.

Sevoflurane is well tolerated when used in patients with impaired hepatic function. Sevoflurane metabolism does not produce trifluroacetylated liver proteins and so sevoflurane do not produce immune mediated hepatotoxicity and also do not cause cross sensitivity in patients previously exposed to halothane.

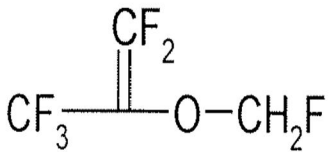
RENAL EFFECTS:

Despite mild decrease in MAP, the renal blood flow is well preserved with sevoflurane. Adequate preoperative hydration abolishes many of the changes in renal function associated with sevoflurane. No degradation of renal function has been found with sevoflurane in renal impaired patients, in elderly patients and those exposed to the drug for greater than 3 hours.

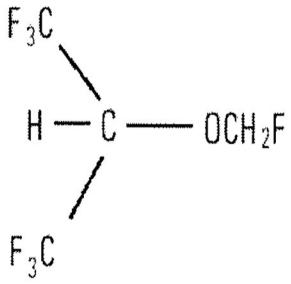
COMPOUND A:

Carbondioxide absorbants (sodalime, barylime) reacts with sevoflurane and eliminate hydrogen fluoride from its isopropyl moiety to form breakdown products.

The degradation product in greatest amounts is compound A. Compound A is a dose dependent nephrotoxin producing proximal renal tubular injury. In patients undergoing surgeries under sevoflurane anaesthesia for more than 5 hours, the average concentration of compound A in the circuit was less than 20PPM and there was no evidence of renal dysfunction.



Compound A



Sevoflurane

Higher concentrations of compound A occur in

1. Presence of barylime probably due to higher absorbent temperature.

2. Increased minute ventilation and

It is recommended to use atleast 2 litres /min fresh gas flow to minimise the concentration of compound A that may accumulate.

The proposed mechanism for nephrotoxicity is metabolism of compound A via the beta-lyase are pathway to a reactive thiol. Because humans have less than one tenth of the enzymatic activity compared to rats, humans are less vulnerable to injury by this mechanism.

SKELETAL MUSCLE EFFECTS:

Sevoflurane produces skeletal muscle relaxation that is about twofold greater than associated with a comparable dose of halothane. Sevoflurane produces dose dependent enhancement of the effects of neuromuscular blocking drugs.

MALIGNANT HYPERTHERMIA:

All volatile anaesthetics including sevoflurane can trigger malignant hyperthermia in genetically susceptible patients. It is inherited as autosomal dominant with incomplete penetrance and generation skipping due to defect in the gene responsible for calcium channels on chromosome 19.

OBSTETRIC EFFECTS:

Sevoflurane produces dose dependent decrease in contractility and blood flow of uterus. These changes are modest at 0.5MAC and become substantial at concentrations of greater than 1MAC. Thus it may be helpful to facilitate removal of retained placenta but has the adverse effect of profound blood loss due to uterine atony.

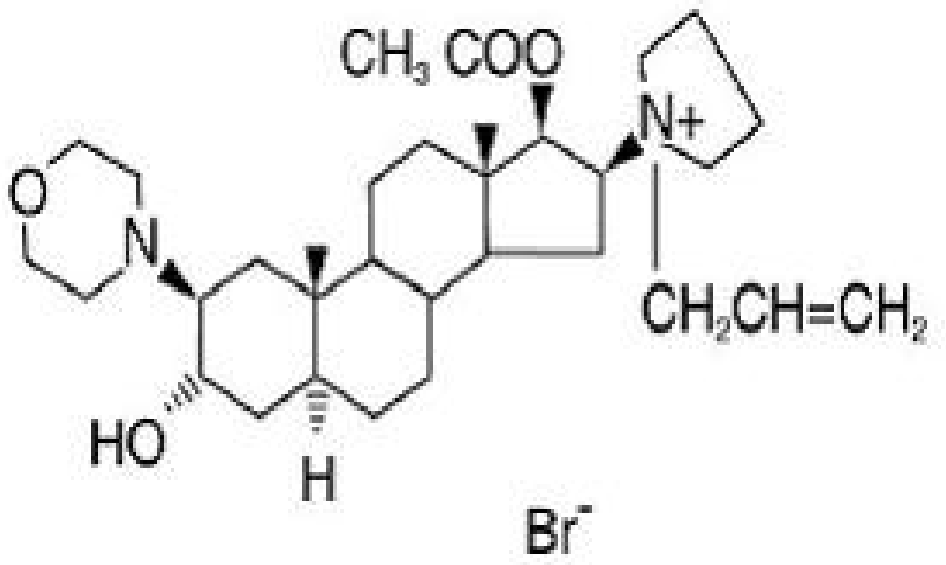
GENETIC EFFECTS:

Compound A formed from sevoflurane degradation might be expected to be an alkylating agent but Ames test which identifies for mutagenecity or carcinogenicity is negative for sevoflurane and also for compound A.

PHARMACOLOGY OF ROCURONIUM

7. PHARMACOLOGY OF ROCURONIUM

Rocuronium bromide, [C32H53BrN2O4] is an aminosteroid non-depolarising neuromuscular blocking agent which is an analogue of the drug vecuronium.



PHYSICAL PROPERTIES:

- Off-white to pale yellow or slightly pink amorphous powder
- soluble in water
- pH 8.9 -9.5.
- In aqueous solutions rocuronium is more stable at acidic pH.

PHARMACOLOGY

Pharmacodynamics

Rocuronium is a non-depolarising neuromuscular blocking agent which acts by competing with acetylcholine and blocks the nicotinic acetylcholine receptors (nAch) located at the motor end-plate of the muscle.It has got a faster onset and intermediate duration of action. Neuromuscular blocking effect occurs only when 80% to 90% of the receptors are blocked. Neostigmine, edrophonium and pyridostigmine are the acetylcholinesterase inhibitors which antagonises the action of rocuronium. The neuromuscular block can also be reversed by sugammadex, a Selective Relaxant Binding Agent. There is no such clinically significant autonomic and cardiovascular effects within the recommended dose range for rocuronium.

The ED90 (dose required to produce 90% depression of the twitch response of the thumb to stimulation of the ulnar nerve) during balanced anaesthesia is approximately 0.3mg.kg-1.

ED95 dose:

Infants - 0.25mg/kg

Children - 0.4mg/kg

Adults - 0.35mg/kg

Duration of action at dose of 0.6mg/kg - 30 to 40mins.

Pharmacokinetics

i.v administration of a bolus dose of rocuronium, the plasma concentration runs in three exponential phases

- elimination half-life is 66-80 minutes
- the volume of distribution is 193-214 mL/kg
- plasma clearance is 3.5 - 3.9 mL/ kg/ min.

It is excreted via renal and biliary system

INDICATIONS:

- Rocuronium is used as an adjunct to general anaesthesia to facilitate endotracheal intubation during routine induction, to provide muscle relaxation in adults, children and infants over 1 month of age.
- Rocuronium is also indicated as an adjunct to general anaesthesia to facilitate endotracheal intubation during rapid sequence induction(RSI) when suxamethonium is contraindicated.

- Rocuronium is also indicated as an adjunct in the intensive care unit (ICU) to facilitate mechanical ventilation.

DOSAGE:

Standard tracheal intubation	:	0.6mg/kg
Rapid sequence induction	:	1.0mg/kg
Maintenance dose	:	0.15mg/kg
Continuous infusion	:	0.3-0.6mg/kg

CONTRAINDICATIONS:

When there is suspicious of hypersensitivity reactions

PRECAUTIONS

- History of previous anaphylactic reactions to rocuronium.

Since rocuronium causes paralysis of the respiratory muscles, ventilatory support is mandatory for patients treated with this drug. Ventilation should be continued until adequate spontaneous respiration is restored. As with all neuromuscular blocking agents, it is important to anticipate intubation difficulties, particularly when used as part of a rapid sequence induction technique. In case of intubation difficulties resulting

in a clinical need for immediate reversal of a rocuronium induced neuromuscular block, the use of sugammadex should be considered. As with other neuromuscular blocking agents, residual curarization has been reported for rocuronium. Geriatric patients (65 years or older) may be at increased risk for residual neuromuscular block.. Anaphylactic reactions can occur following the administration of rocuronium.

Following long term use of neuromuscular blocking agents in the ICU, prolonged paralysis and skeletal muscle weakness has been noted and hence neuromuscular transmission is monitored throughout the use of neuromuscular blocking agents.

- Myopathy after long term administration of other non-depolarizing neuromuscular blocking agents in the ICU in combination with corticosteroid therapy has been reported regularly. Therefore the period of use of the neuromuscular blocking agent should be limited as much as possible.

- If suxamethonium is used for intubation, the administration of rocuronium should be delayed until the patient has clinically recovered from the neuromuscular block induced by suxamethonium.

Prolonged use (> 48 hours) of non-depolarising muscle relaxants in the ICU should be avoided .Patients with multiple organ failure require lower infusion rates.

Infants: Mean onset time and duration of relaxation in infants and children is shorter than in adults.

Hepatic and renal diseases: rocuronium should be cautiously used in hepatic and renal failure patients since the drug is excreted in urine and bile.

Conditions like congestive cardiac failure, ascites, old age results in an increased volume of distribution and hence contribute to a slower onset of action of rocuronium. The duration of action is also prolonged.

Neuromuscular Disease: rocuronium should be used cautiosly in patients with history of neuromuscular disease or polio patient since the response to neuromuscular blocking agents may be altered in these cases.. In myasthenic patients or with Eaton-Lambert syndrome, clinically used dose of rocuronium may have increased effects.

Hypothermia: In surgery with hypothermic conditions, the neuromuscular blocking effect is increased and the duration prolonged.

Obesity:, rocuronium may cause a prolonged duration of action and a prolonged spontaneous recovery in obese patients.

Burns: burns patients are known for developing resistance to NDMR'S.

