"A PROSPECTIVE RANDOMISED STUDY OF COMPARISON OF ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION USING ORAL IVABRADINE AND INTRAVENOUS LIGNOCAINE"

Dissertation submitted in partial fulfillment of

M.D. DEGREE EXAMINATION

M.D. ANAESTHESIOLOGY- BRANCH X

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

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

CHENNAI, TAMILNADU.

APRIL 2017

CERTIFICATE BY THE HEAD OF THE INSTITUTION

This is to certify that the dissertation titled **"A PROSPECTIVE RANDOMISED STUDY OF COMPARISON OF ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION USING ORAL IVABRADINE AND INTRAVENOUS LIGNOCAINE"** submitted by **Dr.K.KAVITHA RANI, D.A** in partial fulfillment for the award of the degree of Doctor of Medicine in anaesthesiology in the April 2017 examination by the Tamilnadu Dr.M.G.R , Medical University, Chennai, is bonafide record of the work done by her in the CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU, during the academic year 2015-2017.

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DECLARATION BY THE CANDIDATE

I, **Dr. K.KAVITHA RANI,D.A** , solemnly declare that the dissertation **"A PROSPECTIVE RANDOMISED STUDY OF COMPARISON OF ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION USING ORAL IVABRADINE AND INTRAVENOUS LIGNOCAINE"** is a bonafide work done by me in the Department of Anaesthesiology, Chengalpattu Medical College & Hospital,Chengalpattu, after getting approval from the Ethical committee under the able guidance of **Dr.S.BALASUBRAMANIAM M.D.,D.A.,** Professor , Department of Anaesthesiology, Chengalpattu Medical College, Chengalpattu.

Place : Chengalpattu **(Dr.K.KAVITHA RANI , D.A)**

Date :

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INSTITUTIONAL ETHICAL COMMITTEE

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

Title of Work	: A Prospective Randomised Study of Comparison of Attenuation of Hemodynamic Response to Larygoscopy and Endotracheal Intubation Using Oral IV Abradube abd Intravenous Lignocaine
Principal Investigator	: Dr.Kavitha Rani
Designation	: 1st Year Anaesthesiology
Co-Investigators	: Dr.Revathy,MD,. Professor of Anaesthesiology Dr.Balasubramanian,MD,. Professor of Anaesthesiology
Department	: Anaesthesiology

The request for an approval From the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.05.2016 at the Medical Education Unit, Government Chengalpattu Medical College, Chengalpattu at 12.00 PM.

The Members of the committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

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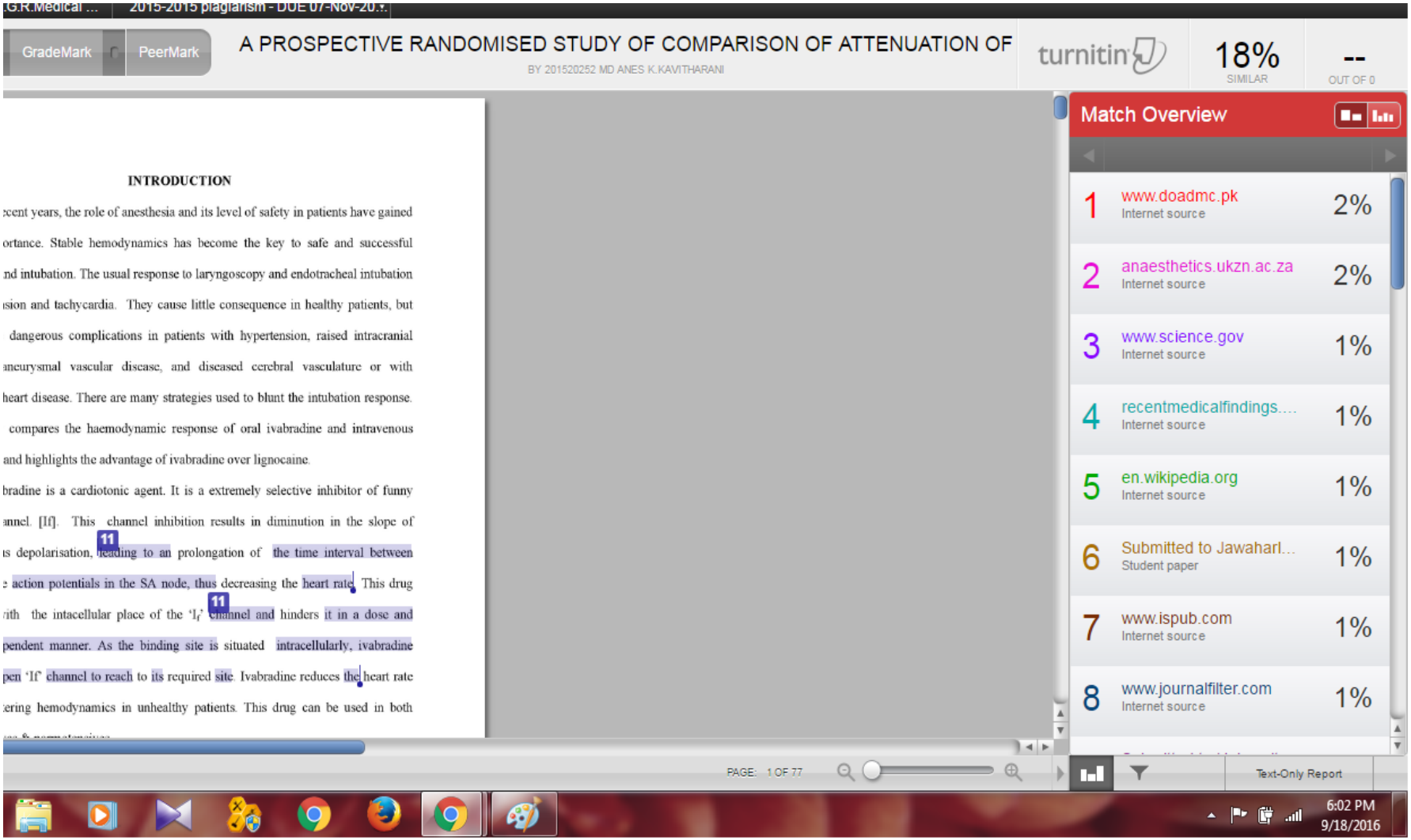
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INTRODUCTION
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CONTENT

INTRODUCTION

In recent years, the role of anesthesia and its level of safety in patients have gained prime importance. Stable hemodynamics has become the key to safe and successful induction and intubation. The usual response to laryngoscopy and endotracheal intubation is hypertension and tachycardia. They cause little consequence in healthy patients, but may cause dangerous complications in patients with hypertension, raised intracranial pressure, aneurysmal vascular disease, and diseased cerebral vasculature or with ischemic heart disease(1). There are many strategies used to blunt the intubation response (2). This study compares the haemodynamic response of oral ivabradine and intravenous lignocaine and highlights the advantage of ivabradine over lignocaine.

Ivabradine is a cardio tonic agent. It is a extremely selective inhibitor of funny current channel. [If]. This channel inhibition results in diminution in the slope of spontaneous depolarization, leading to prolongation of the time interval between consecutive action potentials in the SA node, thus decreasing the heart rate. This drug combine with the intracellular place of the 'I_f' channel and hinders it in a dose and voltage dependent manner. As the binding site is situated intracellular, ivabradine needs an open 'If' channel to reach to its required site. Ivabradine reduces the heart rate without altering hemodynamics

in unhealthy patients. This drug can be used in both hypertensive & normotensives (3) .

Lignocaine is an amide group of local anesthetic . It is used in treatment of patients with ventricular dysarrthmias and as prophylaxis in treatment of ventricular tachyarrthmias especially in connection with myocardial infarction and mechanical irritation of cardiac fibers. The principal metabolite of lignocaine is monoethylglycine xylidide. This metabolite has approximately 80% of the activity of lignocaine for protection against cardiac dysarrythmias. Lignocaine prevents conduction of nerve impulse (conduction blockade). It blocks passage of sodium ions thru ion selective sodium channels in nerve membrane. The Na+ channel is a definite receptor to lignocaine.

Intravenous lignocaine is used to blunt raises in heart rate, B.P, intracranial &intraocular pressure (4). These comprise a direct myocardial depressant effect, a peripheral vasodilating effect(5) .This study aims to compare the hemodynamic response of oral ivabradine and intravenous lignocaine during induction and intubation in ASA-I patients.

ANATOMY

ANATOMY OF AIRWAY (6) (7)

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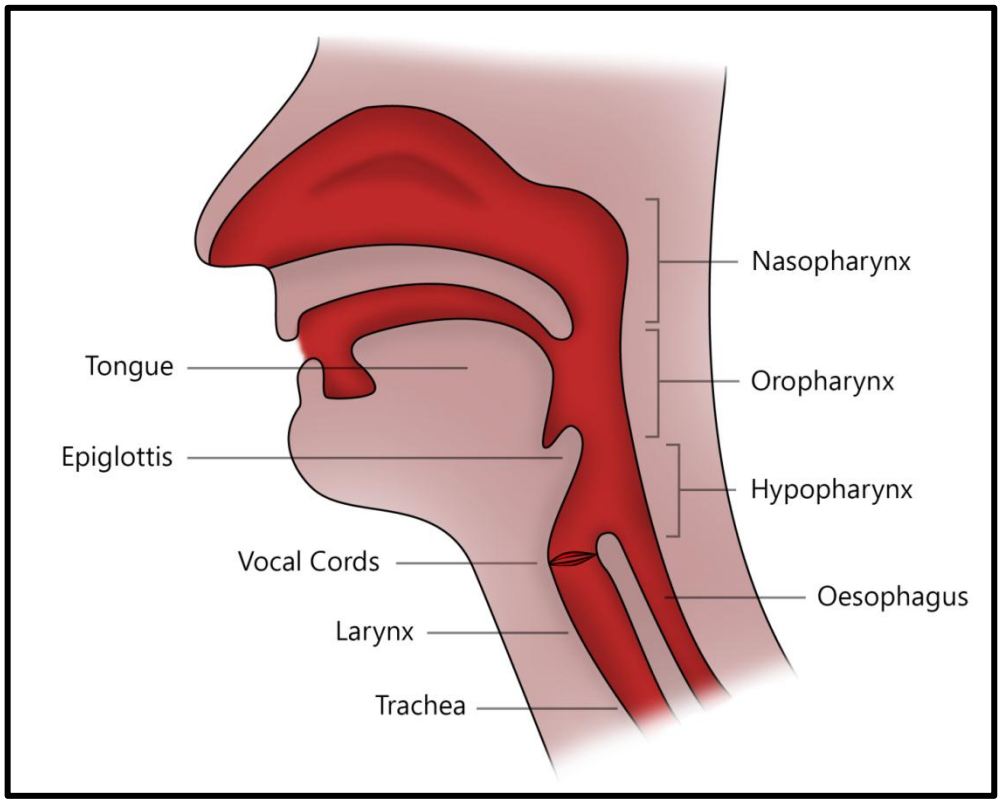
There are two openings to the human airway.

- Nose – continues as nasopharynx
- Mouth –continues as oropharynx.

These passageways are parted anteriorly by the palate. They join posteriorly in the pharynx.



PICTURE.1. ANATOMY OF AIRWAY (6)

Pharynx (6),(7):

The pharynx is a U shaped wide muscular conduit. It starts from the base of the skull and ends at the cricoid cartilage which is at the entry to the oesophagus.

It opens anteriorly in to

- Nasal cavity-nasopharynx
- The mouth-oropharynx
- The larynx-laryngopharynx

The nasopharynx

The nasopharynx lies behindhand the nasal cavity and above the soft palate. It interconnects with the oropharynx over the pharyngeal isthmus. On the lateral wall lies the pharyngeal opening of the pharyngotympanic (Eustachian) tube.

The oropharynx

The oral cavity continues with the oropharynx via the oropharyngeal isthmus, surrounded by the palatoglossal arches, the soft palate and the dorsum of the tongue. The oropharynx itself begins from the soft palate ends at the tip of the epiglottis.

The laryngopharynx

The third portion of the pharynx starts from the tip of the epiglottis and ends at the inferior border of the cricoid cartilage at the level of C6 vertebrae. Oropharynx and laryngopharynx separated functionally by the epiglottis at the floor of the tongue the epiglottis avoids aspiration by wrapping the glottis while swallowing.

Muscles of the pharynx

The muscles of the pharynx are

- superior constrictor- stylopharyngeus
- middle constrictor- salphingopharyngeus and
- inferior constrictor - palatopharyngeus

LARYNX:

It lies against the C4, C5, C6 cervical vertebrae. Larynx comprises a context of articulating cartilages, interconnected by ligament.

The laryngeal cartilages

There are nine cartilages. 3 unpaired cartilages:

1. Thyroid cartilage
2. Cricoid cartilage
3. Epiglottis

3 paired cartilages

1. arytenoid cartilage
2. corniculate cartilage
3. Cuneiform cartilage.

The laryngeal ligaments

These are divided into

- the extrinsic ligaments
- The intrinsic ligaments.

The extrinsic ligaments:

1 The thyro-hyoid membrane-starts from the upper edge of the thyroid cartilage to the hyoid bone.

2 The crico-tracheal ligament- which connects the cricoid and first tracheal ring.

3 The crico-thyroid ligament- connects the thyroid cartilage with the cricoid cartilage.

4 The hyo-epiglottic ligament- lies between the epiglottis and the body of the hyoid.

The intrinsic ligaments:

These are capsules of the synovial joints in between the arytenoid and cricoid cartilage& in-between the thyroid and cricoid cartilages. These are the fibrous structure of the inner larynx.

Muscles of the larynx

They are divided into

The extrinsic group- connects the larynx to its neighbors,

The intrinsic group- accounts for the movement of the laryngeal cartilage.

The **extrinsic muscles:**

- sternothyroid,
- thyrohyoid
- The inferior constrictor of the pharynx.

Some fibers of stylopharyngeus &palatopharyngeus go forward to the posterior edge of the thyroid cartilage.

1 The sternothyroid muscle-starts from the posterior part of the manubrium end at the oblique line situated on the lateral side of the thyroid lamina. It lowers the larynx.

2 The thyrohyoid muscle- goes upwards starting from oblique line of thyroid lamina to the lower edge of the greater horn of the hyoid. It uplifts the larynx.