Conditions which may increase the effects of rocuronium

- Decreased serum potassium (e.g. after severe vomiting, diarrhoea)
- Decreased serum calcium (after massive transfusion)
- Increased serum magnesium.
- Reduced levels of serum protein,
- Dehydration,
- Acidosis,

Use in pregnancy and lactation: rocuronium is not proven teratogenic in humans and is not proven to excrete in the milk of lactating mothers.

Interactions with other drugs

Increased effect

1. Halogenated volatiles are known to potentiate the neuromuscular block of rocuronium

2. After intubation with suxamethonium

3. Long-term use of corticosteroids and rocuronium

Reduced effect:

Prior administration of corticosteroids, antiepileptics.

ADVERSE REACTIONS

The most frequently occuring serious adverse drug reactions is anaphylactic and anaphylactoid reactions. The other frequently occurring adverse reactions are tachycardia, hypotension, pain at the injection site, prolonged neuromuscular block and rarely bronchospasm.

REVIEW OF LITERATURE

8. REVIEW OF LITERATURE

- In the year 1992, Huizinga AC, Vandenbrom RH, Wieda JM, Hommes FD, Hennis PJ, et al, conducted the study of the intubating conditions and onset of neuromuscular blockade of rocuronium and compared it with suxamethonium in which they found that rocuronium (0.6mg/kg) produced good to excellent intubating conditions at 60sec and as well as 90sec when compared to suxamethonium (1.5m/kg).

- In the year 1992, "Cooper R, Mirakhur RK, Clarke RS, Boules Z", et al, studied "the comparision of intubating conditions after administration of rocuronium and suxamethonium". This study was conducted in fourty patients divided into 2 groups

  Group A: patients receive rocuronium(0.8mg/kg) as the muscle relaxant.

  Group B: patients receive suxamethonium(1mg/kg) as the muscle relaxant.

They found that the intubating conditions after rocuronium administration were found to be clinically acceptable (good and

excellent) in 95%patients at 60sec and in all patients at 90sec and in all patients at both times after suxamethonium.

- In the year 1995, Dubois MY, Lea DE, Kataria B, Gadde PL, Tran DQ, Shearrow T, et al, studied the pharmacodynamics of rocuronium with and without prior administration of suxamethonium. This study was conducted in 24patients. They concluded that rapid intubating conditions can be obtained after both suxamethonium and rocuronium administration.

- In the year 1998, Magorian T, Flannery KB, MillerRD, et al, studied the comparision of rocuronium, suxamethonium and vecuronium for rapid sequence induction in adult patients. This study was conducted in 50patients who were randomly designated to receive 3 i.v dose of rocuronium (0.6mg/kg, 0.9mg/kg,1.2mg/kg), vecuronium(0.1mg/kg) and suxamethonium (1mg/kg). The onset time of intubation for patients receiving 0.9mg/kg, 1.2mg/kg of rocuronium and suxamethonium are similar whereas onset time for groups 0.6mg/kg of rocuronium and vecuronium were significantly longer.

- In the year 1998, Mc court KC, Salmela L, Mirakhur RK, Carrroll M, Makinen MT, et al, studied the comparison of

rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. This study was conducted in 50 patients who received inj.rocuronium (0.6mg/kg and 1mg/kg) and suxamethonium1mg/kg. They concluded that the intubating conditions were excellent with rocuronium1mg/kg and suxamethonium 1mg/kg when compared to rocuronium 0.6mg/kg.

- In the year 1998, Lowry DW, Mirakhur RK, Mc carthey GJ, Carroll MT, et al, studied the neuromuscular effects of rocuronium during sevoflurane, isoflurane and I.V anaesthesia. They found that the effects of rocuronium are enhanced by sevoflurane in comparision with isoflurane and propofol anaesthesia.

- In the year 1998, Shorten GD, Uppington J, comunale ME studied the changes in plasma catecholamine concentration and hemodynamic effects of rocuronium and vecuronium in elderly patients. This study was conducted in 30 patients of 65yrs and more who were not on beta blockers. They found out that no significant change in plasma adrenaline or nor-adrenaline concentration in both groups. The use of rocuronium (0.9mg/kg)

does not cause clinically significant change in heart rate, blood pressure and plasma catecholamine concentrations.

- In the year 2002, Yavascoglu B, Cebelli V, Kelebek N, Uckunkaya N, Kutlay O, et al, syudied the comparision of different priming techniques on the onset time and intubating comditions of rocuronium in 75 patients divided into 5 groups.

  Group 1: patients receive a priming dose of rocuronium (0.06mg/kg) followed 2min later by rocuronium (0.5mg/kg)

  Group 2: patients receive a priming dose of 0.1mg/kg followed 2min later by roc (0.5mg/kg)

  Group 3: patients receive a priming dose of roc (0.06mg/kg) followed 3min later by roc(0.5mg/kg)

  Group 4: patients receive a priming dose of roc (0.1mg/kg) followed 3min later by roc (0.5mg/kg)

  Group 5: patients receive placebo injection followed 3min later by roc (0.6mg/kg) They found that the priming with 3min interval shortened the onset time of rocuronium irrespective of the dosage. Clinically acceptable intubating conditions were observed in all patients.

- In the year 2004, Singh A, Bhatia PK, Tulsiani KL studied the comparision of onset time, duration of action and intubating conditions achieved with suxamethonium and rocuronium.

- In the year 2005, Misra MN, Agarwal M, Pandey RP, Gupta A, et al, conducted the comparative study of rocuronium, vecuronium and succinylcholine for rapid sequence intubation.

- In the year 2010, Shobhana Gupta, R Kirubahar, et al, conducted the comparative study of intubating conditions of rocuronium bromide and succinyl choline in adult patients. This study was conducted in thirty patients divided into two groups.

  Group A:patients receive rocuronium (0.6mg/kg)

  Group B: patients receive suxamethonium (1.5mg/kg).

  They found that the intubating conditions were rated as excellent in 90% and good in 10% of patients who receive rocuronium and excellent in 100% of patients who receive suxamethonium.

- In the year 2011, Moazzam Md, Shahnawaz, Bano shahjahan, Sidddiqui suhail, Sarwar, et al, studied the evaluation of intubating conditions after rocuronium bromide in adults

induced with propofol or thiopentone sodium. This study was conducted in sixty patients divided into 2 groups.

Group PR: patients receive propofol2.5mg/kg and rocuronium (0.6mg/kg)

Group TR: patients receive thiopentone 5mg/kg and rocuronium (0.6mg/kg)

They concluded that the clinical intubating conditions after rocuronium bromide (0.6mg/kg) in adults anaesthetised with propofol or thiopentone are same.

- In the year 2011, Hanumanthan Rao H, Andal venkatraman, Malleswari R, et al, studied the comparision of intubating conditions between rocuronium with priming and with out priming in 60 patients divided into two groups.

  Group C: control group

  Group P : patients receive priming dose of roc(0.1mg/kg) and found that the onset time of intubation was earlier in priming group with excellent intubating conditions in both groups.

MATERIALS & METHODS

9. MATERIALS AND METHODS

After getting the Approval of Institutional Ethics Commmitee, informed consent from the patients, this study was done in 60 patients coming under American Society of Anaesthesiology- 1, and ASA- 2 of either male or female and aged between 18-65yr, who undergo elective craniotomy surgery in the Institute of neurosurgery in Madras Medical College hospital.

The study was conducted in Rajiv Gandhi Government General Hospital, Madras Medical College. The patients were randomised into two groups of 30 patients each by closed envelope method.The patients were blinded to the group they belong.

STUDY DESIGN: The study was a prospective, randomised, double blinded, compatative study.

SELECTION OF CASES:

- GROUP RS: Anaesthesia was induced with propofol (2mg/kg) and 2% sevoflurane and intubated with rocuronium (0.8mg/kg). Anaesthesia was maintained with 1 MAC sevoflurane.

- GROUP R: Anaesthesia was induced with propofol (2mg/kg) and intubated with rocuronium (0.8mg/kg). anaesthesia maintained with 1 MAC sevoflurane.

DURATION OF STUDY : FOUR MONTHS

INCLUSION CRITERIA:

- Age : patient between 18-65 years of age
- ASA : I,II
- Surgery : Elective Craniotomy procedures
- Who have given valid informed consent.
- Patient having GCS 15/15
- Patients with normal haematological and biochemical parameters.

EXCLUSION CRITERIA:

- Not satisfying inclusion criteria
- Patients posted for emergency surgeries
- Lack of written informed consent

- Patients with anticipated difficult airway and intubation
- Patients with history of neuromuscular diseases
- Pregnancy patients
- Breastfeeding patients
- Patients receiving drugs which interfere with neuromuscular function

Materials:

- IV cannula 18G, 16G
- Drugs–Inj.GLYCO, inj.RANITIDINE, inj.EMESET, inj.PROPOFOL, inj.FENTANYL, inj.ROCURONIUM, SEVOFLURANE and emergency drugs.
- Monitors – ECG, NIBP, SPO_2, $EtCO_2$ neuromuscular monitor, agent analyser
- 2ml syringe, 5ml syringe, 10ml syringe

PARAMETERS OBSERVED

PRIMARY OUTCOME MEASURES :

- Onset time of paralysis with TOF stimuli
- Intubating conditions by using Cooper scoring system

SECONDARY OUTCOME MEASURES:

- Heart rate, systolic blood pressure, diastolic blood pressure and MAP measurements.

ANAESTHESIA PROTOCOL

The patients satisfying the above mentioned criteria were detailed about the study, procedure,advantages and side effects.

- Informed written consent was obtained from all the patients.
- They were thoroughly investigated and assessed before surgery.For all patients,age,height and weight are noted.
- Patients shifted inside OT.
- Monitors like ECG, pulse oximeter, NIBP, TOF monitor were connected. All the vital parameters like Heart rate,Systolic Blood

Pressure,Diastolic Blood Pressure, Mean Arterial Pressure and baseline TOF ratio were recorded pre operatively.