3 The inferior constrictor starts from the oblique line of the thyroid lamina, as a tendinous arch above the cricothyroid muscle and from the sideways of the pharynx. This is a constrictor of the pharynx.

Muscles involved in the indirect movement of the larynx are

Indirect elevators are-

- mylohyoid,
- stylohyoid
- geniohyoid

Indirect depressors

- sternohyoid
- Omohyoid.

Intrinsic muscles of the larynx

- Posterior cricoarytenoids muscle
- Lateral cricoarytenoids muscle
- Interarytenoid muscles

- Thyroarytenoid muscle
- Vocalis
- Cricothyroid muscle

The actions of the intrinsic laryngeal muscles

1] Abductors of the cords: posterior cricoarytenoids;

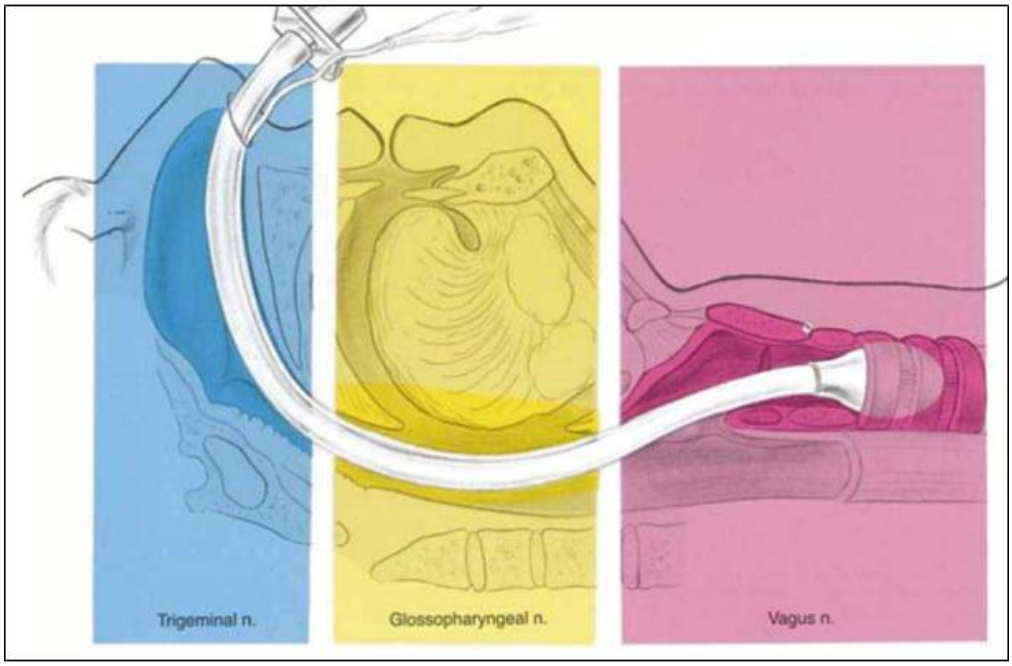
2] Adductors of the cords: lateral cricoarytenoids& interarytenoid

3] Sphincters to vestibule: aryepiglottics& thyroepiglottis

4] Regulators of cord tension: cricothyroid are tensors of cord,

Thyroarytenoid (relaxation of cords) & Vocalis (fine adjustment).

SENSORY NERVE SUPPLY OF UPPER AIRWAY (8):



PICTURE 2.SENSORY NERVE SUPPLY OF UPPER AIRWAY

The pharynx:

Sensory nerve supply:

Glossopharyngeal nerve innervates

- the posterior third of the tongue
- the fauces
- tonsils,
- anterior epiglottis
- Parts of the pharynx with visceral sensory innervation.

Motor supply:

Efferent supply- Vagus nerve thru its pharyngeal branch.

The larynx:

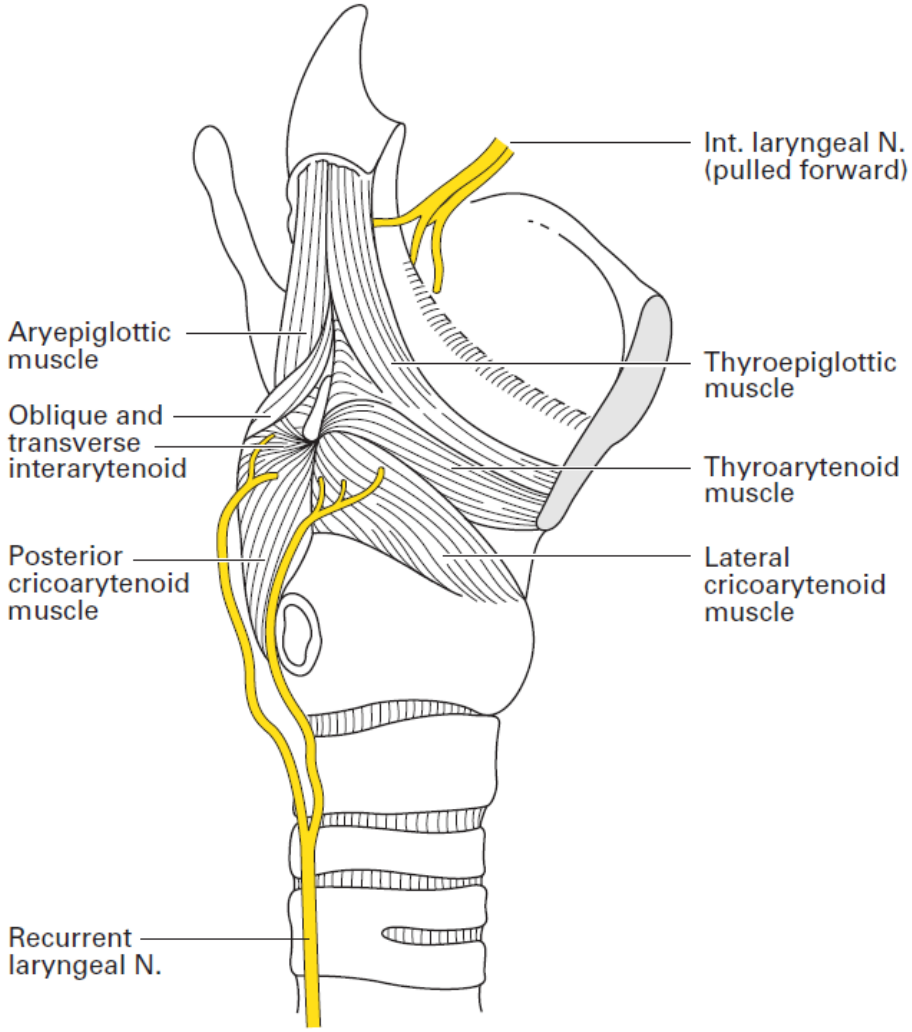
Sensory nerve supply:

The internal laryngeal Nerve- It is a branch of the superior laryngeal nerve. From the posterior epiglottis to the vocal cords .

The recurrent laryngeal Nerve - the larynx below the vocal cords the trachea.

Motor supply:

Recurrent Laryngeal Nerve - Intrinsic muscles of the larynx except the cricothyroid muscles.



PICTURE.3. NERVE SUPPLY OF LARYNX (7):

PHYSIOLOGY OF INDUCTION AND INTUBATION

Mechanism of hemodynamic responses during induction (9),(10),(11)

Intravenous induction of general anesthesia is often associated with hypotension. Several mechanisms have been thought responsible for the decrease in blood pressure and are classified into two broad categories namely

1) Direct effects
2) Indirect effects

Direct effects (11):

This occurs primarily due to the effect of drug on the contractility of the myocardium. Measurement of this intrinsic myocardial contractility is more accurately performed in in-vitro models. Possible mechanism for this are probably due to interference with the calcium transport across myocardial cells and a decrease in neural nitric oxide synthetase activity.

Indirect effects (11):

- Preload
- Afterload
- Sympathetic activity
- Baroreflex activity
- Central nervous system activity

Of all the above mentioned factors, the baroreflex activity is the single most important point in induction .Basically this reflex is started by stretch receptors known as baroreceptor /pressure receptors. They are situated in the walls of the huge systemic arteries .A increase in pressure in systemic arteries will stretch the baroreceptors and affect them to conduct signals into CNS and response signals will send back via the ANS to the systemic circulation to decrease arterial pressures towards the normal level.

Physiological anatomy of baroreceptors and their innervations

These are spray variety of nerve terminals lying on the wall of the vessels that are aroused when stretched. Some baroreceptors are sited on the wall of nearly all single big blood vessel of the thoracic and neck region. They are extremely abundant on the wall of both internal carotid artery somewhat directly above the carotid bifurcation. This area is recognized as carotid sinus& wall of aortic arch.

Response of baroreceptor to pressure

The carotid baroreceptors, which are not aroused by pressures between Zero to Sixty mm of Hg, they react gradually and hastily and reach a high pressure of 180 mm of Hg. The response to the arch of aorta baroreceptors are alike carotid baroreceptors excluding that they will respond at pressure limits of around 30 mm of Hg or more .Baroreceptors react enormously to variations in arterial blood pressures. Indeed the degree of impulse firing rises

throughout systole and reduces yet again during diastole. Moreover the baroreceptors react very rapidly to sudden changes of BP somewhat to static pressures.

Reflex pathway of baroreceptor system

Transmission of signals from both carotid sinus via very small Herrings nerve to glossopharyngeal Nerve. Then they reach tractus solitaries in medulla oblongata .Secondary impulses impede the center of vasoconstrictor within the medulla and stimulate the vagal centre. The end results are

- Vasodilatation throughout peripheral circulation
- Decreased heart rate &strength of myocardial contraction

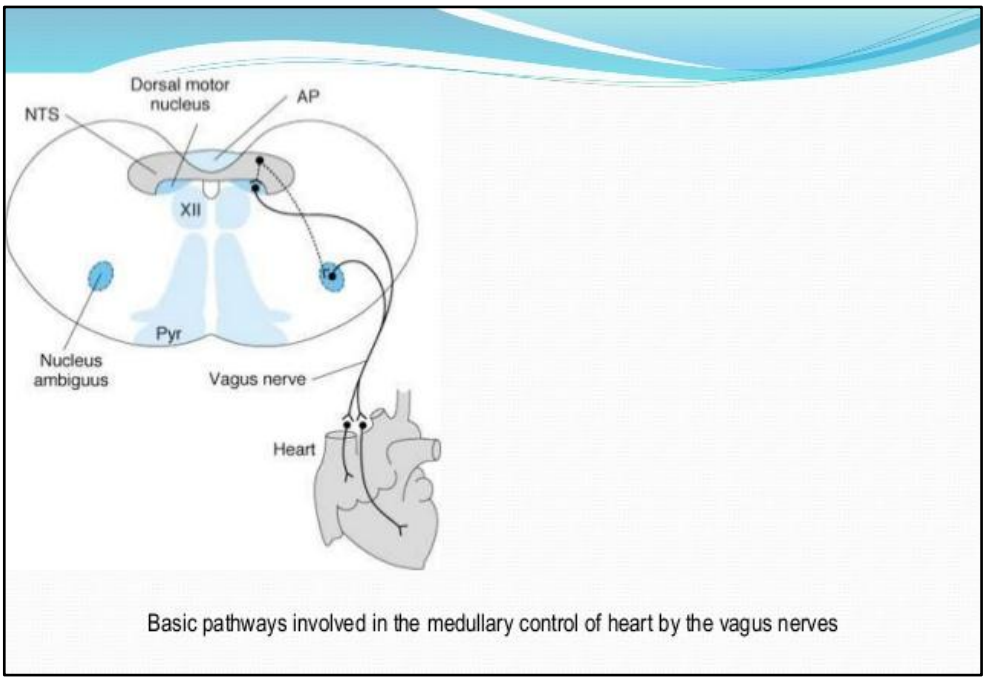
Conversely, low pressures have a contrary effect producing the pressure to augmentation back towards basal.

Mechanism of haemodynamic responses during Intubation (11)(12)

Endotracheal intubation is associated with a temporary escalation in blood pressure and rate of the heart and with an increase in the plasma concentration of epinephrine. All studies have shown that haemodynamic response which occurs during intubation is mainly due to stimulation of sympathetic nervous system. Exact cause for the haemodynamic response is

not known. It could be because of activation of the Somato-visceral reflex due to stimulation of the base of the tongue and epiglottis.

Basic pathways involved in medullary control of heart rate and blood pressure (9)(10)



PICTURE.4. MEDULLARY CONTROL OF HEART RATE AND BLOOD PRESSURE -BASIC PATHWAY

Somato-visceral reflex:

Provocation of proprioceptors situated on the base of the tongue during intubation induces surge in pressure changes and rate of the heart. Subsequent attempts recruit additional receptors that further augment hemodynamic and catecholamine concentration. Probable pathway for Somato visceral reflex resulting in hemodynamic changes is given below.

Afferent pathway

The afferent fibers mainly arise from the various receptors which are present in the larynx and trachea. The various receptors are pain receptors carried by unmyelinated C fibers, touch receptors which are more in the lower half of true vocal cords, chemical receptors and thermal receptors mainly in the supraglottic and epiglottis area, joint and pressure receptors and stretch receptors. The afferent response from these receptors (general visceral afferent) is transmitted along the Vagus nerve to the tractus solitaries.

Central-vasomotor center:

Nerve fibers from tractus are projected into the superficial ventrolateral reticular area of reticular activating system .This area is mainly concerned with cardiovascular, baroreceptors, chemoreceptors and respiratory reflexes and probably forms the vasomotor center.

Efferent pathway:

Reticulospinal efferent from this ventrolateral reticular region (vasomotor center) terminate bilaterally on the preganglionic neurons of sympathetic system in the thoracic spinal nerves. Along sympathetic nerve it is distributed to all the vessels except capillaries, precapillaries, precapillary sphincter and Meta arterioles.

Other probable pathways

A . Activation of pain pathway

Pain impulse from the respiratory tract and oral cavity are mainly transmitted by unmyelinated C fibers .Pain pathways from the head and neck synapse in spinal sensory nucleus of trigeminal nerve. The fibers from here cross to the opposite side. Here they divided into two pathways. One ascends in ventral trigeminal-thalamic tract and end in thalamus, other fibers pass into the reticular formations where they synapse with ascending reticulo-thalamic fibers and end in thalamus. Few example, stimulus of motor cortex rouses center of vasomotor by the signals conveyed downwards into the hypothalamus and thereafter into the center of vasomotor. Stimulus of vasomotor center causes increase in heart rate and blood pressure. Stimulation of hypothalamus will also activate hypothalamo -pituitary axis as part of stress response.