- Intravenous access obtained.
- Intravenous fluids preferentially RL was started at rate of 250 ml/hr.
- The patients are pre-medicated with inj. ranitidine 50 mg, inj.emeset 4mg, inj.midaz 0.01 mg/kg, inj.glycopyrrolate 10mcg/kg and inj.fentanyl 2 μg/kg
- Patients were pre-oxygenated with 100% oxygen.
- Group RS patients were induced with propofol (2mg/kg) and 2%(1 MAC) sevoflurane.
- Group R patients were induced with propofol (2mg/kg)
- After loss of verbal response, supramaximal stimuli applied to the ulnar nerve and baseline train of four ratio noted.
- Intubating dose of rocuronium (0.8mg/kg) was given.

- Supramaximal train of four stimuli applied again and repeated every 15sec to assess for loss of thumb adduction and loss of T1 of TOF stimuli.

- Onset time of paralysis is calculated which is the time between intubating dose of rocuronium to loss of T1 of TOF stimuli.

- Intubation was carried by well experienced anaesthesiologist.

- Intubating conditions were assessed and graded using cooper scoring system.

- Intraop vitals like heart rate, systolic blood pressure, diastolic blood pressure and MAP were recorded before induction, and also at 0min, 1min and 3min after induction and noted.

- Anaesthesia was maintained with 1 MAC value of Sevoflurane in 30% 0_2& 70% N_20. Patients were ventilated to obtain $PaCO_2$ values between 25-30mmHg.

- Mannitol (0.5-1g/Kg IV) was administered to avoid rise in ICP. Patients with Intracranial Tumours were also given 10mg of Dexamethasone IV.

- At the end of surgery, after adequate neuromuscular recovery, patient was reversed with Inj.Glycopyrrolate(0.005mg/kg) and Inj.Neostigmine(40mcg/kg) . Then Patients were extubated.

OBSERVATION, RESULTS AND ANALYSIS

10. OBSERVATION, RESULTS AND ANALYSIS

STATISTICAL ANALYSIS:

The patients in this study were divided into two groups consisting of thirty patients each.

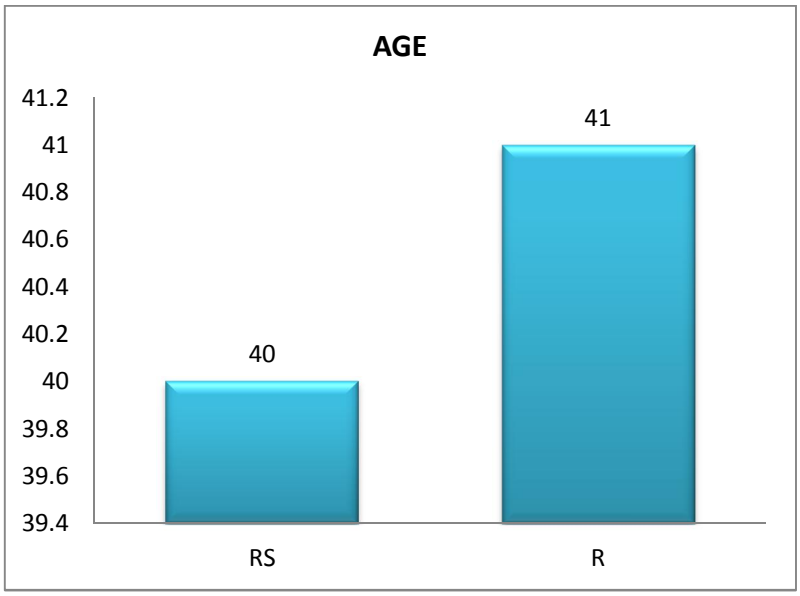
Group RS – patients who receive 2%sevoflurane and rocuronium.

Group R - patients who receive rocuronium.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the unpaired sample t-test was used. To find the significance in categorical data Chi-Square test and Fisher's Exact test was used. In both the above statistical tools the probability value .05 is considered as significant level.

Demographic variables:

AGE:



GROUP STATISTICS

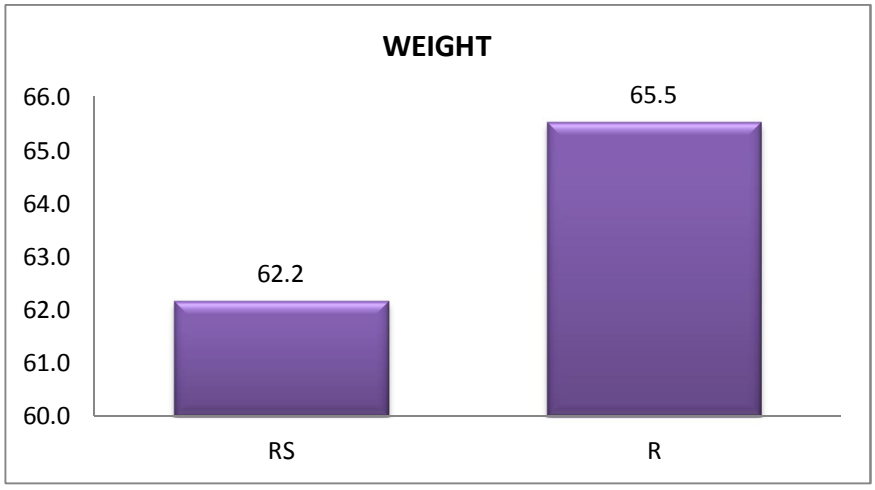
Groups	N	Mean	Std. Deviation	Std. Error Mean	P Value
RS	30	40.40	10.934	1.996	0.82
R	30	41.03	10.785	1.969	

INDEPENDENT SAMPLE TEST

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Diffe-rence	Std. Error Diffe-rence	95% Confidence Interval of the Difference	
									Lower	Upper
AGE	Equal variances assumed	.049	.825	-.226	58	.822	-.633	2.804	-6.246	4.979
	Equal variances not assumed			-.226	57.989	.822	-.633	2.804	-6.246	4.979

The mean age in group RS is 40.4 years and in group R is 41 yrs. The two groups were similar with respect to age distribution; the difference was statistically insignificant.

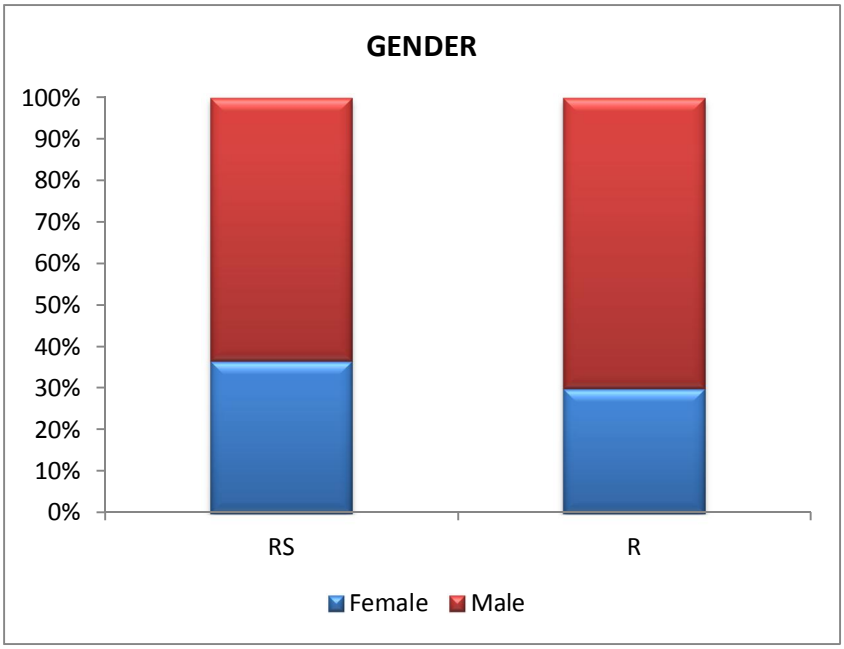
WEIGHT



Group		N	MEAN	SD	Std ER mean	P value
WT	RS	30	62.17	9.355	1.708	0.029
	R	30	65.53	11.101	2.027	

The mean weight in the group RS was 62.1 kgs and in the group R was 65.5 kgs. There was no statistically significant difference among the two groups with respect to weight distribution.

GENDER:



CROSS TABLE

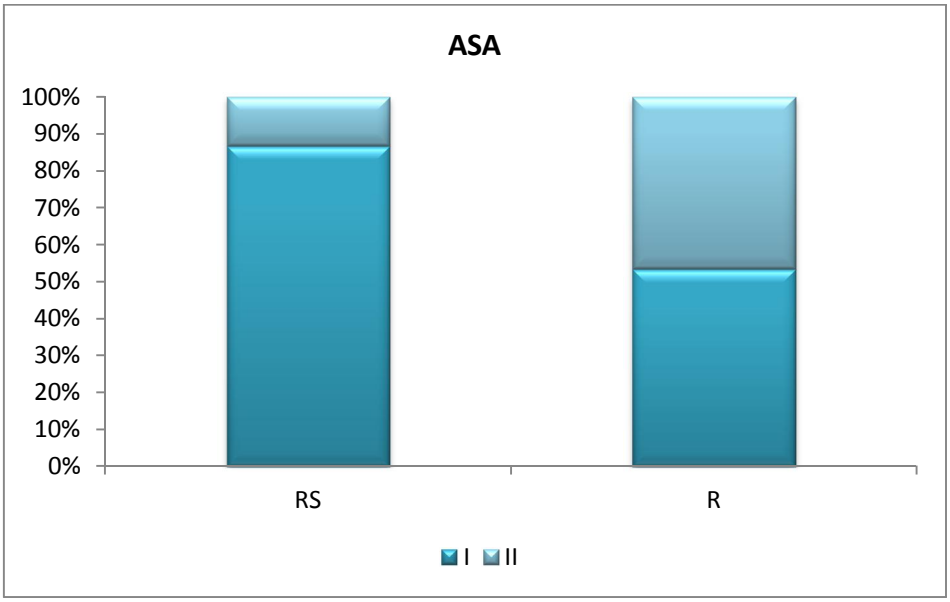
			Groups		
			RS	R	Total
SEX	F	Count	11	9	20
		% within Groups	36.7%	30.0%	33.3%
	M	Count	19	21	40
		% within Groups	63.3%	70.0%	66.7%
Total		Count	30	30	60
		% within Groups	100.0%	100.0%	100.0%

CHI- SQUARE TEST

	Value	**df**	**Asymp. Sig. (2-sided)**	**Exact Sig. (2-sided)**	**Exact Sig. (1-sided)**
Pearson Chi-Square	.300[a]	1	.584		
Continuity Correction[b]	.075	1	.784		
Likelihood Ratio	.300	1	.584		
Fisher's Exact Test				.785	.392
N of Valid Cases	60				

As p value is 0.584(>0.05), there is no statistically significant difference among the two groups regarding gender distribution.