B. Hypothalamo pituitary adrenal axis stimulation as a part of these stress response:

The afferent response from the upper airway larynx and trachea is transmitted along the vagus nerve to the tractus solitarious. Nerve fibers from the tractus solitarious are projected into the superficial ventrolateral area of reticular activating system .Fibers from here ascend and synapse in supraoptic and Para ventricular areas of the hypothalamus. Excitation of these cells causes release of vasopressin from neurohypophysis. Medullary noradrenergic

cell groups A1and A2 in the ventrolateral reticular area also innervate directly or indirectly the median eminence and control the release of ACTH which in turn acts on adrenal cortex to release cortisol. This cortisol in turn acts on the adrenal medulla to secrete catecholamine. These catecholamines in turn act on the cardiovascular system and cause alteration in blood pressure.

Neural regulation of the circulation (9),(10)

The nervous system switches the circulation virtually via the ANS, mainly by sympathetic nervous system. It controls the cardiovascular system by two mechanisms:

1) Through definite sympathetic nerves which supply the blood vessels and heart.

2) Through catecholamine release.

Cardiac innervation:

The efferent preganglionic cardiac sympathetic fibers arise in the upper four or five thoracic spinal segments, while the parasympathetic is from the Vagus. Impulses from the nor-adrenergic sympathetic nerves supply of the heart raise rate of heart and force of heart contraction. They also impede the end result of vagal stimulus. Impulse conduction from cholinergic vagal heart fibers reduces heart rate. A reasonable quantities of tonic release takes place in the heart sympathetic nerves at resting conditions. But there are worthy pact of tonic vagal release in humans

Innervation of the blood vessels:

Though the arterioles and the additional resistant vessels are utmost compactly innervated, capillaries and venules that contains smooth muscles and get motor nerve supply from the sympathetic part of the ANS. Regulation of tissue blood flow and arterial pressure are maintained through the nerve fibers of resistance blood vessels. Blood vessels of all parts of the body are innervated by nor adrenergic fibers. They are vasoconstrictor in nature. The resistance blood vessels of the skeletal muscles are innervated by both cholinergic and nor adrenergic nerve fibers.

Vasomotor control:

Sympathetic nerve fiber constricts arterioles and veins and raise heart rate and stroke volume in a stimulant manner, blood pressure is modified by variations in the frequency of this tonic liberation. Spinal reflex action affects pressure in the blood vessels, but the chief regulation of blood pressure is exercised by collections of neurons in the medulla oblongata, are at times called as the vasomotor area or vasomotor center.

Factors affecting the activity of the vasomotor are in the medulla.

1. Direct stimulation

    - Carbon dioxide
    - Hypoxia

2. Excitatory inputs

- From the cortex via hypothalamus
- From pain pathways and muscles
- From chemoreceptors of carotid& aortic bodies

3. Inhibitory inputs

- From the cortex thru hypothalamus
- From lungs
- From carotid, aortic and cardio-pulmonary baroreceptors.

Nerve supply to adrenal glands (11)

Sympathetic nerve fibers innervating the adrenal glands arise from the T8-L1 segments. Many preganglionic fibers from these segments pass through the paired paravertebral ganglion to form the splanchnic nerves; most do not synapse until in celiac ganglion, whereas others innervate the adrenal medulla directly. Majority of the fibers to adrenal gland contains myelinated nerve fibers and few unmyelinated nerve fibers. Adrenal gland receives larger autonomic supply than any other organ. Preganglionic fibers directly synapse with large chromaffin cells in adrenal medulla. Stimulation of these fibers directly cause release of catecholamines, thereby they act similar to post ganglionic fibers.

Coronary perfusion (11):

Coronary perfusion is distinctive in that it has intermittent to some extent than continues, as in other structures, during contraction, pressure in intra myocardium of the LV reaches systemic blood pressure. The potency of the left ventricle contraction virtually occludes the intramyocadial portion of the coronary arteries actually; flow of blood might transiently inverse in epicardial blood vessels. In the last part of diastole, left ventricular pressure ultimately surpasses right atrial pressure. Therefore pressure of coronary perfusion is commonly decided by the variation between aortic pressure and ventricular pressure, left ventricle is getting blood supply completely during diastole. In disparity the right ventricle is getting blood supply both during systole and diastole. Furthermore, as a element of myocardial blood flow, arterial diastolic pressure is added significant than mean arterial pressure. Coronary perfusion pressure = Arterial diastolic pressure - Left ventricular end diastolic pressure

Decrease in aortic or increase in L.V end diastolic pressure could reduce pressure of coronary perfusion. Increase in rate of heart also decreases perfusion of the heart, since unduly more reduction in diastolic time as the rate of the heart increases. As it is exposed to the maximum intramural pressure during systole, the endocardium has a predisposition to ischemia during reduction in pressure coronary perfusion.

Regulation of coronary blood flow (11):

Blood supply of heart is normally equals myocardial metabolic needs. In the normal adult man and at rest blood flow to the heart is around 250 ml/min at rest. The myocardium controls its individual blood flow meticulously between perfusion pressures of 50 mm of Hg -120 mm of Hg, afar this range, circulation becomes increasingly depends on pressure.

Under normal circumstances, fluctuations in blood flow are completely due to variants in coronary artery tone in reaction to metabolic need. Hypoxia whichever directly or indirectly over the discharge of adenosine leads to coronary vasodilatation. Autonomic influences were commonly weak. Both adrenergic receptors α1&β 2 are exists in coronary arteries. The α1 adrenergic receptors are chiefly positioned on great epicardial vessels, whereas β2 adrenergic are generally located on the smaller intramuscular & subendocardial blood vessels. Sympathetic stimulus usually rises the myocardial blood flow owing to an rise in myocardial need and a majority of β2 receptor stimulation. Parasympathetic possessions on coronary vasculature are usually slight and are faintly vasodilatory.

Regulation of myocardial oxygen supply- demand (11):

Myocardial oxygen need is ascribed by many processes

- Basal metabolism -20%

- Electrical activity- 17
- Blood volume work
- Pressure work (64%).

Usually, the myocardium abstracts more oxygen from the blood (65%) compared to other tissues of the body (25%). The coronary sinus oxygen saturation is usually 30%. Thus when demands by the myocardium are increased, the oxygen extraction cannot be augmented as occurs in others parts of the body. Thus the needs can be met with only by increasing the blood flow to the myocardium.

Factors influencing myocardial oxygen supply-demand balance (11):

- Blood supply
  - Rate of heart
  - Time for diastole
- Coronary perfusion pressure
  - arterial diastolic blood pressure
  - left ventricular end diastolic pressure
- arterial oxygen content(Cao2)
- Pao2
- hemoglobin content
- Coronary vessel diameter

- Demand
- Basal requirements
- Heart rate
- Tension in the wall
    - preload
    - afterload
    - Contractility

Mechanism of intubation response

The exact mechanism of intubation response is indefinable, but it involves both a sympathetic and parasympathetic systems. The net effect is temporary taking place 30 seconds after intubation and maintained for less than 10 minutes (13).

Sympathetic reflex:

The sympathetic reflex is a polysynaptic pathway with the involvement of glossopharyngeal and Vagus nerve creating the afferent arc to the sympathetic nervous system thru the brain stem and spinal cord. This will lead to profound autonomic response at the efferent end. It includes augmented firing of the cardio-accelerator fibres and discharge of adrenergic mediators like norepinephrine, epinephrine &vasopressin. The end effect is hypertension,

tachycardia, and raise in pulmonary artery wedge pressure &decline in ejection fraction.

Parasympathetic reflex:

It is a monosynaptic pathway & is seen often in children. It may occur in adults also. The response is mediated by augmented vagal tone at Sino-atrial node (14).

The haemodynamic response to laryngeal &endo- tracheal intubation is temporary. In many of the patients supposed to be of diminutive consequence. In patients with coronary artery disease, raised blood pressure, increased intra cranial and intra ocular pressure it might related with myocardial ischemia& infarction, dysrhythmias, heart failure, pulmonary oedema& intra cranial haemorrhage (15). The procedure of intubation consists of different phases and these change the haemodynamic responses uniquely. Endotracheal intubation comprises of two phases:

1. Direct laryngoscopy
2. Introduction of endotracheal tube through the vocal cord & trachea (16).

PHARMACOLOGY OF IVABRADINE

Ivabradine Hydrochloride (17):

Generic Name: Ivabradine Hcl**.**

Introduction:

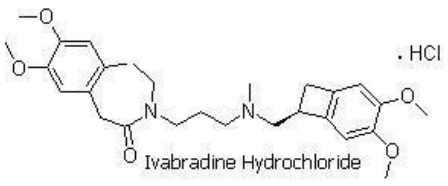
It is a 'pure' heart rate lowering drug. It has been introduced recently as an alternative to β blockers. It is a cardio tonic drug .Ivabradine, the first selective & specific inhibitors of the funny current channel. Ivabradine affords reduction in heart rate without changing myocardial contractility of myocardium. It is useful for the symptomatic relief of chronic stable angina in persons with normal rhythm who were intolerant to β blockers.

Chemical Name:

3(3-{[(7S)-3,4-dimethoxybicyclo[4.2.o] octa-3, 5-trien-7-yl) methyl amino}propyl)-1,3,4,5-tetrahydro-7,8-dimethoxy-2H-3-benzazepine-2-one,hydrochloride

Chemical formula: C27H36N2O5

Structural formula:



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PICTURE.5. STRUCTURAL FORMULA OF IVABRADINE

Molecular Weight: 468.585 g/mol

Physical form: White to pale yellow powder

Solubility:

It is readily soluble in water,DMSO, methanol and methylene chloride and ethanol. It is soluble in acetone to some extent.

Category:

Used to treat symptoms of long standing stable angina, adults with coronary artery disease with normal sinus rhythm. This drug is also used in patients who are contraindicated or intolerance to β blockers. Ivabradine is also used in symptomatic treatment of tachycardia.

Stability and storage:

Store at temperature not exceeding 30 degree centigrade

Mechanism of action (17):

The only significant action of ivabradine is blockade of cardiac pacemaker (Sino-atrial) cell ‘f’ channels. The ‘funny’ cation channels are present in the S.A node. The If channels that open during early part of slow diastolic (phase 4) depolarization. The resulting inward current (If) determines the slope of phase 4 depolarization. Selective blockade of If current by ivabradine results in heart rate reduction without altering electrophysiological

or negative inotropic or negative lucitropic (slowing of myocardial relaxation) effect. Heart rate reduction decreases cardiac O2demand and prolongation of diastole tends to improve myocardial perfusion (O2 supply)(18),(19).

PHARMACODYNAMICS:

Ivabradine decreases heart rate about 10 beats per minute in the course of exercise &at resting condition. It will lead to decrease in myocardial oxygen usage and work load. Ivabradine do not affect intracardiac contractility, conduction and myocardial contractility. This drug mainly reduces the frequency of angina attacks as effective as β blockers and reduces short acting nitrates consumption along with β blockers.

PHARMACOKINETICS:

Absorption:

Ivabradine is quickly and entirely absorbed after oral intake. It reaches peak plasma concentration in 60 minutes in fasting conditions. Food delays its absorption.

Distribution:

It binds 70% to plasma protein .The Cmax is 0.22 µg/ml.Volume of distribution -1001.

Metabolism:

Bioavailability of Ivabradine is 40%.Metabolised by liver and GIT by CYP3A4 oxidation.

Elimination:

The half- life of Ivabradine is about 120 minutes in serum. Renal clearance - 70%. The total clearance is about 400ml/min. Excretion of metabolites occurs via feces and urine. And about 4% excreted unchanged in urine after oral administration.

Indications

- chronic stable heart failure
- stable angina
- Intolerant to to β blocker
- Contraindication to β blockers
- inappropriate sinus tachycardia.

Contraindications:

- Sick sinus syndrome
- Hypertension
- Stroke
- Liver failure

- Renal failure
- Runny nose
- Pregnancy and lactation

Should not be used along with CYP3A4 like azole antifungal, macrolide antibiotics, nafazodone & antiretroviral nelfinavir and ritonavir. Concomitant use of verapamil and diltiazem

Adverse effects: Heart:

- Bradycardia
- Palpitations
- 1 degree AV block. Ventricular extra systoles
- Difficulty in breathing
- Giddiness
- Central nervous system: Headaches, dizziness
- Eyes: Luminous phenomenon- sensations of heightened brightness in a fully maintained visual field. This is due to If channel block situated in the retina.
- Gastro intestinal tract: Nausea, vomiting and constipation
- Musculo skeletal: muscle cramps and weakness

Dose: Initially 5 mg BD, increase if needed to 7.5 mg BD,

Elderly 2.5 mg BD.

PHARMACOLOGY OF LIGNOCAINE

LIGNOCAINE HYDROCHLORIDE

History

Lignocaine is the first tertiary amide–type local anesthetic drug. It was first synthesized in 1943(20),(21)(22).In early days, it was named as 'xylocaine'. Lignocaine was first synthesized by Nils Lofgren in Sweden. Bengt Lundqvist, who executed the first injection anesthesia on himself (20). It came to market in 1949.

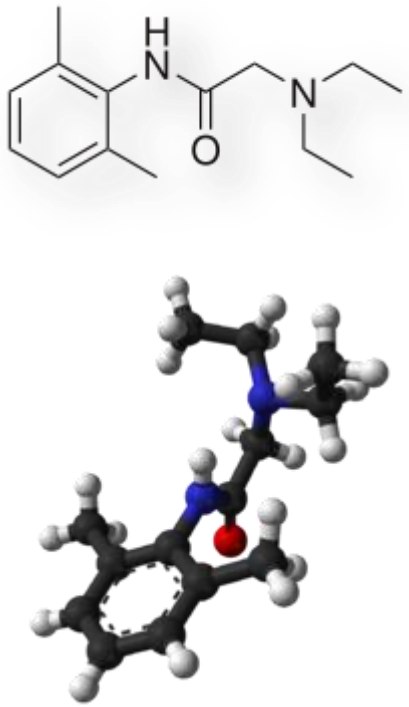
It is currently most widely used LA. It is a versatile LA, good both for surface applications well as injection .It is available in a variety of forms. Injection of Lignocaine surrounding a nerve will block impulse conduction within 3 min and produces anesthesia & is more intense and longer lasting. Vasodilatation occurs at the injected area. It is useful for surface application, infiltration, nerve block, epidural, spinal and intravenous regional block anesthesia(17).

Chemical Name:

2-(diethyl amino) - *N*-(2, 6-dimethylphenyl) acetamide

Chemical Formula: C14H22 N20

Structural Formula:



PICTURE.6.STRUCTURE OF LIGNOCAINE

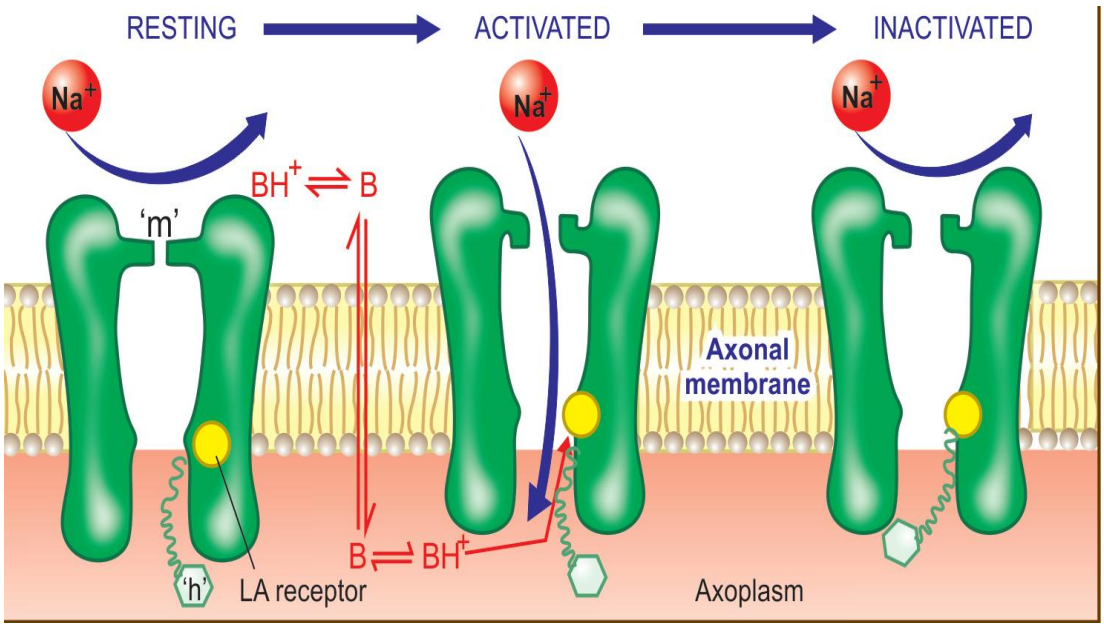
Molecular weight **:** 234.34 g/mol

Melting point **:** 68 degree (154F)

Mechanism of action (17)

Lignocaine act mainly by inhibiting sodium influx through voltage-gated sodium channels in the neuronal cell membrane. Once the entry of sodium is blocked in to the cell, action potential will not rise &there will be no signal conduction. The receptor site for local anesthetic is found at the inner lot of the NA channel& this drug combine with this channel in activated state. The time taken for the onset of neuronal blockade was quicker in neurons. This action is denoted as dependent blockade.

Lignocaine is a weak base. They are formulated by means of hydrochloride salt as to make them water-soluble. At equal pH& pKa, the ionized as well as unionized forms of the particle exist in equal quantities. The unionized base disseminates readily across cell membranes. As soon as the local anesthetic drug is ionized and in equilibrium it will not go out of the cell membrane. This action is called by means of "ion-trapping". When the local anesthetic in ionized form, it binds to the LA binding site on the inner portion of the sodium channel at the cytoplasmic end. Majority of local anaesthetic drugs act on the inner side of the cell membrane. Local anesthetic drug should enter the cell membrane when in non-ionized state.



PICTURE.7. SITE AND MECHANISM OF ACTION OF LOCAL ANAESTHETICS (17)

PHARMACOKINETICS

Bioavailability:

35 % (oral)

3 % (topical)

Distribution:

The volume of distribution is 1.1-2.1 l/kg. About 60-80% circulates bound to the protein alpha$_1$ acid glycoprotein.

Metabolism:

Lignocaine 95% metabolized in the liver-95%. Dealkylation chiefly by CYP3A4.It will form active& inactive metabolites namely monoethylglycine xylidide and glycine- xylidide. Active form has a longer half compared to lignocaine. It is a weak NA channel blocker.

Onset of action: within 1.5 min (i.v)

Duration of action:

10minutes to 20 minutes (IV) 30 minutes to 180 minutes (injection)

Elimination:

The elimination half-life- 1.5to 2 hours. . It is excreted (90% as metabolites) & 10% as unchanged drug in the urine (24).

Dosage and administration:

“Lignocaine is commonly used in the formula of lignocaine hydrochloride. Preparations of Lignocaine are

- Injected local anesthetic
- Dermal patch (sometimes combined with prilocaine in a eutectic mixture)
- I.V. injection
- I.V. infusion
- Intra osseous Injection
- Nasal spray with phenylephrine
- Oral “viscous lidocaine" or abbreviated "lidocaine visc" or "lidocaine Hcl visc"; used as teething gel)
- Oral solution
- Topical gel
- “Topical liquid”
- Lidocaine Hcl 2% jelly, combined with hypromellose, to anesthetize and lubricate the urethra, etc., for inserting a catheter or instrument
- Topical patch (lidocaine 5%),
- Over the counter patch (lidocaine 4%) since 2015.
- Topical aerosol spray

- Inhaled by nebulizer
- Ear drops”

USES OF LIGNOCAINE(25),(260:

Regional Anesthesia:

- topical or surface anesthesia
- local infiltration
- peripheral nerve block
- intravenous regional anesthesia (Bier block)
- epidural anesthesia
- spinal (subarachnoid) anesthesia.

Analgesia

The administration of I.V.(lidocaine) to provide analgesia is limited. In addition to attenuating ventricular cardiac dysrhythmias, the I.V.Lignocaine will raise the defibrillation threshold.

Suppression of Generalized Tonic-Clonic Seizures

Anti-inflammatory Effects

It is useful in modifying perioperative inflammatory injury

Bronchodilation

Inhaled lidocaine blunt histamine-induced bronchospasm .It enhances airway anesthesia

Tumescent Liposuction

Infiltration of large volumes of diluted lidocaine around 0.05% to 0.10%with epinephrine (1:100,000) the subcutaneously. Lignocaine the dose ranges from 35 -55 mg/kg .This is known as mega dose lignocaine. "Lignocaine toxicity is the commonest complication in tumescent liposuction.

Heart arrhythmias

Lignocaine is classified as-1b antiarrhythmic type of drug. Intravenous Lignocaine is indicated in the treatment of ventricular arrhythmias associated with acute myocardial infarction , digoxin poisoning due to digoxin and cardio version or the conditions in which amiodarone was not available or could not be used.

"Intravenous or topical administrations of lidocaine have been used with variable success to blunt hemodynamic response to tracheal intubation & extubation and suppress cardiac dysrhythmias". Instrumentation of the upper airway will result in coughing, constriction of the bronchus and additional airway responses. I.V. Lignocaine effectively depresses airway reflexes due to instrumentation (29). This action is mediated by decreasing c movement of calcium in the smooth muscle cells of the airway.

"Doses of intravenous lignocaine from 2 to 2.5 mg/kg are needed to consistently blunt hemodynamic and airway responses to tracheal

instrumentation. Intravenous lignocaine is also effective for attenuating increases in intraocular pressure, intracranial pressure, and intra-abdominal pressure during airway instrumentation. Attenuation of all these responses may be beneficial in selected clinical situations (e.g., corneal laceration or increased intracranial pressure)" (27), (28).

Insensitivity (30):

Relative insensitivity to lignocaine is genetic.

- Attention deficit hyperactivity disorder - hypokalemic sensory overstimulation.
- In dental anesthesia- unexpected positions of nerves.
- Ehlers-Danlos syndrome

Adverse effects:

- Allergic reactions
- Systemic toxicity

Allergic Reactions (31)

Allergic reactions are infrequent and less than 1% .

Cross-Sensitivity

Cross-sensitivity amongst local anesthetics was due to the shared metabolite para-aminobenzoic acid.

Systemic Toxicity (32)

Systemic toxicity occurs due to excess concentration of local anesthetic drug. CNS symptoms generally occur when blood plasma concentrations were low. Cardiovascular effects usually manifests at higher concentrations, even though cardiovascular system may collapse at lower concentrations.

Central Nervous System

- At low plasma concentrations - numbness of the tongue and circumoral tissues are because of delivery of L.A. to vessel rich tissues. Central nervous system excitation first to occur.
- At higher plasma concentrations - skeletal muscle twitching's (tonic-Clonic seizures) & CNS depression.
- Neurotoxicity
- Transient Neurologic Symptoms
- Cauda Equina Syndrome
- Anterior Spinal Artery Syndrome

Cardiovascular System

Toxic effects of high plasma concentrations towards CVS are more resilient than the CNS.

- Fall in blood pressure
- Reduction in heart rate

- Dysrhythmias
- Facial flushing
- Decreased venous return
- Pulmonary edema
- Cardiac arrest

Respiratory System:

- Bronchoconstriction
- Difficulty in breathing
- Reduced respiration
- Respiratory arrest

Gastrointestinal System:

- perception of metallic taste
- nausea &vomiting

Ears - Tinnitus

Eyes:

- Burning sensation in the eyes
- Congestion of conjunctiva
- Corneal ulceration
- Diplopia
- Corneal opacity

Methemoglobinemia

Ventilatory Response to Hypoxia

Hepatotoxicity

Dysphoria

Dose-Dependent Systemic Effects of Lidocaine(26)

PLASMA CONCENTRATION (μg/mL)	EFFECT
1–5	Analgesia
5–10	Lightheadedness Tinnitus Numbness of tongue
10–15	Seizures Unconsciousness
15–25	Coma Respiratory arrest
>25	Cardiovascular depression

Interactions(33)

- Drugs that increase CYP3A4 and CYP1A2 enzyme induction
- .Drugs that precipitate Methemoglobinemia
- Dronedarone
- Liposomal morphine

Contraindications:

Absolute contraindications:

- 2degree heart block /3 degree without pacemaker
- S.A Nodal block (Severe) without the presence of pacemaker
- H/O reactions caused by amide group of local anesthetic drugs
- Hypersensitivity reactions related to corn food products
- Adams Stokes syndrome and W-P-W syndrome
- Concomitant intake of drugs like quinidine, flecainide, disopyramide, procainamide

Exercise caution with:

- Hypotension not related to arrhythmia
- Reduced heart rat
- Accelerated idioventricular rhythm
- Old patients
- Deficiency of pseudo choline esterase enzyme
- "acute intermittent porphyria"
- Impairment of liver function –patients with reduced hepatic function might have an adverse reaction due to repetitive administration of lignocaine

Over dosage:

Disproportionate administration of

- Topical
- Parenteral routes,
- unintentional oral intake of topical preparations
- Accidental I.V. injection
- prolonged use of tumescent anesthesia

REVIEW OF LITERATURE

1) C. G. Raghu ram, Deep raj Singh, Aditya Vikram Kabra (1) in (2014)evaluated the effect of oral ivabradine on the hemodynamics during intubation in patients undergoing surgical procedures under general anesthesia& conducted in 50 ASA- I adult patients in two groups. . Received oral Ivabradine 5mg one Tab. at 9.00 pm on the evening before the day of surgery and another one 5mg tab one hour before intubation& placebo. Hemodynamic variables were recorded from pre-operative period to 10 minutes after intubation. : There were no significant escalation in the hemodynamic changes in during laryngoscopy and orotracheal intubation in the Test group, compared to the control group . Minimal raise also returned to baseline within a minute. Ivabradine is useful to prevent abnormal increase in heart rate and minimizes hypertension seen during laryngoscopy and endotracheal intubation.

2) Kunwar et al (34) in 2016 evaluated the role oral Ivabradine on haemodynamics during laryngoscopy and intubation of trachea during general anaesthesia.They conducted the study in 50 ASA grade-I patients undergoing various procedures under general anaesthesia in two groups 25 each. Received oral Ivabradine 5mg one Tab. at 9.00 pm on the evening before the day of surgery and another one hour before intubation and the placebo. The result

was haemodynamic parameters were more stable in ivabradine is compared to Control group. Ivabradine is extremely useful drug to prevent the abnormal increase in rate of heart& blood pressure in the process of direct laryngoscopy and endotracheal intubation.

3) Couvreur et al(35) in 2010 was investigated that alterations of left ventricular work load and calcium control to prolonged heart rate reduction with ivabradine in reperfused heart .Rabbits were underwent occlusion of coronary artery for 20 minutes and reperfusion 0f heart was done for 3 weeks. For the period of reperfusion, rabbits received ivabradine (10 mg/kg/day) or placebo (Control). Ivabradine decreased heart rate by around 20% and improved both +35% of ejection fraction&26% of systolic displacement after the interval of 3 weeks of treatment. Injection of a single i.v.bolus of ivabradine (1 mg/kg) in control group of rabbits at 3 weeks interval of reperfusion also considerably enhanced ejection fraction & systolic displacement. Prolonged heart rate drop protects the myocardium contrary to ventricular dysfunction stimulated by myocardial ischemia followed by 3 weeks duration of reperfusion. Along with heart rate control, ivabradine has improved global and regional contractile function of the reperfused heart over a double mechanism concerning a direct mechanical influence and a long-term tolerance in calcium handling.

4) Cappato et al(36) in (2012) in have evaluated “ the role of ivabradine in the treatment of symptomatic inappropriate sinus tachycardia

using ivabradine" .Because of its funny current channel blocking properties, selectively mitigate the high release of rate from S.A nodal cells in patients with increased heart rate. Twenty-one patients have been randomly divided in to 2 group. One group received placebo drug (10 patients) or ivabradine 5 mg 2 times daily (10 patients)over a period of 6 weeks. After 6 weeks duration, patients underwent symptom assessment and heart rate assessment at beginning and end of each phase. Ivabradine group patients, relieved of symptoms of around 70%& with 47% of them felt whole elimination. These effects were accompanied with a significant decrease in heart rate at rest. .