ASA STATUS:



CROSS TABLE

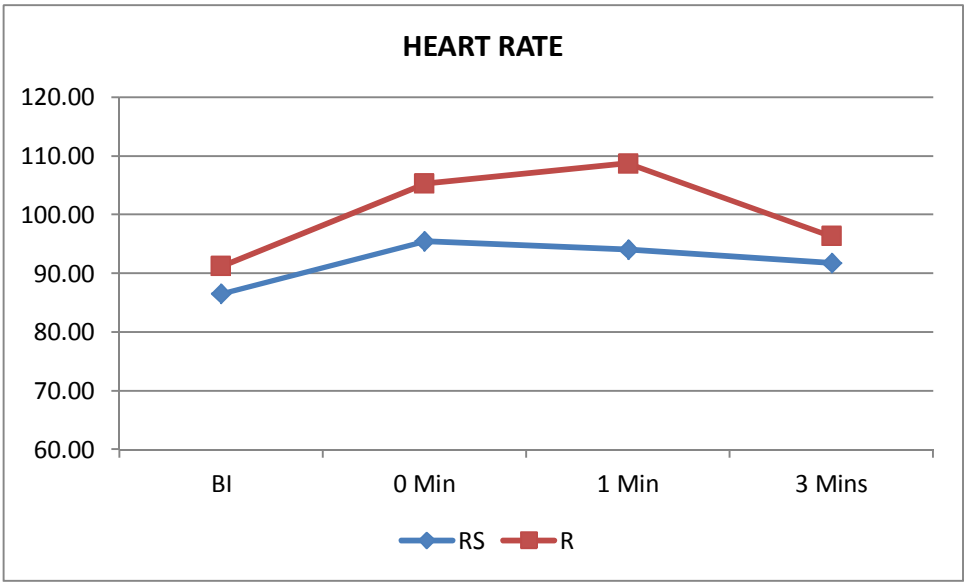
			Groups		Total
			RS	R	
ASA	I	Count	26	16	42
		% within Groups	86.7%	53.3%	70.0%
	II	Count	4	14	18
		% within Groups	13.3%	46.7%	30.0%
Total		Count	30	30	60
		% within Groups	100.0%	100.0%	100.0%

CHI-SQUARE TEST

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.937[a]	1	.005		
Continuity Correction[b]	6.429	1	.011		
Likelihood Ratio	8.288	1	.004		
Fisher's Exact Test				.060	.005
N of Valid Cases	60				

As the p value is 0.06(>0.05), there is no statistical significant difference among the two groups with respect to ASA status.

HEART RATE:



GROUP STATISTICS

Group		N	mean	SD	Std Er.mean
HR BI	RS	30	86.53	3.617	.660
	R	30	91.23	11.389	2.079
HR 0 min	RS	30	95.47	4.869	.889
	R	30	105.27	10.586	1.933
HR 1 min	RS	30	94.07	4.346	.794
	R	30	108.73	7.492	1.368
HR 3 min	RS	30	91.77	4.232	.773
	R	30	96.33	7.448	1.360

INDEPENDENT SAMPLE TEST

		Levene s test for Equality of variables		t-Test for Equality of Means						
		F	SIG	t	df	Sig [2 tailed]	Mean differrence	Std error of differ-ence	95% confidence Interval of the Difference	
									Lower	Upper
HR BI	Equal variances assumed	19.889	.000	-2.154	58	.035	-4.700	2.182	-9.067	-.333
	Equal variances not assumed			-2.154	34.792	.038	-4.700	2.182	-9.130	-.270
HR 0 min	Equal variances assumed	17.655	.000	-4.607	58	.000	-9.800	2.127	-14.058	-5.542
	Equal variances not assumed			-4.607	40.744	.000	-9.800	2.127	-14.097	-5.503
HR 1 min	Equal variances assumed	7.583	.008	-9.274	58	.000	-14.667	1.581	-17.832	-11.501
	Equal variances not assumed			-9.274	46.534	.000	-14.667	1.581	-17.849	-11.484
HR 3 min	Equal variances assumed	3.317	.074	-2.920	58	.005	-4.567	1.564	-7.697	-1.436
	Equal variances not assumed			-2.920	45.958	.005	-4.567	1.564	-7.715	-1.418

- The mean heart rate before induction in the group RS is 86.53 beats per minute and in the group R is 91.23 beats per minute.

- The mean heart rate at 0min (immediately after induction) in the group RS is 95.47 beats per minute compared to 105.27 beats per minute in the group R.

- The mean heart rate at 1minute after induction in the group RS is 94.07 beats per minute compared to 108.73 beats per minute in the group R.

- The mean heart rate 3 minutes after induction in the group RS is 91.77 beats per minute compared to 96.77 beats per minute in the group R.

STATISTICAL SIGNIFICANCE:

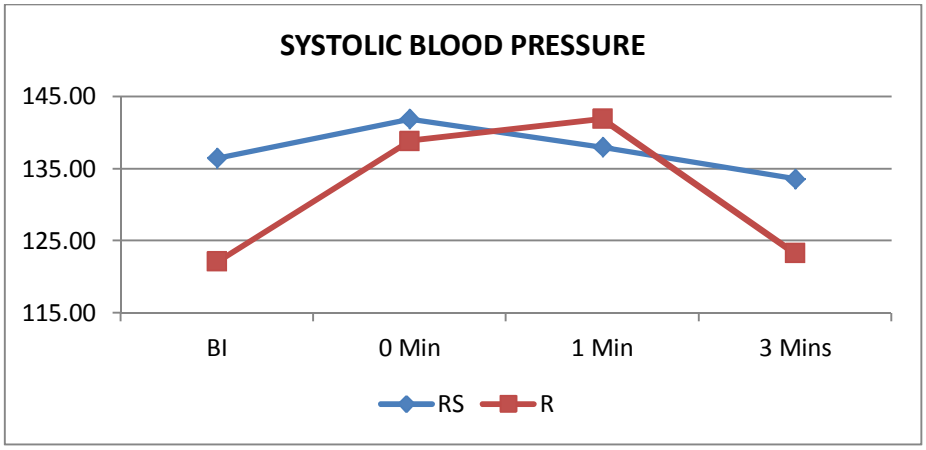
- The mean heart rate before induction is decreased by 4.70 beats per minute in the group RS compared to the group R with p value of 0.06 and hence considered to be statistically insignificant.

- The mean heart rate at 0min after induction is decreased by 9.8 beats per minute in the group RS compared to the group R with p value of 0.001 and hence considered to be statistically significant.

- The mean heart rate 1minute after induction is decreased by 14.69 beats per minute in the group RS compared to the group R with p value of 0.00 and hence considered to be statistically significant.

- The mean heart rate 3 minute after induction is decreased by 5.0 beats per minute in the group RS compared to group R with p value of 0.005 and hence considered to be statistically significant.

SYSTOLIC BLOOD PRESSURE:



GROUP STATISTICS

GROUP		N	Mean	SD	Std error of Mean
S BI	RS	30	122.13	4.462	.815
	R	30	136.50	13.567	2.477
S 0 min	RS	30	138.83	4.071	.743
	R	30	141.90	10.306	1.882
S 1 min	RS	30	138.80	3.851	.703
	R	30	141.90	8.310	1.517
S 3 min	RS	30	123.27	3.616	.660
	R	30	133.6	10.007	1.827

INDEPENDENT SAMPLE TEST

		Levenes test for equality of variances		t-Test for equality of Means						
		F	Sig	t	df	Sig(2 tailed)	Mean difference	Std error of difference	95% Confidence interval of the difference	
S BI	Equal variances assumed	28.442	.000	5.510	58	.000	14.367	2.607	9.147	19.586
	Equal variances not assumed			5.510	35.203	.000	14.367	2.607	9.074	19.659
S 0 min	Equal variances assumed	15.778	.000	1.516	58	.0135	3.067	2.023	-.983	7.116
	Equal variances not assumed			1.516	37.836	.0138	3.067	2.023	-1.029	7.163
S 1 min	Equal variances assumed	11.405	.001	-2.332	58	.023	-3.900	1.672	-7.247	-.553
	Equal variances not assumed			-2.332	40.904	.025	-3.900	1.672	-7.277	-.523
S 3 min	Equal variances assumed	23.700	.000	5.319	58	.000	10.333	1.943	6.445	14.222
	Equal variances not assumed			5.319	36.447	.000	10.333	1.943	6.395	14.271

- The mean systolic blood pressure before induction in the group R is 136.50mm Hg and 122.13mmHg in the group RS.

- The mean systolic blood pressure 0 minute after induction in the group R is 141.90mm Hg and 138.83mmHg in the group RS.

- The mean systolic blood pressure 1 minute after induction in the group R is 141.90mmHg and 138.80mm Hg in the group RS.

- The mean systolic pressure 3 minute after induction in the group R is 133.60mm Hg and 123.27mmHg in the group RS.