5) A.G.Shirbman et al (37) in 1987 ("The catecholamine and cardiovascular responses to laryngoscopy"). This study evaluated the effect of direct laryngoscopy &endotracheal intubation. This study was conducted in24 patients were randomly divided into two groups. Premeditated with Inj. fentanyl and induced with Inj. thiopentone sodium, Inj. atracurium was injected and artificial ventilation given via anatomical face mask for 2 minutes with 67% of nitrous oxide with 33% oxygen. Subsequent to direct laryngoscopy, the vocal cords had been visualized for the duration of 10 seconds. "Arterial pressure, heart rate and plasma noradrenaline and adrenaline concentrations were measured before and after induction and at 1, 3 and 5 min after laryngoscopy". Increases in arterial pressure & elevated concentrations of circulating catecholamine were found during laryngoscopy

with or without intubation. Intubation was associated with significant increases in heart rate. There was no change in the laryngoscopy group.

6) Sanjeev Singh et al(38) in 2013 evaluated " the efficacy and safety of esmolol and lidocaine for suppressing cardiovascular response to laryngoscopy and tracheal intubation in a normotensive African population".. This study was evaluated in 120 adult patients. They were ASA physical status I or II and posted for elective surgeries .Divided them into three groups, about 40 patients in each group. First group patients has received no drug (control) as placebo, another group received 1.5 mg /kg I.V.Lignocaine and the third group received Inj.esmolol IV 2 mg/ kg 2 minutes prior to intubation. Mean arterial pressure and rate-pressure product were measured at preoperatively as baseline and after intubation at 1, 3, and 5minutes respectively.. After induction of with inj.thiopentalsodium and vecuronium bromide, the test solution was injected 2 min before endotracheal intubation. Alterations in haemodynamics were recorded .There was a rise in HR, SBP, DBP, MAP, and RPP from the base line in control group at 1 min with onward declines at 3 and 5 min respectively after intubation. They concluded that Esmolol in the dose of 2 ml/kg can be given prophylactically to blunt the cardiovascular response to endotracheal intubation.

7) Shruthi Jain et al (39) in 2015 investigated that Intravenous (IV) Lignocaine in bolus dose during perioperative period was infused to blunt haemodynamic variations pertaining to intubation as well as extubation in

elective laparoscopic cholecystectomies. This study was carried out in 60 patients were divided into two groups of 30 each& gave bolus of 6 ml normal saline over 10 minutes duration followed by infusion of the same at 6ml/hr. and 2% lignocaine 1.5 mg/kg IV bolus (diluted to a volume of 6 ml with normal saline) for 10 minutes and after that an infusion at a rate of 1.5 mg/kg/h The increase in heart rate and M.A.P are minimal in i.v .lignocaine group. ($P < 0.05$) during endotracheal intubation and during extubation. There was extended pain-less post-op duration of 5½ h as compared to 54.43 min in normal saline group ($P < 0.05$).

8) Gulabaní et al (40) in 2015 compared the efficacy of lignocaine with two different doses of dexmedetomidine for attenuating the haemodynamic changes. They conducted the study in 90 adults in the age group of 18-65 years of both sexes, were normotensives assessed as ASA Grade I or II, Divided into three groups. Group D1- IV Dexmedetomidine 0.5μg/kg over 10 minutes, Group D2- IV Dexmedetomidine 1μg/kg over 10 minutes and Group X- preservative free Lignocaine 1.5mg/kg diluted in 10 ml normal saline. They conclude that dexmedetomidine 1μg/kg adequately attenuated the cardiovascular response to direct laryngoscopy and endotracheal intubation when matched with dexmedetomidine 0.5μg/kg and lignocaine 1.5mg/kg.in pressor response to laryngoscopy and endotracheal intubation (ETI).

9) Malde and sarode et al (41) in 2006 conducted a study to evaluate the effectiveness of Fentanyl (2µg/kg) - single bolus dose/intravenous Lignocaine (1.5 mg/kg) for attenuation haemodynamic changes in 90 patients. They received fentanyl /lignocaine / saline 5 minutes prior to endotracheal intubation.

The fentanyl group showed minimal increase in heart rate compared to lignocaine and Control group. The rise heart was persisted upto10 min in fentanyl, lignocaine & control groups respectively. The lignocaine group had minimal rise in systolic BP (12.1%) when compared to Control group (25.8%) (p=0.000) at endotracheal intubation& remained for 3 &10 minutes in both groups. The fentanyl group significantly reduced systolic BP after injection, which return back to normal at 1 - 3 minutes following endotracheal intubation and once again reduced after 4 minutes of endotracheal intubation. There was no side effects were noted in both groups. They concluded that "Lignocaine attenuated the rise in blood pressure with intubation whereas fentanyl prevented it totally".

10) Sarvesh P.sing et al (42) in 2010 evaluated the" efficacy of esmolol and labetalol, in low doses, for attenuation of sympathomimetic response to laryngoscopy and intubation." This study was conducted in 75 ASA physical status I and II adult patients, (18-45 yrs.) posted for elective surgeries and who required G.A and endotracheal intubation in three groups (25 each).Group C (control) 10 ml 0.9% saline i.v Group E (esmolol) 0.5

mg/kg added normal saline to make 10 ml i.v and Group L (labetalol) 0.25 mg/kg added with normal saline to make10 ml i.v In the control group 10 ml of 0.9% saline was given both at 2 &5 min respectively before endotracheal intubation. In the esmolol group 0.5 mg/kg of esmolol was given 2 minutes before and 10 ml of 0.9% saline 5 min before intubation. In the labetalol group 10 ml of normal saline was administered 2 min before and 0.25 mg/kg of labetalol 5 min before endotracheal intubation. All the participants were exposed to the same standard anesthetic technique .Changes in haemodynamics have been recorded prior to induction, at time of endotracheal intubation and 1, 3, 5, and 10 min after intubation. M.A.P.and RPP were calculated. They also recorded abnormal ECG changes .They found that" esmolol (0.5 mg/kg), labetalol (0.25 mg/kg) significantly attenuated the rise in heart rate, systolic blood pressure, and RPP during laryngoscopy and intubation" and they are not statistically significant among the values for DBP and MAP in lower doses. They concluded that labetalol (0.25 mg/kg) better drug than esmolol (0.5mg/k 0 in attenuating the sympathomimetic response to direct laryngoscopy and endotracheal intubation.

AIM OF THE STUDY

To compare the efficacy of oral ivabradine and intravenous lignocaine to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation

MATERIALS AND METHODS

The study was conducted at Chengalpattu medical college between 2015- 2016. After obtaining ethical committee approval, 100 ASA I adult patients undergoing surgical procedures under general anaesthesia are randomly allotted into two groups

STUDY DESIGN: A Prospective randomized study

SAMPLE SIZE: 100 patients were selected and allocated in two groups Randomly. 50 patients in each group.

INCLUSION CRITERIA:

- ASA -I patients who were posted for various procedures under G.A.
- Age group -20-45 years
- Both sexes
- Normal ECG
- Mallampatti grading I&II

EXCLUSION CRITERIA:

- Patient Refusal
- H/0 Chest pain /palpitations/syncope/H/o Respiratory problems,
- Hepatic or renal problems

- Base line HR<60, base line systolic BP <100 mm Hg.
- Patients with ECG abnormality
- Patients with difficult airway

PRE OP PREPARATION:

On the day of surgery Patients who satisfy the inclusion criteria were selected, written Informed consent obtained from all the patients. Preoperative evaluation including detailed history, clinical evaluation, investigations and airway assessment were done. Intravenous canulation was done with 18G cannula after shifting the patient into the waiting area of the operation theater, and connected to a drip of Ringers lactate.

PREMEDICATION:

Inj. Glycopyrrolate 0.2 mg I.M 45 Minutes before surgery and Inj. Ondensetron 4 mg sloe I.V and Inj. Fentanyl 2µg/kg before induction.

MATERIALS USED:

- Laryngoscope, Macintosh laryngoscope blades size 3&4
- Appropriate size cuffed endotracheal tubes
- Inj. Thiopentone Sodium 500mg vial
- Inj. Succinylcholine 500 mg vial
- Inj.Atracurium 25 mg ampule

- Inj.Lignocaine preservative free
- Tab. Ivabradine 5 mg

METHODOLOGY

Patients were randomly allocated into two groups, Test and Control [having 50 patients in each group]

GROUP- I: received oral Ivabradine 5 mg one tab 2 hour before intubation and received 5 ml of normal saline 90 seconds before intubation.

GROUP-II: received Tab.B Complex 2 hours before intubation& I.V. Lignocaine 1.5 mg/kg 90 seconds before induction

These drugs were given by the anesthesiology residents who were not included in this study.

Monitoring:

Continuous ECG, automated intermittent noninvasive blood pressure monitoring, Spo2 monitoring done.

Pre oxygenation: 100% o2 for 3 min.

Induction:

Inj.Thiopentone sodium 5 mg/kg I.v and succinylcholine 2 mg/kg I v. Inj .Lignocaine 1.5 mg/kg I.V (groupII). & Normal saline5ml (group I) given 90 seconds before intubation.

Intubation:

after 120 min intubation was achieved with appropriate size cuffed, endotracheal tube by the aid of Macintosh laryngoscope blade. Time for intubation did not exceed 20 sec.

Maintenance:

Atracurium bisylate 0.5 mg/kg top-up dose. N2O:O2 in 2:1, intermittent positive pressure ventilation using circle absorber system connected to the Boyles machine. Surgery was not allowed to commence till the recordings were completed up to 10 min.

Parameters recorded were heart rate, systolic BP, diastolic BP, Mean arterial pressure. Ten minutes after intubation, after taking the recordings of hemodynamic parameters, inhalational agent was introduced into the anesthetic technique.

Reversal:

Inj.Neostigmine 0.05 mg/kg and Inj.Glycopyrrolate 0.01 mg/kg. All patients were monitored for adverse effect effects of ivabradine in post op period. The recordings were noted at

- preoperative (after premedication)
- At induction
- At intubation

- 1 min after intubation
- 3min after intubation
- 5min after intubation
- 8 min after intubation
- 10 min after intubation.
- 30 min after intubation
- 1 hour after intubation
- 2 hours after intubation
- 4 hours after intubation
- 6 hours after intubation
- 12 hours after intubation

STATISTICAL ANALYSIS

Data were analyzed using SPSS16.0V.Software. Two sided independent students' t tests to analyze continuous data and chi square test for categorical data were used. P<0.05 was considered as statistically significant.

DEMOGRAPHIC DATA

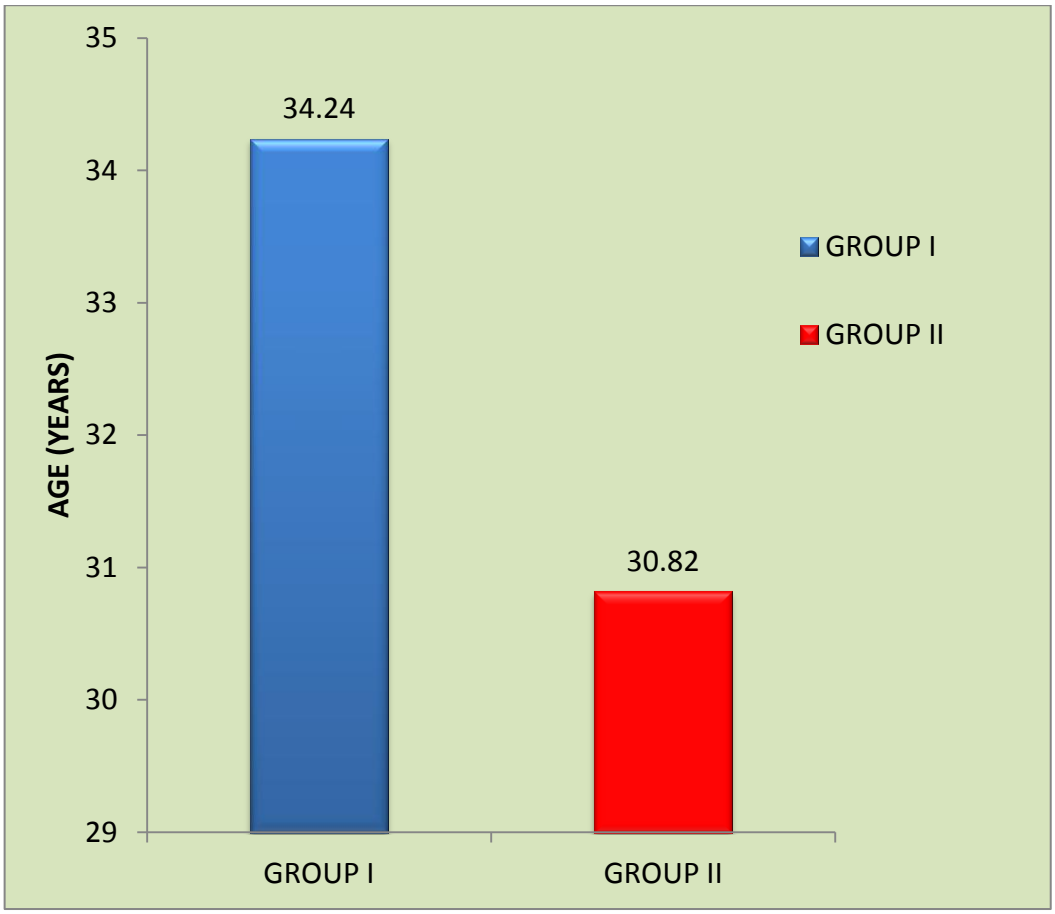
The two groups were comparable with respect to their age, weight, sex. There is no statistically significant difference among two groups in demographic profile.