STATISTICAL SIGNIFICANCE:

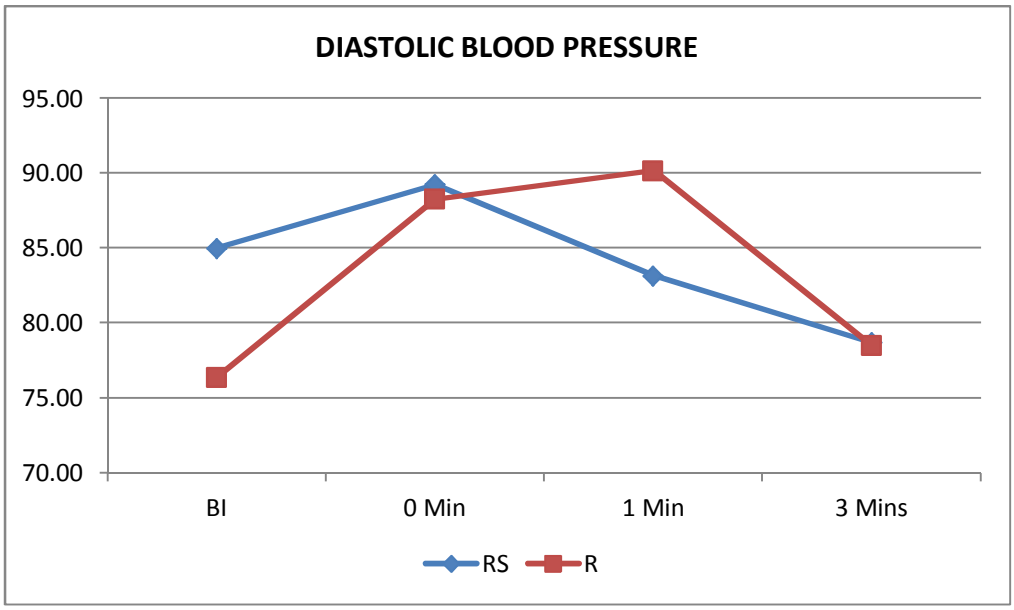
- The mean systolic blood pressure before induction is increased by 14.37mm Hg in the group R than in the group RS and the p value is 0.32 and hence statistically not significant.

- The mean systolic blood pressure 0 minute after induction is increased by 3.07mm Hg in the group R than in the group RS and the p value is 0.0138 and hence statistically significant.

- The mean systolic blood pressure 1 minutes after induction is increased by 3 mm Hg in the group R than in the group RS and the p value is 0.025 and hence statistically significant.

- The mean systolic pressure 3minutes after induction is increased by 10.33 mmHg in the group R than in the group RS and the p value is 0.00 and hence statistically significant.

DIASTOLIC BLOOD PRESSURE:



GROUP STATISTICS

GROUP		N	MEAN	SD	Std.error mean
D BI	RS	30	76.37	4.983	.910
	R	30	85.00	7.275	1.328
D 0 min	RS	30	89.27	4.500	.822
	R	30	88.23	6.264	1.144
D 1 min	RS	30	83.17	3.887	.710
	R	30	90.17	5.515	1.007
D 3 min	RS	30	78.50	3.984	.727
	R	30	78.70	5.722	1.045

INDEPENDENT SAMPLE TEST

		Levene"s test for equality of Variances		t-Test for Equality of Means						
		F	Sig	t	Df	Sig(2 tailed)	Mean Difference	Std.error of difference	95% confidence interval of the difference	
									lower	upper
DBI	Equal variances assumed	5.196	.026	5.363	58	.000	8.633	1.610	5.411	11.856
	Equal variances not assumed			5.363	51.299	.000	8.633	1.610	5.402	11.865
D 0 min	Equal variances assumed	2.284	.136	.686	58	.0495	.967	1.408	-1.852	3.785
	Equal variances not assumed			.686	52.640	.0495	.967	1.408	-1.858	3.792
D 1 min	Equal variances assumed	2.007	.162	-5.682	58	.000	-7.000	1.232	-9.466	-4.534
	Equal variances not assumed			-5.682	52.108	.000	-7.000	1.232	-9.472	-4.528
D 3 min	Equal variances assumed	2.100	.153	.157	58	.040	.200	1.273	-2.348	2.748
	Equal variances not assumed			.157	51.767	.046	.200	1.273	-2.355	2.755

- The mean diastolic blood pressure before induction in the group R is 85.0mm Hg and 76.37mmHg in the group RS.

- The mean diastolic blood pressure 0minutes after induction in the group R is 89.23mm Hg and 88.27 mmHg in the group RS.

- The mean diastolic pressure 3 minutes after induction in the group R is 83.17mm Hg and 90.17mm Hg in the group RS.

- The mean diastolic pressure 5 minutes after induction in the group R is 78.70mm Hg and 78.50 mm Hg in the group RS.

STATISTICAL SIGNIFICANCE:

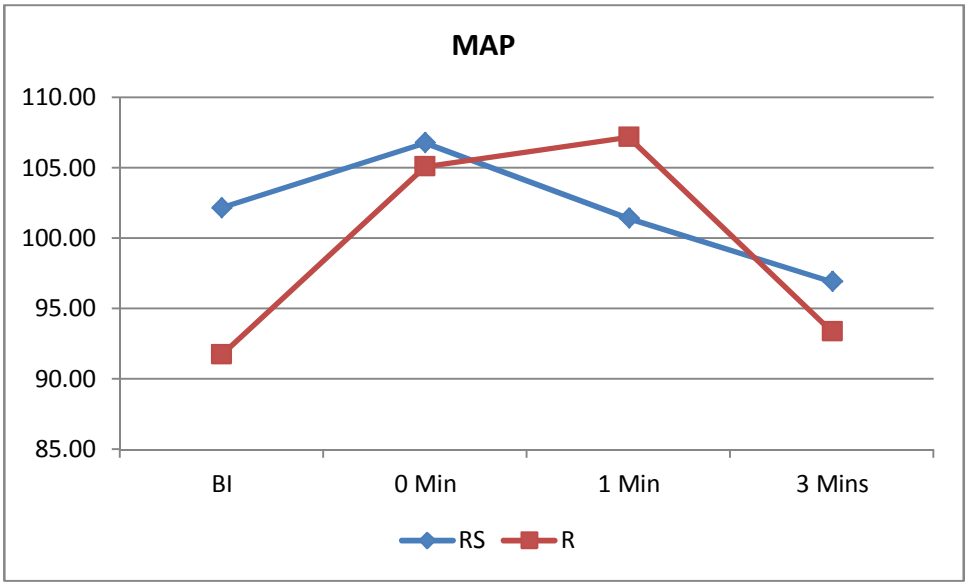
- The mean diastolic blood pressure before induction is increased by 8.63 mm Hg in the group R than in the group RS and the p value is 0.00 and hence statistically significant.

- The mean diastolic blood pressure 0 minute after induction is increased by 0.96 mm Hg in the group R than in the group RS and the p value is 0.049 and hence statistically significant.

- The mean diastolic blood pressure 1 minute after induction is decreased by 7 mm Hg in the group RS than in the group R and the p value is 0.01 and hence statistically significant.

- The mean diastolic blood pressure 3 minute after induction is increased by 0.2 mm Hg in the group RS than in the group R and the p value is 0.046 and hence statistically significant.

MEAN ARTERIAL PRESSURE:



GROUP STATISTICS

Group		N	MEAN	SD	Std error Mean
MAP BI	RS	30	91.753	4.6951	.8572
	R	30	102.173	8.0555	1.4707
MAP 0 min	RS	30	105,093	4.0755	.7441
	R	30	106,787	5.9718	1.0903
MAP 1 min	RS	30	101.417	3.4952	.6381
	R	30	107.187	5.1732	.9445
MAP 3 min	RS	30	93.390	3.4738	.6342
	R	30	96.930	5.5156	1.0070

INDEPENDENT SAMPLE TEST

		Levene's test for equality of Variances		t-Test for Equality of means						
		F	Sig	T	df	Sig(2 tailed)	Mean difference	Std.error difference	95% confidence interval of the difference	
									Lower	Upper
MAP BI	Equal variances assumed	9.750	.003	6.121	58	.000	10.4200	1.7023	7.0125	13.8275
	Equal variances not assumed			6.121	46.665	.000	10.4200	1.7023	6.9948	13.8452
MAP 0 min	Equal variances assumed	4.880	.031	1.283	58	.0205	1.6933	1.3200	-.9489	4.3356
	Equal variances not assumed			1.283	51.198	.0205	1.6933	1.3200	-.9564	4.3431
MAP 1 min	Equal variances assumed	5.548	.022	-5.062	58	.000	-5.7700	1.1399	-8.0517	-3.4883
	Equal variances not assumed			-5.062	50.911	.000	-5.7700	1.1399	-8.0585	-3.4815
MAP 3 min	Equal variances assumed	6.209	.016	2.975	58	.004	3.5400	1.1901	1.1578	5.9222
	Equal variances not assumed			2.975	48.878	.005	3.5400	1.1901	1.1483	5.9317

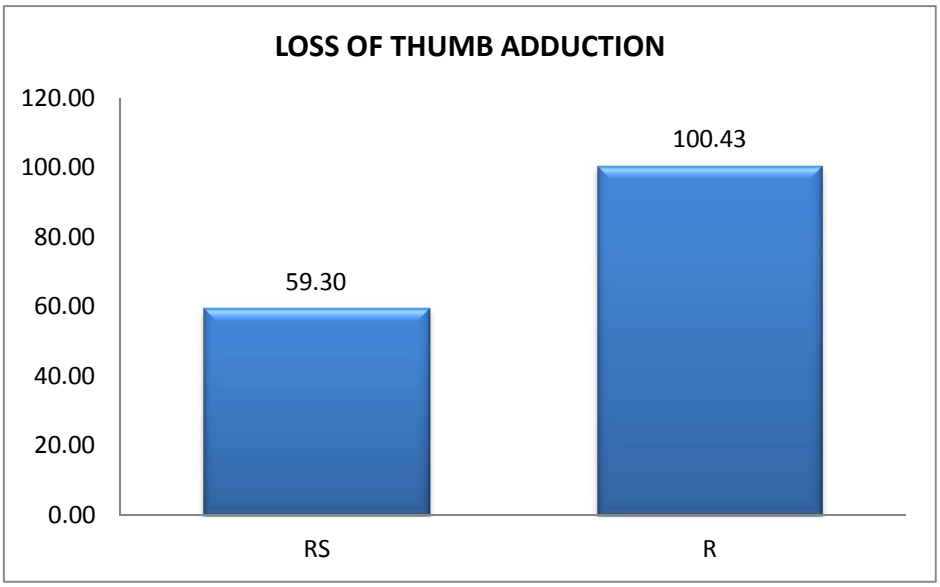
- The mean MAP before induction in the group R is 102.17 mm Hg and 91.75 mm Hg in the group RS.
- The mean MAP 0 minute after induction in the group R is 106.78 mm Hg and 105.09 mm Hg in the group RS.
- The mean MAP 1 minute after induction in the group RS is 101.47 mm Hg and 107.18 mm Hg in the group R.
- The mean MAP 3 minutes after induction in the group R is 96.93 mm Hg and 93.39 mm Hg in the group RS.

STATISTICAL SIGNIFICANCE:

- The mean MAP before induction is decreased by 10.42mm Hg in the group RS than in the group R and the p value is 0.01 and hence considered to statistically significant.
- The mean MAP 0 minutes after induction is decreased by 1.6 mm Hg in the group RS than in the group R and the p value is 0.0205 and hence statistically significant.
- The mean MAP 1 minute after induction is decreased by 5.77 mm Hg in the group RS than in the group R and the p value is 0.00 and hence statistically significant.

- The mean MAP 3 minute after induction is decreased by 3.6 mm Hg in the group RS than in the group R and the p value is 0.005 and hence considered to be statistically significant.

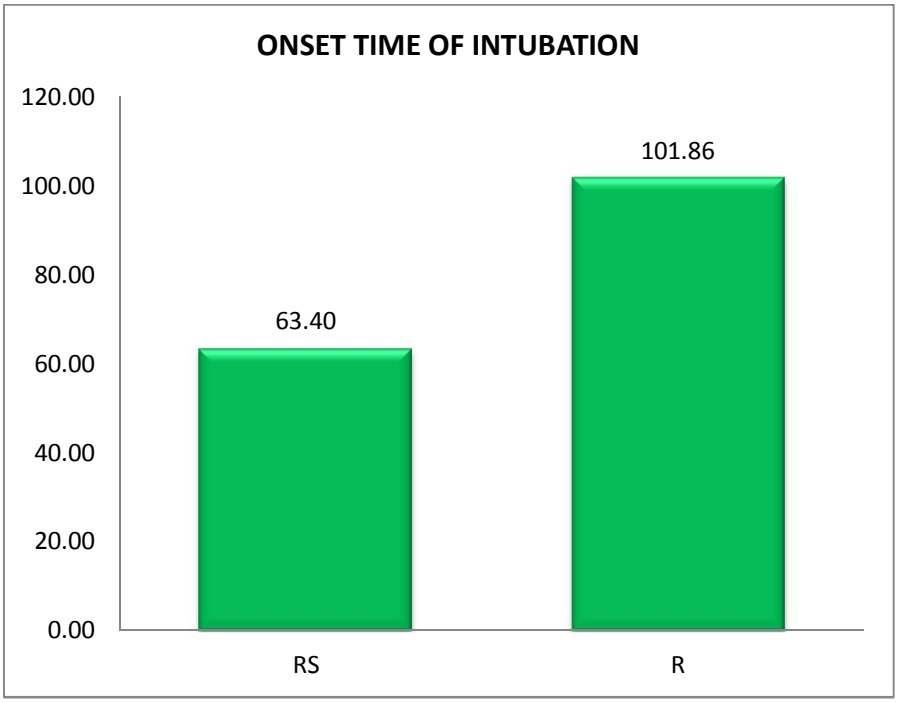
LOSS OF THUMB ADDUCTION:



Group		N	Mean	SD	Std.err mean	P value
LOSS OF THUMB ADDUCTION	RS	30	59.300	1.4179	.2589	0.001
	R	30	100.433	3.2557	.5944	

- The mean time for loss of thumb adduction in the group RS is 59.30 seconds compared to 100.43 seconds in the group R.
- The mean time for loss of thumb adduction is reduced by 41.13 seconds in the group RS than in the group R with p value of 0.001 and therefore statistically significant.

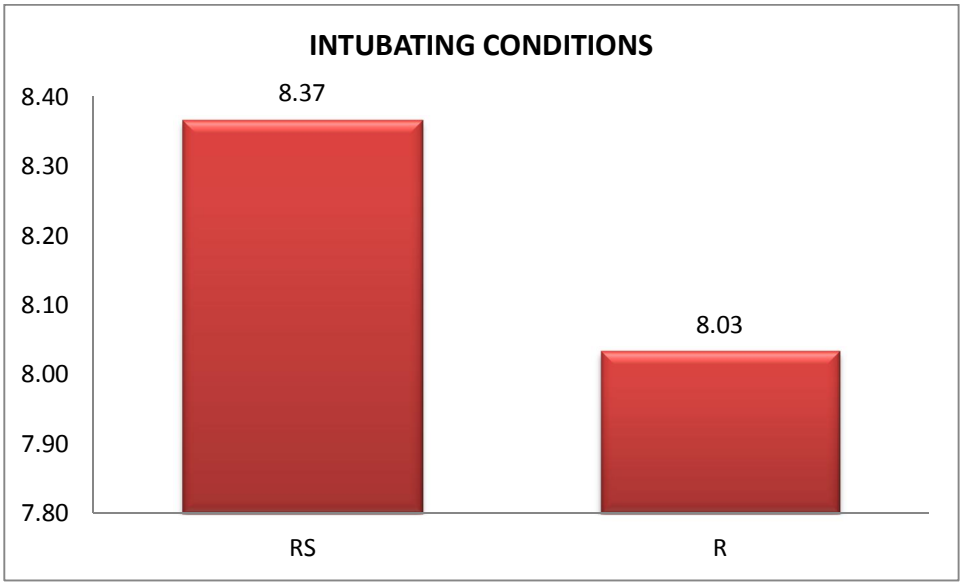
ONSET TIME OF INTUBATION:



Group		N	Mean	SD	St d err mean	P value
ONSET TIME OF INTUBATION	RS	30	63.400	1.7927	.3273	0.002
	R	30	101.857	3.2500	.5934	

- The mean onset time for intubation in the group RS is 63.40 seconds compared to 101.85 seconds in the group R.
- The mean onset time for intubation is decreased by 38.45 seconds in the group RS than in the group R with p value of 0.002 and hence considered to be statistically significant.

INTUBATING CONDITIONS:



Group		N	Mean	SD	Std. err mean	P. Value
INTUBATING CONDITIONS	RS	30	8.37	.615	.112	0.116
	R	30	8.03	.964	.176	

The mean intubation condition score in the group RS is 8.37 compared to 8.03 in the group R with p value of 0.116 and hence statistically not significant.

DISCUSSION

11. DISCUSSION

This prospective, randomized, double blinded controlled study is to assess and compare the effect of sevoflurane on intubating conditions with rocuronium in patients undergoing Elective Craniotomies in Rajiv Gandhi Government General hospital – Madras Medical College.

Sixty patients belonging to ASA1 and 2, between 18 to 65 years of either sex, satisfying inclusion criteria were randomized into two groups containing 30 patients each.

- **Group RS** patients received rocuroium(0.8mg/kg) along with 2%sevoflurane

- **Group R** patients received rocuronium(0.8mg/kg).

1. In my study it has been found that the usage of rocuronium (0.8mg/kg) along with 2% sevoflurane resulted in earlier onset of loss of thumb adduction and earlier onset of intubation than in the group in which rocuronium alone is used.

2. Also the intubating conditions were comparable in both the groups which is clinically insignificant.

These results are in correlation with the following studies as mentioned below.

Magorian T, Flannery KB, Miller RD conducted the study of comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients in which they found that Rocuronium at doses of 0.9 mg/kg and 1.2 mg/kg has been shown to result in rapid onset of action with comparable intubating conditions to that of succinylcholine 1 mg/kg for rapid sequence induction with endotracheal intubation.

Cooper R, Mirakhur RK, Clarke RS, Boules Z, et al, studied the comparison of intubating conditions after administration of rocuronium and suxamethonium in which they found that the time to achieve maximum blockade was 89 s with rocuronium 0.6 mg/kg with clinically acceptable intubating conditions at 60–90 s in a previous study.

McCourt KC, Salmela L, Mirakhur RK, Carroll M, Mäkinen MT, Kansanaho M, *et al.studied the* comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia in which they found that Rocuronium at 1 mg/kg produces clinically acceptable intubating conditions at 60 s and it has been suggested as an

alternative to succinylcholine 1 mg/kg in rapid sequence intubation in the absence of anticipated difficult airway conditions.

Wright PM, Caldwell JE, Miller RD" studied the Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans in which they concluded that the onset time of rocuronium, in doses more than 0.8 mg/kg was comparable to that of succinylcholine 1 mg/kg at the adductor pollicis but was significantly delayed at the laryngeal adductors.

Lowry DW, Mirakhur RK, McCarthy GJ, Carroll MT, McCourt KC studied the Neuromuscular effects of rocuronium during sevoflurane, isoflurane, and intravenous anesthesia pn which they found that effect of rocuronium 0.6 mg/kg was enhanced by 1.5 MAC of sevoflurane in comparison with isoflurane or propofol anaesthesia.