AGE

	GROUP	N	Mean	Std. Deviation	p value
AGE	Group I	50.00	34.24	9.290	0.058
	Group II	50.00	30.82	8.535	

The mean age in years was 34.24± 9.290 (Years) in group I and 30.82 ± 8.535 (Years) in group II. There was statistically no significant difference between two groups (p>0.05)

AGE


35
34
33
32
31
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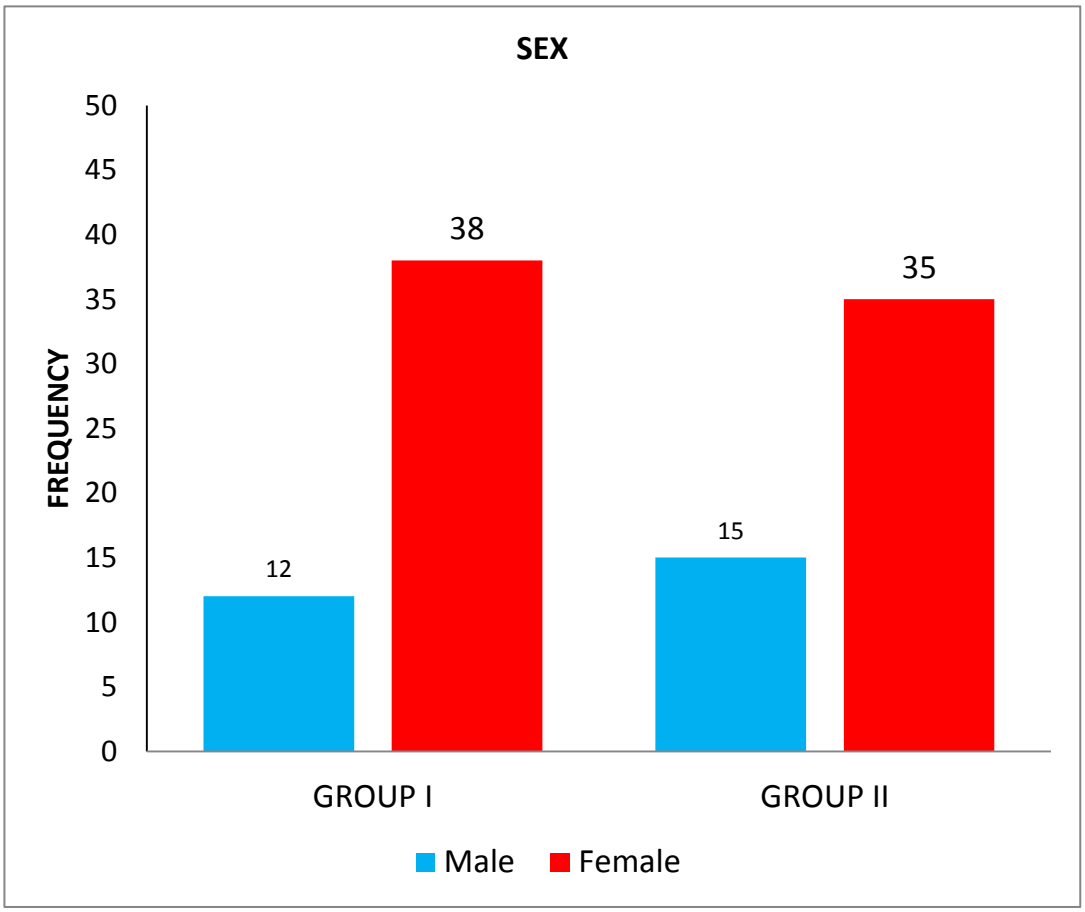
29
AGE (YEARS)
34.24
30.82
GROUP I
GROUP II
GROUP I
GROUP II

SEX DISTRIBUTION

	Group I	Group II
Male	12	15
Female	38	35

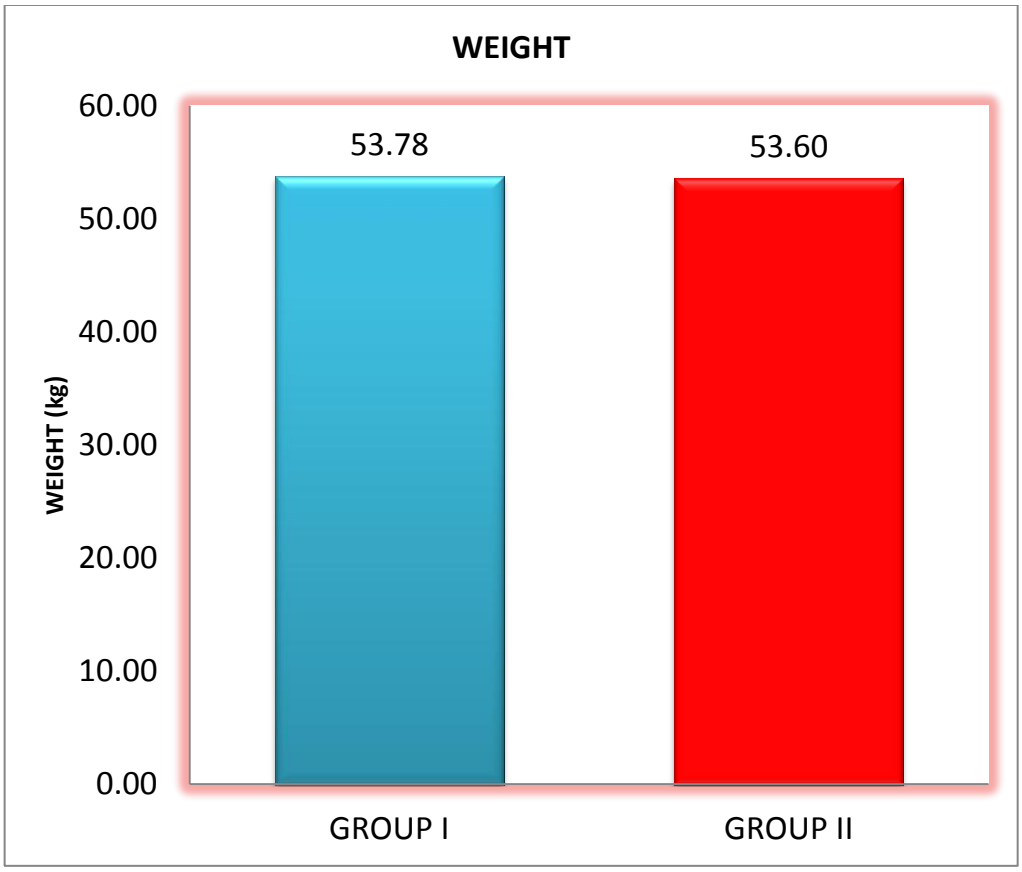
In our series of 100 patients 27 were male and73 were females.



WEIGHT

	GROUP	N	Mean	Std. Deviation	P value
WEIGHT	Group I	50.00	53.78	4.705	0.830
	Group II	50.00	53.60	3.580	

In our study mean Weight in kilograms was 53.78±4.705 (Kg) in group 1 and53.60 ± 3.580(Kg) in group 2. There was statistically no significant difference between two groups(p>0.05)

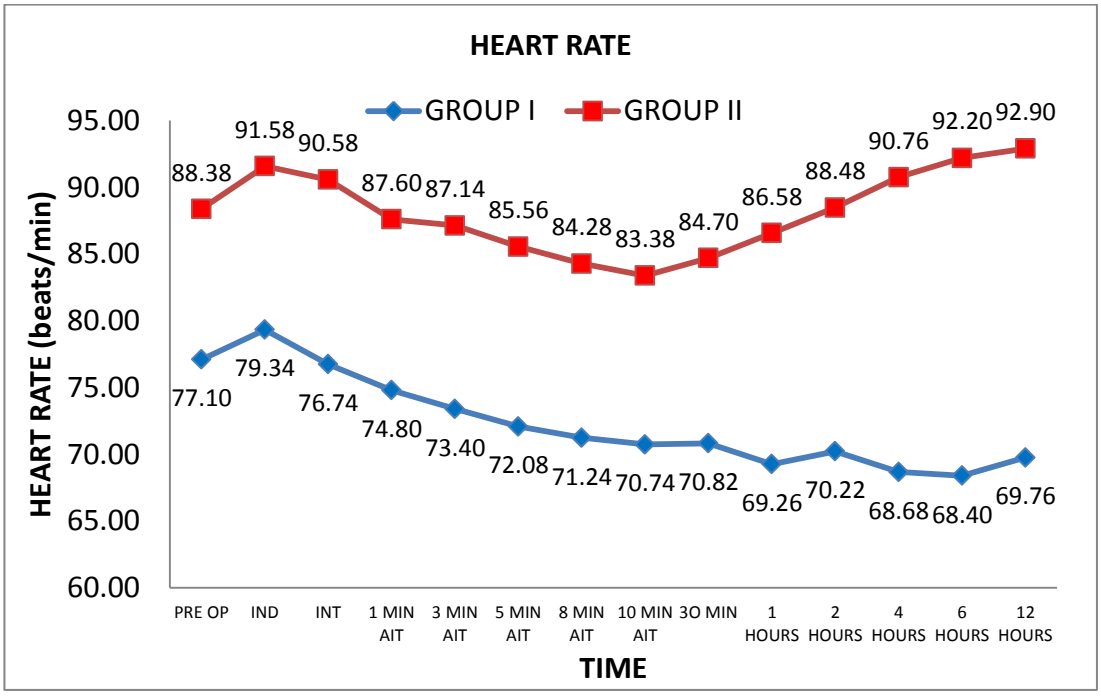


HEART RATE

	GROUP	N	Mean	Std. Deviation	p value
PRE OP	Group I	50.00	77.10	7.947	<0.0001
	Group II	50.00	88.38	7.214	
AT INDUCTION	Group I	50.00	79.34	7.657	<0.0001
	Group II	50.00	91.58	6.737	
AT INTUBATION	Group I	50.00	76.74	7.575	<0.0001
	Group II	50.00	90.58	6.795	
1MIN AIT	Group I	50.00	74.80	7.426	<0.0001
	Group II	50.00	87.60	9.532	
3MIN AIT	Group I	50.00	73.40	7.253	<0.0001
	Group II	50.00	87.14	6.612	
5MINAIT	Group I	50.00	72.08	7.182	<0.0001
	Group II	50.00	85.56	6.181	
8 MIN AIT	Group I	50.00	71.24	7.061	<0.0001
	Group II	50.00	84.28	6.331	
10 MIN AIT	Group I	50.00	70.74	6.866	<0.0001
	Group II	50.00	83.38	5.966	
30 MIN	Group I	50.00	70.82	6.492	<0.0001
	Group II	50.00	84.70	5.776	
1 HOUR	Group I	50.00	69.26	11.091	<0.0001
	Group II	50.00	86.58	5.786	
2HOUR	Group I	50.00	70.22	6.254	<0.0001
	Group II	50.00	88.48	6.004	

	GROUP	N	Mean	Std. Deviation	p value
4HOUR	Group I	50.00	68.68	10.580	<0.0001
	Group II	50.00	90.76	5.546	
6HOUR	Group I	50.00	68.40	10.508	<0.0001
	Group II	50.00	92.20	5.322	
12HOUR	Group I	50.00	69.76	6.150	<0.0001
	Group II	50.00	92..90	5.471	

In our series. The mean heart rate of all patients in both groups were calculated and compared from pre- operative to up to 12 hours post-operatively. The change in heart rate in group I and group II were statistically significant.

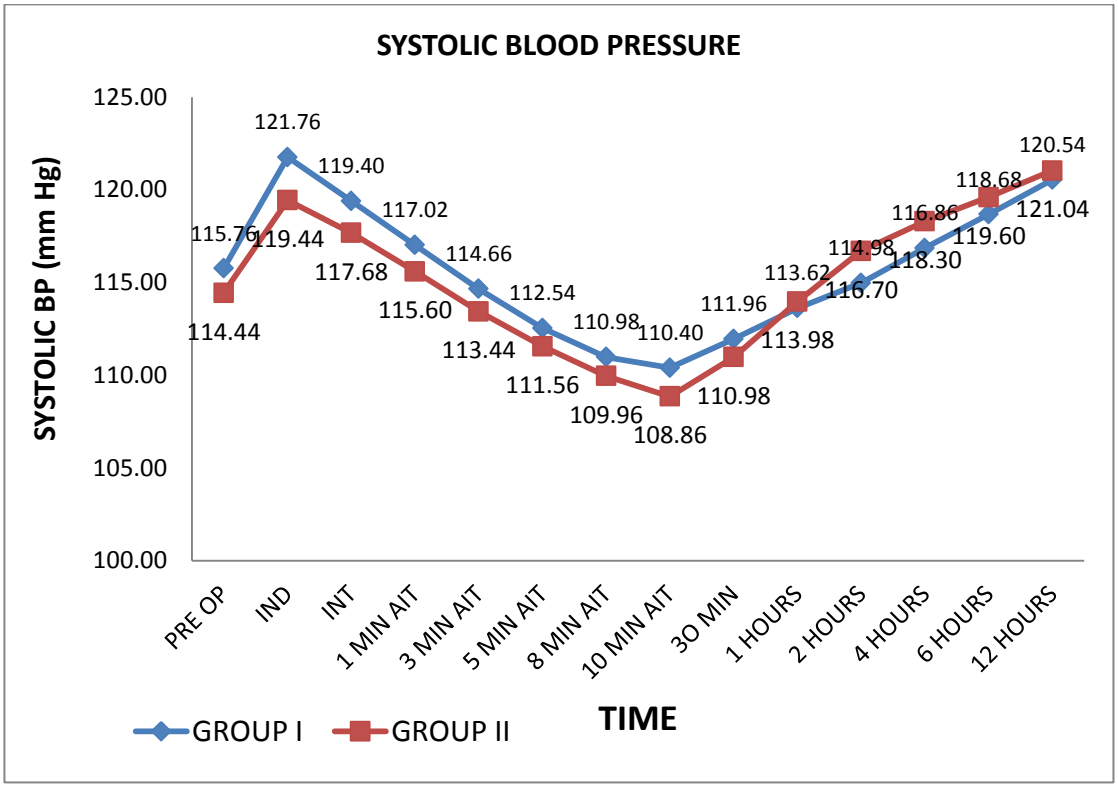


SYSTOLIC BLOOD PRESSURE

	GROUP	N	Mean	Std. Deviation	P value
PRE OP	Group I	50.00	115.76	6.620	0.362
	Group II	50.00	114.44	7.752	
AT INDUCTION	Group I	50.00	121.76	6.793	0.108
	Group II	50.00	119.44	7.506	
AT INTUBATION	Group I	50.00	119.40	6.540	0.226
	Group II	50.00	117.68	7.542	
1MIN AIT	Group I	50.00	117.02	6.653	0.327
	Group II	50.00	115.60	7.722	
3MIN AIT	Group I	50.00	114.66	6.675	0.392
	Group II	50.00	113.44	7.500	
5MINAIT	Group I	50.00	112.54	6.584	0.479
	Group II	50.00	111.56	7.180	
8 MIN AIT	Group I	50.00	110.98	6.268	0.450
	Group II	50.00	109.96	7.140	
10 MIN AIT	Group I	50.00	110.40	6.273	0.254
	Group II	50.00	108.86	7.120	
30 MIN	Group I	50.00	111.96	5.938	0.442
	Group II	50.00	110.98	6.720	
1 HOUR	Group I	50.00	113.62	5.678	0.763
	Group II	50.00	113.98	6.206	
2HOUR	Group I	50.00	114.98	5.408	0.119
	Group II	50.00	116.70	5.534	
4HOUR	Group I	50.00	116.86	5.718	0.179
	Group II	50.00	118.30	4.883	

6HOUR	Group I	50.00	118.68	5.332	0.348
	Group II	50.00	119.60	4.375	
12HOUR	Group I	50.00	120.54	5.338	0.605
	Group II	50.00	121.04	4.242	

In our study series, mean systolic blood pressure was raised during induction and returned to preoperative level within 3 minutes of after intubation. Mean systolic pressures were within normal limits. There was statistically no significant difference between two groups (p>0.05)

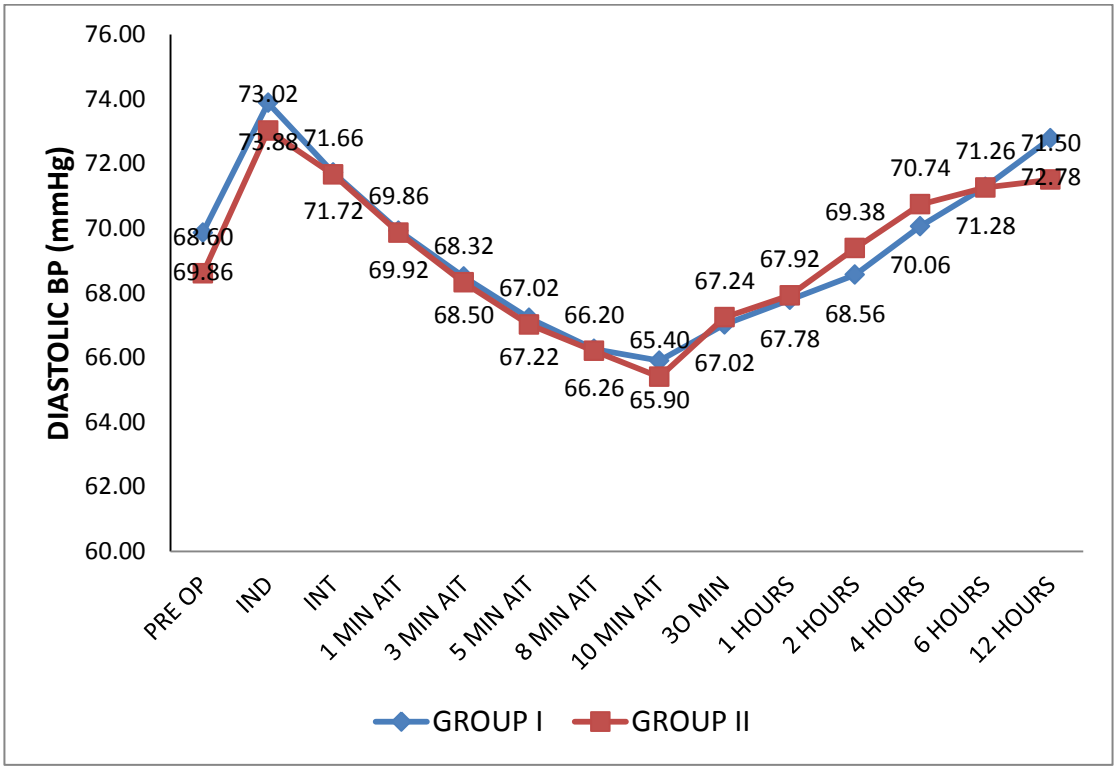


DIASTOLIC BLOOD PRESSURE

	GROUP	N	Mean	Std. Deviation	P value
PRE OP	GROUP I	50.00	69.86	5.548	0.334
	GROUP II	50.00	68.60	7.301	
INDUCTION	GROUP I	50.00	73.88	5.610	0.503
	GROUP II	50.00	73.02	7.100	
INTUBATION	GROUP I	50.00	71.72	5.620	0.963
	GROUP II	50.00	71.66	7.050	
I MIN AIT	GROUP I	50.00	69.92	5.721	0.963
	GROUP II	50.00	69.86	6.966	
3 MIN AIT	GROUP I	50.00	68.50	5.779	0.888
	GROUP II	50.00	68.32	6.915	
5 MIN AIT	GROUP I	50.00	67.22	5.604	0.873
	GROUP II	50.00	67.02	6.784	
8 MIN AIT	GROUP I	50.00	66.26	5.268	0.960
	GROUP II	50.00	66.20	6.676	
10 MIN AIT	GROUP I	50.00	65.90	5.108	0.675
	GROUP II	50.00	65.40	6.673	
30 MINS	GROUP I	50.00	67.02	5.332	0.862
	GROUP II	50.00	67.24	7.170	
1 HOUR	GROUP I	50.00	67.78	5.549	0.908
	GROUP II	50.00	67.92	6.490	
2 HOURS	GROUP I	50.00	68.56	5.350	0.476
	GROUP II	50.00	69.38	6.094	

4 HOURS	GROUP I	50.00	70.06	5.024	0.545
	GROUP II	50.00	70.74	6.107	
6HOURS	GROUP I	50.00	71.28	5.507	0.986
	GROUP II	50.00	71.26	6.141	
12HOURS	GROUP I	50.00	72.78	5.144	0.255
	GROUP II	50.00	71.50	6.011	

In our study series, mean diastolic blood pressure was raised during induction and returned to preoperative level within 3 minutes of after intubation. Mean diastolic pressures were within normal limits. There was statistically no significant difference between two groups (p>0.05)

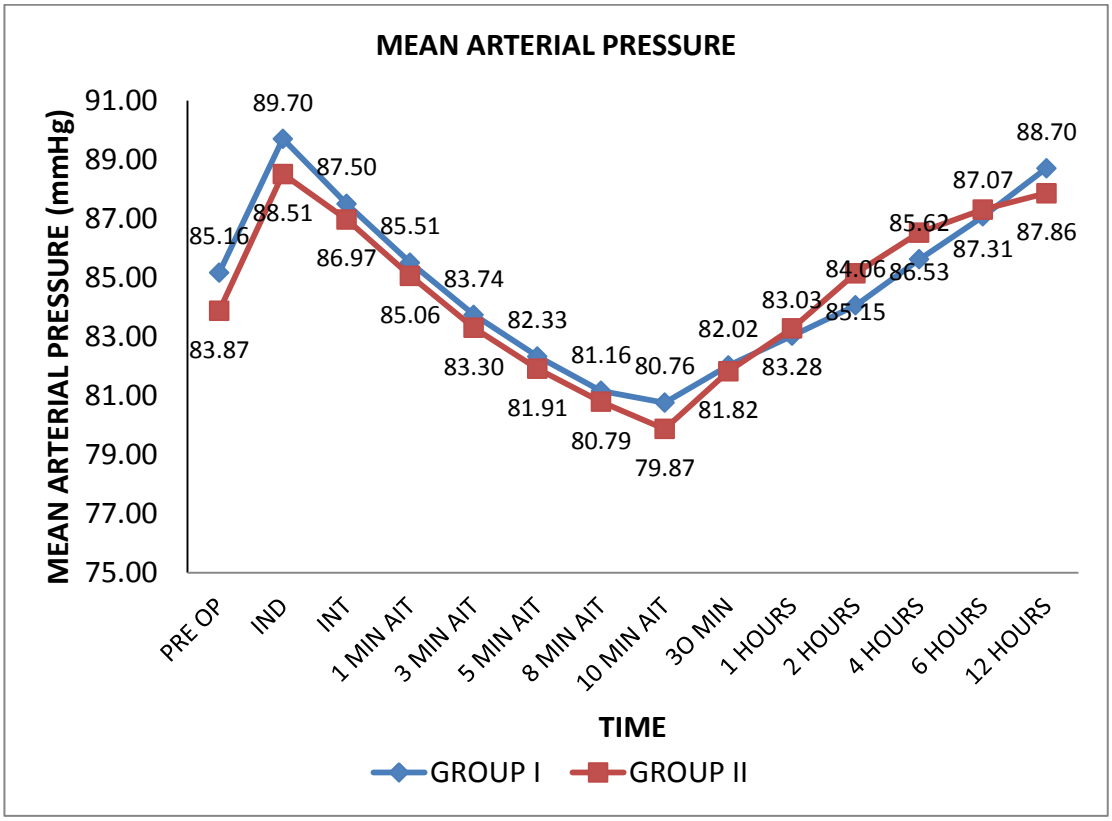


MEAN ARTERIAL PRESSURE

	GROUP	N	Mean	Std. Deviation	P value
PRE OP	GROUP I	50.00	85.16	4.792	0.279
	GROUP II	50.00	83.87	6.869	
INDUCTION	GROUP I	50.00	89.70	5.064	0.313
	GROUP II	50.00	88.51	6.588	
INTUBATION	GROUP I	50.00	87.50	5.025	0.648
	GROUP II	50.00	86.97	6.568	
I MIN AIT	GROUP I	50.00	85.51	5.058	0.704
	GROUP II	50.00	85.06	6.499	
3 MIN AIT	GROUP I	50.00	83.74	5.484	0.713
	GROUP II	50.00	83.30	6.420	
5 MIN AIT	GROUP I	50.00	82.33	5.004	0.714
	GROUP II	50.00	81.91	6.275	
8 MIN AIT	GROUP I	50.00	81.16	4.737	0.736
	GROUP II	50.00	80.79	6.117	
10 MIN AIT	GROUP I	50.00	80.76	4.654	0.416
	GROUP II	50.00	79.87	6.140	
30 MINS	GROUP I	50.00	82.02	4.770	0.863
	GROUP II	50.00	81.82	6.334	
1 HOUR	GROUP I	50.00	83.03	4.793	0.812
	GROUP II	50.00	83.28	5.643	

2 HOURS	GROUP I	50.00	84.06	4.717	0.274
	GROUP II	50.00	85.15	5.164	
4 HOURS	GROUP I	50.00	85.62	4.678	0.360
	GROUP II	50.00	86.53	5.153	
6HOURS	GROUP I	50.00	87.07	4.863	0.815
	GROUP II	50.00	87.31	5.089	
12HOURS	GROUP I	50.00	88.70	4.479	0.378
	GROUP II	50.00	87.86	5.028	

In our study series, mean arterial pressures were elevated. There was statistically no significant difference between two groups (p>0.05)



DISCUSSION

Rapid and dramatic hemodynamic changes are adversely affecting the patient. It may occur during perioperative period. Hypertension and tachycardia have been recognized since 1950's as commonly associated with intubation under light anaesthesia and is most evident during laryngoscopy and manipulation of epiglottis. The effect is temporary arising in 30 seconds after endotracheal intubation and lasts for less than 10 minutes thereafter.

Sympathetic response to laryngoscopy has been studied and managed in past by topical anaesthesia of pharynx, superior laryngeal nerve block, tracheal spray of lignocaine, increasing the depth by inhalational agents, alpha and beta blockers, both alpha and beta blockers e.g. Labetalol, Nitroprusside, Calcium channel blockers, Nitroglycerine and strong narcotics etc.

"King et al in 1951 described pressor response to laryngoscopy and intubation in anaesthetised patients" (1)

In the present study, oral Ivabradine and intravenous Lignocaine were used to attenuate the haemodynamics. Blood pressure and heart rate response to direct laryngoscopy and endotracheal intubation was studied in both the groups. The pre-induction parameters of haemodynamic (i.e. after premedication) values were taken as basal values. After induction and intubation the surgeon was not allowed to operate till ten minutes (duration of

observation) because ivabradine has no analgesic properties and skin incision could have raised the heart rate and blood pressure giving false result.

Heart Rate:

In our study, oral ivabradine reduces heart rate significantly than intravenous Lignocaine. Mean heart at intubation in oral ivabradine group (group I) was 76.74 ±7.575, whereas in group II mean heart rate at intubation was about 90.58± 6.795.

C. G. Raghu ram, Deep raj Singh, Aditya Vikram Kabra (1) observed that there was not a very significant rise in the heart rate in response to direct laryngoscopy and endotracheal intubation in ivabradine group, when compared to the control group. There was a raise in heart rat returned to baseline within a minute. In the control group the baseline reading was high and the increase in pulse rate though decreased was above the normal value.

Kunwar et al (34) concluded that Ivabradine is a useful drug to blunt the abnormal increase in heart rate &blood pressure during direct laryngoscopy and endotracheal intubation.

Blood Pressure:

In our study, mean systolic blood pressure in group I is 119 ± 6.540 mmHg during intubation and returned to normal within 3 minutes. In

group II mean systolic blood pressure is 117.68 ± 7.542 & returned to normal within a minute. But there was no statistical significance between two groups.

The mean diastolic pressure during intubation is 71.72 ± 5.620 in group I and 71.66±7.050 in group II . There is a small raise in diastolic pressure during induction and come to base line within 3 minutes.

The mean arterial pressure during intubation is 87.50±5.025 in group I an86.97±6.56in group II. Mean arterial pressure was mildly elevated in both groups. There was no statistically significant change mean arterial pressure in both groups.

C. G. Raghu ram, Deep raj Singh, Aditya Vikram Kabra (1)found that oral Ivabradine minimizes hypertension during laryngoscopy and endotracheal intubation.

Kunwar et al (34) evaluated that haemodynamic parameters were more stable in ivabradine and also it prevents abnormal increase in heart rate & blood pressure during direct laryngoscopy and endotracheal intubation.