3. In my study it has also been found that usage of rocuronium (0.8mgkg) along with 2% sevoflurane is associated with stable intraop hemidynamics than in the group in which rocuronium alone is used.

The group in which rocuronium along with 2%sevoflurane used results in significant reduction in heart rate at 0min, 1 min, and 3 min after induction than in the other group.

The group in which rocuronium along with 2% sevoflurane used resulted in significant reduction in systolic blood pressure at 0min, 1 min and 3 min after induction than in the other group.

The group in which rocuronium along with 2% sevoflurane used resulted in significant reduction in diastolic blood pressure at 0min, 1 min and 3 min after induction than in the other group.

The group in which rocuronium along with 2% sevoflurane used resulted in significant reduction in MAP at 0min, 1 min and 3 min after induction than in the other group.

LIMITATIONS OF THE STUDY:

- Only ASA I and ASA II patients were included.
- No patients with Glascow ComaScale (GCS) below 15 were included in the study
- Direct estimation of ICP was not attempted. Only the hemodynamic responses were noted

- Only elective patients were included in this study. Emergency neurosurgical patients were not included.

- No placebo group included to highlight the differences in the hemodynamic responses, since both the groups have been proven superior to placebo in different studies.

SUMMARY

To summarize, on performing the double blinded prospective randomized comparative trial comparing the effect of sevoflurane on intubating conditions with rocuronium in patients undergoing elective craniotomies, the following observations were made,

- There were significant difference in intraop hemodynamics between the two groups. The use of sevoflurane with rocuronium resulted in statistical significant reduction in heart rate, systolic blood pressure, diastolic blood pressure and MAP.

- The use of sevoflurane with rocuronium resulted in earlier onset time of intubation.

- The use of sevoflurane with rocuronium resulted in better intubating conditions.

CONCLUSION

12. CONCLUSION

In conclusion, inj. Rocuronium when used at a dose of 0.8 mg/kg along with 2% sevoflurane (1 MAC) provides excellent intubating conditions within 60–66 sec without any adverse effects in elective neurosurgeries. This can be used for rapid sequence intubation (RSI) during anaesthesia in neurosurgical patients.

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BIBLIOGRAPHY

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PROFORMA

NAME:
DATE:

AGE: SEX: IP NO:

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

Ht: cms CVS: Rs:

Wt: kgs BT: CT: Hb: g% Platelets:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O bleeding diathesis

H/O documented difficult airway

H/O previous surgeries

INFORMED CONSENT IN TAMIL:

RANDOMISATION: Tick the following

GROUP A: ROCURONIUM

GROUP B: ROCURONIUM WITH 2% SEVOFLURANE

IV LINE

Premedication

Monitors

BASELINE VITAL PARAMETERS:

Heart rate	
NIBP	
Spo2	
Baseline TOF Ratio	

MEASURES OF STUDY OUTCOME:

ONSET TIME OF INTUBATION

	TIME (SECONDS)
GROUP A	
GROUP B	

INTUBATING CONDITIONS:

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
GROUP A				
GROUP B				

HEMODYNAMICS INTRA OPERATIVE:

TIME	BASELINE	PRE INDUCTION	POST INDUCTION	AT INTUBATION	IMMEDIATELY AFTER INTUBATION (0 MIN)	1 MIN	3 MIN
HEART RATE							
SYSTOLICBP							
DIASTOLIC BP							
MAP							

INFORMATION TO PARTICIPANTS

Investigator: Dr.S. GAYATHIRI

Name of the Participant:

Title:

"A Prospective, randomised, double blind comparative study of the effect of sevoflurane on intubating conditions with rocuronium" in patients undergoing Elective Craniotomies

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria. We want to compare and study the onset time of intubation with rocuronium vs rocuronium with 2% sevoflurane, intubating conditions and hemodynamic responses in patients undergoing Elective Craniotomies

What is the Purpose of the Research:

To compare the effect of sevoflurane on intubating conditions with rocuronium in patients undergoing Elective Craniotomies based on

- Onset time of paralysis
- Intubating conditions
- Hemodynamic measurements

The Study Design:

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

Group RS-patients receiving rocuronium (0.8mg/kg) with 2% sevoflurane

Group R: Patients receiving rocuronium (0.8mg/kg)

Benefits

The combination of rocuronium (0.8mg/kg) with 2% sevoflurane provides early onset of neuromuscular blockade, better intubating conditions and haemodynamics.

Discomforts and risks

Discomfort and pain during supramaximal TOF stimuli- this will be reduced by rescue analgesic. Hypotension , bradycardia may occur – emergency drugs are readily available.

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

Time :

Date :

Place :

Signature / Thumb Impression of Patient
Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study title : "A Prospective, randomized double blind comparative study of the effect of sevoflurane on intubating conditions with rocuronium" in patients undergoing Elective Craniotomies"

Study center: Institute of Anaesthesiology & Critical care,
Rajiv Gandhi Government General Hospital,
Madras Medical College,
Chennai.

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

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

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

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

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

Time:

Date: Signature / thumb impression of patient

Place: Patient name:

Signature of the investigator: Name of the investigator:

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.Gayathiri.S.
II Year Post Graduate in M.D. (Anaesthesiology)
Madras Medical College & RGGGH
Chennai 600 003

Dear Dr.Gayathiri.S,

The Institutional Ethics Committee has considered your request and approved your study titled **"A PROSPECTIVE, RANDOMIZED DOUBLE BLIND COMPARATIVE STUDY OF EFFECT OF SEVOFLURANE ON INTUBATING CONDITIONS WITH ROCURONIUM IN PATIENTS UNDERGOING ELECTIVE CRANIOTOMIES " - NO.26032016.**

The following members of Ethics Committee were present in the meeting hold on **01.03.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Dr.Baby Vasumathi, Director, Inst. of O&G,Ch-8	: Member
7.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3	: Member
8.Prof.Srinivasagalu,Director,Inst.of Int.Med.,MMC,Ch-3	: Member
9.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

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

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

Member Secretary - Ethics Committee

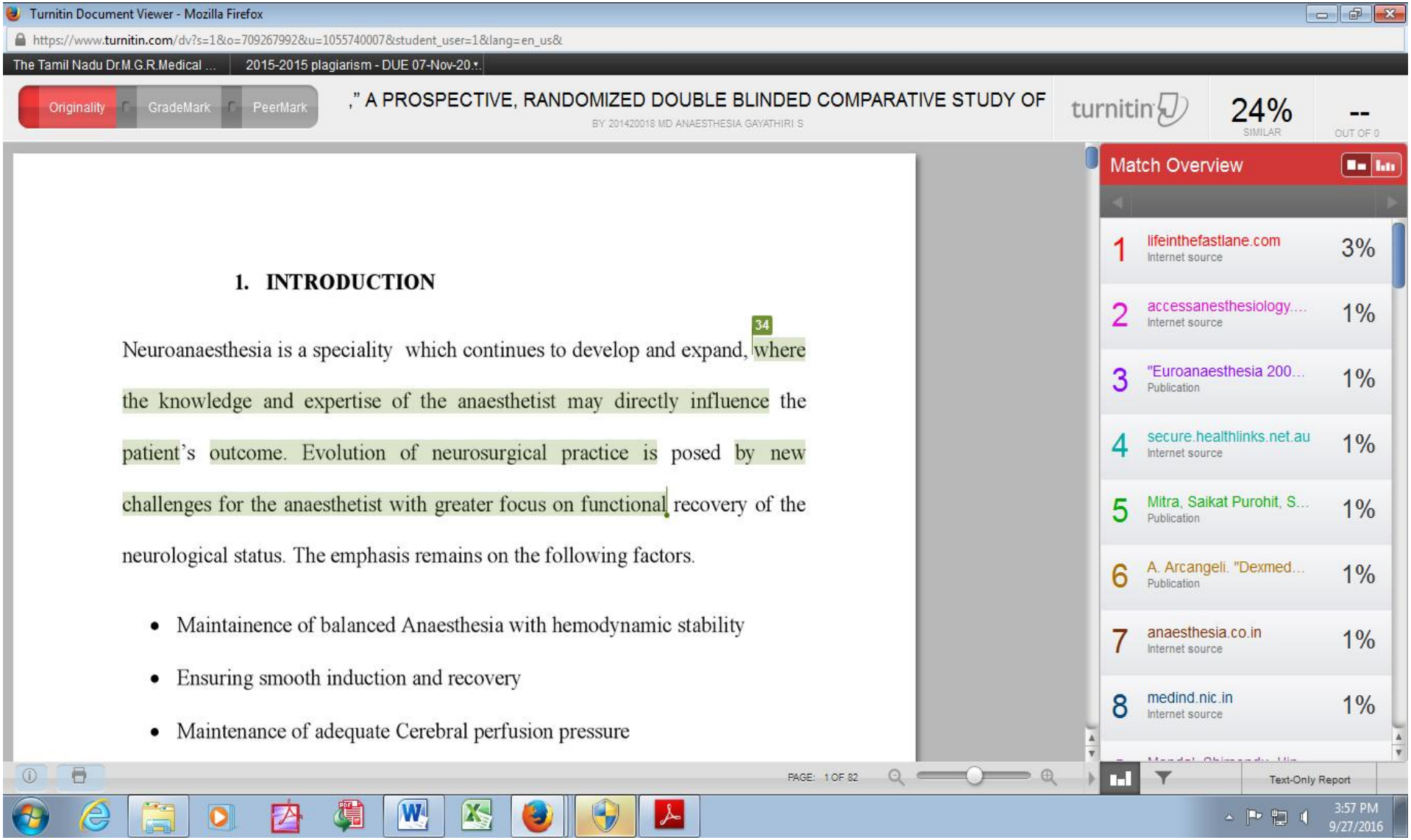
MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

MASTER CHART - RS GROUP

S.NO	GROUP-RS	IP NO	AGE	SEX	WT	ASA	HR BI	HR 0 min	HR 1 min	HR 3 min	S BI	S 0 min	S 1 min	S 3 min	D BI	D 0 min	D 1 min	D 3 min	MAP BI	MAP 0 min	MAP 1 min	MAP 3 min	LOSS OF THUMB ADDUCTION	ONSET TIME OF INTUBATION	INTUBATING CONDITIONS
1	1	125678	45	M	45	I	80	90	87	82	136	144	140	140	84	90	82	80	101.3	108	101.3	100	59	61	9
2	1	159703	29	M	59	I	82	86	86	87	140	144	139	136	90	94	90	86	106.7	110.7	106.3	102.7	58	60	8
3	1	124521	59	M	64	II	84	89	88	85	136	139	136	132	82	86	85	81	100	103.7	102	98	60	63	8
4	1	130981	43	M	67	I	80	85	87	86	138	140	134	131	85	89	84	79	102.7	106	100.7	96.3	58	61	8
5	1	130432	49	M	75	I	91	98	95	93	135	140	138	134	83	84	80	77	100.3	102.7	99.3	96	59	62	9
6	1	129034	29	M	69	I	90	95	96	94	142	146	140	134	86	88	84	78	104.7	107.3	102.6	96.7	60	64	9
7	1	136098	20	F	46	I	85	90	89	88	139	142	139	132	87	90	86	80	104.3	107.3	103.6	97.3	63	66	8
8	1	131200	34	M	62	I	87	96	96	93	137	143	141	136	85	86	81	79	102.3	105	101	98	60	62	8
9	1	134100	39	F	65	I	85	93	91	90	136	140	137	134	84	88	82	76	101.3	105.3	100.3	95.3	61	65	8
10	1	123761	30	M	72	I	90	98	97	96	138	142	139	135	87	91	84	79	104	108	102.3	97.6	58	62	7
11	1	133598	29	F	54	I	91	100	98	96	140	147	144	139	89	90	83	79	106	109	103.3	99	58	61	8
12	1	130051	49	F	52	I	84	90	90	88	141	143	142	136	92	95	88	84	108.3	111	106	101.3	59	63	8
13	1	130891	51	M	59	I	82	96	95	93	143	146	142	137	95	98	90	90	112	114	107.3	105.6	59	65	9
14	1	139983	40	F	71	I	84	98	95	95	138	145	143	136	90	94	89	84	106	111	107	101.3	60	64	8
15	1	131019	32	F	50	I	86	97	96	94	134	140	137	134	89	90	86	81	103.3	106.7	103	98.6	62	66	9
16	1	134312	37	M	60	I	90	100	102	100	130	136	132	130	80	88	84	79	96.7	104	100	96	61	65	8
17	1	141230	54	M	76	II	92	98	95	93	126	132	133	129	78	83	78	73	94	99.3	96.3	91.6	60	66	9
18	1	139087	40	M	61	I	84	90	90	88	138	142	139	135	83	85	80	76	101.3	104	99.6	95.6	58	63	8
19	1	141003	41	M	54	I	88	98	96	91	137	145	142	138	85	90	84	78	102.3	108.3	103.3	96.6	58	64	8
20	1	138600	50	M	60	I	86	94	92	90	134	140	136	131	84	88	82	77	100.7	105.3	100	95	59	65	9
21	1	140089	32	F	69	I	88	98	97	95	139	148	142	130	86	91	86	78	103.7	110	104.6	95.3	60	64	8
22	1	139876	23	F	56	I	92	90	86	83	140	146	142	136	91	96	84	78	107.3	112.7	103.3	97.3	62	66	7
23	1	129996	41	M	65	I	90	103	100	94	142	146	139	134	93	96	87	82	109.3	112.7	104.3	99.3	59	63	9
24	1	137610	52	M	69	I	93	100	98	94	132	139	132	128	82	88	81	76	98.7	105	98	93.3	58	62	9
25	1	133129	43	M	59	I	86	106	97	96	136	140	134	134	83	85	80	74	100.7	103.3	98	94	**58**	**61**	9
26	1	134290	22	F	53	I	88	98	96	95	125	132	128	122	74	79	72	70	91	96.7	90.6	87.3	**59**	**64**	8
27	1	138076	62	F	56	II	84	97	98	95	134	143	139	134	76	83	78	75	95.3	103	98.3	94.6	59	65	9
28	1	135409	46	M	60	I	84	96	96	93	132	140	135	131	79	86	79	74	96.7	104	97.6	93	57	61	8
29	1	133901	38	F	70	I	87	98	97	94	134	139	135	134	80	90	84	80	98	106.3	101	98	58	63	9
30	1	140012	53	M	87	II	83	97	96	92	143	148	141	136	88	96	82	78	106.3	113.3	101.6	97.3	59	65	9

MASTER CHART - R GROUP

S.NO	GROUP-RS	IP NO	AGE	SEX	WT	ASA	HR BI	HR 0 min	HR 1 min	HR 3 min	S BI	S 0 min	S 1 min	S 3 min	D BI	D 0 min	D 1 min	D 3 min	MAP BI	MAP 0 min	MAP 1 min	MAP 3 min	LOSS OF THUMB ADDUCTION	ONSET TIME OF INTUBATION
1	2	132202	45	F	65	I	96	108	110	100	132	142	145	140	84	90	93	89	100	107.3	110.3	106	101.3	102.9
2	2	142210	39	M	72	II	89	104	122	98	120	139	144	132	72	88	92	78	88	105	109.3	96	99.6	100.4
3	2	133244	63	M	56	II	104	110	107	97	116	132	139	124	70	84	88	80	85.3	100	105	94.6	110.1	111.5
4	2	132180	43	M	76	I	92	99	109	96	108	133	140	116	65	74	79	68	79.3	93.6	99.3	84	98.2	99.3
5	2	140089	31	F	51	I	109	122	113	114	143	154	149	140	77	89	93	70	99	110.6	111.6	93.3	108.3	109.6
6	2	128756	51	M	59	II	100	113	109	98	137	148	151	130	90	95	99	89	103.6	112.6	116.3	102.6	103	104
7	2	140234	57	M	87	II	91	98	108	89	122	139	144	109	71	87	91	82	88	104.3	108.6	91	101	103
8	2	132434	24	M	49	I	88	97	100	96	100	132	124	104	66	79	84	80	77.3	96.6	97.3	88	99.1	101
9	2	133745	29	M	70	I	75	98	103	86	107	128	136	112	74	89	94	80	85	102	108	90.6	97.2	98.5
10	2	140092	45	M	56	I	77	89	98	100	130	144	151	139	70	87	90	76	90	106	110.5	97	106.6	107.8
11	2	139852	39	F	60	II	99	109	115	102	109	118	127	120	86	98	100	80	93.6	104.6	109	93.3	102	104
12	2	140345	41	M	74	I	69	100	98	91	144	159	153	140	76	88	92	80	98.6	111.6	112.3	100	99	100
13	2	140123	30	F	80	I	89	99	105	100	132	145	140	122	80	92	88	78	97.3	109.6	105.3	92.6	98	100
14	2	134534	39	M	71	II	103	118	107	100	141	149	154	130	84	97	90	78	103	114.4	111.3	95.3	96.4	97.9
15	2	145322	50	M	77	II	98	109	110	98	126	140	144	122	68	80	77	70	87.3	100	99.3	87.3	98.1	100
16	2	140923	19	M	52	I	85	96	101	90	104	118	131	121	73	84	88	70	83.3	95.3	102.3	87	100	101
17	2	134563	24	F	53	I	94	100	109	99	121	137	142	117	77	80	94	78	91.6	99	110	91	102	103.6
18	2	140123	34	F	44	II	90	98	107	101	118	129	137	112	69	84	80	78	85.3	99	99	89.3	104	105
19	2	140234	43	M	61	II	101	116	120	104	103	123	134	130	82	94	89	80	89	103.6	98	96.6	101	102
20	2	139012	50	M	66	II	93	102	110	98	116	131	144	123	77	87	93	80	90	101.6	110	94.3	97.7	99
21	2	139923	31	M	73	I	99	109	118	94	123	142	149	131	90	98	84	88	101	112.6	105.6	102.3	99	100
22	2	140321	43	F	70	I	104	119	122	102	148	157	160	135	80	96	90	82	109.3	116.3	113.3	99.6	100	102
23	2	142678	53	M	72	II	66	85	99	74	135	148	151	123	84	94	98	89	101	112	115.6	100.3	98	99
24	2	142123	42	F	61	II	72	89	102	99	122	135	143	120	78	89	93	80	92.6	104.3	109.6	93.3	99	100
25	2	139023	49	M	60	I	79	103	120	94	113	142	133	120	66	79	84	70	81.6	100	100.3	86.6	**101.4**	**102.8**
26	2	140923	38	F	50	I	88	104	116	103	109	135	140	112	70	89	92	77	83	104.3	108	88.6	**99**	**100**
27	2	140912	61	M	74	II	94	122	119	100	104	133	141	114	76	85	93	70	85.3	101	109	84.6	97	98
28	2	140812	32	M	82	I	110	126	103	97	137	151	144	130	70	88	91	77	92.3	109	108.6	94.6	99	101.4
29	2	139098	39	M	79	I	97	119	101	82	127	141	134	120	88	98	90	78	101	112.3	104.6	92	100	102
30	2	140921	47	M	66	II	86	97	101	88	117	141	133	110	78	86	96	80	91	104.3	108.3	90	98	100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1. INTRODUCTION
Neuroanaesthesia is a speciality which continues to develop and expand, where the knowledge and expertise of the anaesthetist may directly influence the patient's outcome. Evolution of neurosurgical practice is posed by new challenges for the anaesthetist with greater focus on functional recovery of the neurological status. The emphasis remains on the following factors.
Maintainence of balanced Anaesthesia with hemodynamic stability
Ensuring smooth induction and recovery
Maintenance of adequate Cerebral perfusion pressure
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