Shruthi Jain et al (39) found that the increase in pulse rate &mean arterial pressure are less in i.v .lignocaine group during intubation as well as extubation.

Malde and sarode et al(41) evaluated the efficacy of single bolus doses of Fentanyl (2µg/kg) or Lignocaine (1.5 mg/kg) for attenuation haemodynamic

response that Lignocaine blunt the increase in blood pressure with endotracheal intubation. But fentanyl prohibited it totally.

Gulabaní et al (40) compared the efficacy of lignocaine with two different doses of dexmedetomidine for attenuating the pressor response and concluded that dexmedetomidine 1μg/kg adequately attenuated the hemodynamic response to laryngoscopy and endotracheal intubation when compared with dexmedetomidine 0.5μg/kg and lignocaine 1.5mg/kg.

C .D. Miller and S .J .Warren (43) used intravenous lignocaine to blunt the cardiovascular responses to direct laryngoscopy and endotracheal intubation. There was no significant change in haemodynamics in I.V. Lignocaine group in that study.

SIDE -EFFECTS:

All the patients in the study group were monitored for 12 hours. There were no side effects were found in the patients.

SUMMARY

"This Prospective randomised study was conducted to compare the effect of oral ivabradine and i.v lignocaine on the haemodynamics during laryngoscopy and endotracheal intubation in patients undergoing surgical procedures under general anaesthesia in 100 patients.50 patients in each group. Premedication, induction agent and muscle relaxant to facilitate intubation were standardized for both the groups.

In both groups surgery was not allowed for 10 minutes till the recordings were completed. Changes in heart rate, systolic blood pressure, diastolic blood pressure &mean arterial pressure were monitored.

According to this study significant changes in heart rate were observed. Heart Rate: Group I (oral Ivabradine) patients showed statistically significant change Heart rate.

Blood Pressure: There was no statically significant change in blood pressure in both Groups. And also these patients were monitored post – operatively for upto 12 hours. Side effects like bradycardia and visual disturbances were not found in the patients.

Advantages of oral Ivabradine in this study is

- Good attenuation of heart rate response

- There was good heart rate control during perioperative period.
- There was good heart reduction during extubation also.
- The drug has minimal side effects. No side effects were observed during the study.
- The drug is easily available& easy to administer.

CONCLUSION

To conclude that oral Ivabradine has better heart rate control than Intravenous Lignocaine for attenuation of haemodynamics during laryngoscopy and endotracheal intubation in ASA I patients without side effects.

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GLOSSARY:

- PR Pulse Rate
- HR Heart Rate
- M.A.P Mean Arterial Pressure
- SBP Systolic Blood Pressure
- DBP Diastolic Blood Pressure
- NIBP Non invasive Blood Pressure
- CVS Cardiovascular System
- RS Respiratory System
- CNS Central Nervous System
- WT Weight
- Kg Kilogram
- Ml Milliliter
- I.M Intra muscular
- I.V. Intra Venous
- Mg Milligram
- ASA American Society of Anaesthesiologist
- MPC Mallampatti Classification
- AIT After Intubation

PROFORMA

- Name :
- Age /sex:
- IP no :
- Date of admission :
- Date of surgery :
- Address for communication:
- Contact no:
- Diagnosis :
- Surgery :
- Weight :
- PR:
- BP:
- CVS:
- RS:
- ABDOMEN:
- CNS:
- Mallampati classification class:
- ASA PS class :
- Investigations :
  - ✓ Hb:
  - ✓ TC
  - ✓ DC

- ✓ Platelets
- ✓ RFT:
- ✓ Urine routine:
- ✓ ECG:
- ✓ CXR:
- ✓ Electrolytes:
- ✓ Others :

❖ Premedication :

❖ Pre oxygenation:

❖ Induction drugs given :

❖ Intubation:

❖ Hemodynamic monitoring :PR , Systolic BP ,Diastolic BP ,Mean arterial BP are recorded at

TIME	PR	Systolic BP	Diastolic BP	Mean Arterial Pressure
Preoperative				
At induction				
At Intubation				
1min AIT				
5min AIT				
8min AIT				
10min AIT				
30min AIT				
1 Hour				
2 Hours				

4 Hours				
6 Hours				
12 Hours				

- ❖ Maintenance:
- ❖ Relaxation:
- ❖ Reversal:
- ❖ Extubation
- ❖ Other side effects:

சுயஒப்புதல்படிவம்

ஆய்வுசெய்யப்படும்தலைப்பு : மூச்சுகுழாய்குள் செயற்கை மூச்சுக்குழல் பொருத்தும் பொழுது ரத்த ஓட்டத்தில் ஏற்படும் மாறுதல்களை குறைப்பதில் இவாபிராடின் மற்றும் லிக்னொகெயின் மருந்துகளை தொலைநோக்கு ஆராய்ச்சியில் ஒப்பிட்டு பார்த்தல்

ஆய்வுசெய்யப்படும்இடம்:

பங்குபெறுபவரின்பெயர்:

பங்குபெறுபவரின்வயது: **பங்குபெறுபவரின்எண் :**

மேலேகுறிப்பிட்டுள்ளமருத்துவஆய்வின்விவரங்கள்எனக்குவிளக்கபட்டுள்ளது.நான்இவ்வாய்வில்தன்னிச்சையாகபங்கேற்கின்றேன்.எந்த காரணத்தினாலோ, எந்தசட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில்இருந்து விலகிக்கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதைசார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர், என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவை இல்லை என அறிந்து கொள்கிறேன். இந்தஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ளமறுக்க மாட்டேன். இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்: **சாட்சியாளரின் கையொப்பம்**

இடம்: **இடம்:**

தேதி: **தேதி :**

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்:

ஆய்வாளரின் கையொப்பம்:

இடம்: **தேதி:**

GROUP-I (ORAL IVABRABINE)

S.NO.	NAME	AGE/SEX	IP NO	WEIGHT	DIAGNOSIS	HEART RATE PREOP	IND	INTU	1 MIN AIT	3MIN AIT	5MIN AIT	8MIN AIT	10MIN AIT	30MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT
1	Shankaran	43/M	14652	60Kgs	Lf lateral canthus soft tissue loss	80	82	80	78	77	75	74	74	75	75	75	75	75	75
2	Gokulakrishnan	45/M	13783	59 kgs	Rt.lateral canthus soft tissue loss	84	88	86	82	80	79	77	76	74	74	74	74	74	73
3	Sivathanu	38/M	15077	54Kgs	Lt.Eye ectropion	74	78	75	73	71	70	69	69	70	70	70	70	69	69
4	Guru	33/M	14400	55Kgs	Lf lateral canthus soft tissue loss	88	91	87	85	84	83	81	80	80	78	78	78	78	78
5	Udhayakumar	20/M	16839	56kgs	subacute appendicitis	67	70	68	66	65	63	63	62	65	65	65	65	65	65
6	Malliga	45/F	17281	49Kgs	Solitary nodular goitre Lt Lobe	65	68	66	64	63	62	60	60	60	60	60	60	60	60
7	Ramya	25/F	17748	47Kgs	Fibroadenoma Lt.Breast	70	75	71	69	68	66	64	63	65	65	65	65	65	66
8	Kala	45/F	17914	52	Carcinoma Lt.Breast	83	85	81	78	75	73	70	70	70	70	70	70	70	73
9	Kanniyamma	45/F	15387	57	SOlitary nodular goitre Rt Lobe	60	63	61	60	59	58	58	58	60	60	60	60	60	60
10	Logumary	45/F	17268	59	Multi nodular goitre	92	93	89	87	86	85	84	83	85	85	85	83	8	83
11	Vanitha	30/F	18544	46	Fibroadenoma Rt.Breast	72	75	73	72	71	69	68	68	68	68	70	70	70	70
12	Maharajan	35/M	18556	59	Recurrent appendicitis	62	63	60	59	59	58	58	58	60	60	60	60	58	58
13	Padmavathy	33/F	18967	62	Fibroadenoma Lt.Breast	87	89	87	85	83	82	81	80	80	80	80	8	80	79
14	Usha	30/F	20003	43	Fibroadenoma Lt.Breast	82	84	81	80	78	79	78	78	78	75	75	75	75	75
15	Usha	40/F	21372	45	Carcinoma Lt.Breast	84	85	82	80	78	75	76	74	75	75	74	74	72	72
16	Bakiam	43/F	20480	52	Carcinoma Rt.Breast	63	65	63	62	60	60	60	59	59	58	58	59	58	58
17	Kanakambaram	37/F	20806	55	RIF Pain for Evaluation	76	79	76	75	72	71	70	70	70	70	70	70	70	70
18	Akila	20/F	21343	47	SOlitary nodular goitre Rt Lobe	79	81	79	78	76	74	72	70	70	70	70	68	68	68
19	Kanchana	21/F	21350	54	Fibroadenoma Lt.Breast	88	90	87	85	84	83	82	81	80	80	80	79	79	79
20	Kala	37/F	21916	48	Fibroadenoma Rt.Breast	72	73	71	69	67	66	65	65	65	65	65	65	65	65
21	Manimegalai	35/F	26128	50	RIF Pain for Evaluation	80	84	82	80	78	75	73	73	73	70	70	70	70	70
22	Kanagasundari	45/F	19920	54	SOlitary nodular goitre Rt Lobe	80	82	80	78	76	75	73	73	73	70	70	70	70	70
23	Eshwari	37/F	22396	54	Fibroadenoma Rt.Breast	73	75	73	72	71	70	69	68	66	65	65	67	67	65
24	Madhan	22/M	22627	57	RIF Pain for Evaluation	89	90	88	86	85	84	82	80	80	80	78	78	78	78
25	Eliammal	45/F	21407	57	Cholelithiasis	91	91	89	86	85	83	82	81	80	80	79	79	79	77
26	Kamatchi	20/F	22834	45	subacute appendicitis	76	78	76	74	73	71	70	68	68	68	68	68	68	65
27	Velu	35/M	22824	59	subacute appendicitis	75	77	74	72	70	70	69	68	68	67	65	66	66	65
28	Veerammal	45/F	22732	52	Solitary nodular goitre Lt Lobe	75	78	74	72	71	70	70	70	70	70	69	69	69	67
29	Minnala	45/F	23856	60	Cholelithiasis	85	86	84	82	80	79	79	78	75	75	75	75	74	73
30	Yashodha	42/F	24033	56	Solitary nodular goitre Lt Lobe	78	80	77	75	75	73	72	72	70	70	70	68	68	68
31	Mariammal	45/F	24181	54	Cholelithiasis	74	77	73	72	71	70	70	70	70	70	70	70	69	69
32	Devagi	43/F	24192	57	Colloid goitre	70	71	69	67	66	65	65	65	65	65	65	63	63	63
33	Saravanan	20/M	24126	56	Cholelithiasis	69	71	70	68	67	65	65	64	65	65	65	65	62	62
34	Jayanthi	40/F	24345	58	Multi nodular goitre	81	83	81	78	76	75	75	74	74	73	72	72	72	71
35	Geetha	31/F	24201	55	Solitary nodular goitre Lt Lobe	79	81	80	78	77	75	75	75	75	75	74	74	74	76
36	Jeevarathinam	31/F	25571	48	Fibroadenoma Rt.Breast	77	79	76	75	73	72	72	72	72	72	70	70	70	70
37	Kalaimathi	20/F	25244	54	Fibroadenoma Rt.Breast	69	72	70	68	67	65	64	64	65	6	65	65	65	65
38	Jeeva	25/F	25478	53	Fibroadenoma Rt.Breast	75	77	74	72	72	71	70	70	70	70	70	70	70	70
39	Alamelu	25/F	24183	51	Multi nodular goitre	88	90	87	85	83	82	82	82	80	80	80	80	80	80
40	Vijaya	45/F	26202	53	Multi nodular goitre	68	71	68	66	65	63	62	62	62	62	62	62	62	62
41	Saraswathy	44/F	26205	64	Solitary nodular goitre Lt Lobe	83	85	83	81	80	78	77	77	77	75	75	75	75	75
42	Megala	20/F	26475	52	Pelvic mass for evaluation	77	79	75	73	70	69	69	69	70	70	68	68	68	68
43	Saroja	42/F	24126	56	Carcinoma Lt.Breast	89	90	86	84	83	82	81	80	80	80	80	80	79	79
44	Kumarasen	25/M	16264	57	Rt Brachial plexus injury	69	72	68	65	64	64	63	63	63	63	63	63	64	65
45	Bharathi	23/F	16265	53	Fibroadenoma Rt.Breast	74	76	74	72	70	69	66	65	65	65	65	65	65	64
46	Venuraghavan	27/M	15193	56	Thyroglossal cyst	72	74	72	70	70	68	68	68	68	68	68	68	70	70
47	Thilaga	42/F	15532	50	Solitary nodular goitre Lt Lobe	69	72	68	65	64	63	63	63	63	63	63	63	63	64
48	Thenmozhi	20/F	17075	47	subacute appendicitis	80	83	82	80	78	76	76	76	76	75	75	75	73	73
49	Rajendren	30/M	16963	54	subacute appendicitis	86	88	85	84	82	80	80	79	79	78	78	78	78	78
50	Varalakshmi	33/F	16971	58	Cholelithiasis	76	78	76	73	72	71	70	70	70	70	70	70	70	70

S.NO.	SYSTOLIC BLOOD PRESSURE PREOP	IND	INTU	1MIN AIT	3MIN AIT	5MIN AIT	8MIN AIT	10MIN AIT	30MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT
1	121	127	125	123	123	122	120	120	120	123	125	125	125	125
2	117	125	123	121	121	119	118	116	115	115	118	118	120	120
3	123	130	126	124	123	121	119	119	120	120	120	123	123	125
4	115	124	120	118	116	114	114	114	115	115	115	115	120	120
5	110	118	115	113	110	107	107	105	105	108	110	110	110	115
6	123	128	125	120	118	115	115	115	115	115	120	122	125	125
7	115	123	118	114	112	110	110	110	110	115	115	115	118	120
8	124	130	127	125	122	118	115	115	115	118	118	120	120	120
9	109	110	108	105	105	100	100	100	100	100	105	105	110	110
10	118	124	122	120	118	115	112	112	112	115	115	115	120	120
11	107	115	113	112	110	108	107	105	108	110	112	115	115	115
12	120	126	123	120	119	117	115	115	115	115	120	122	124	126
13	106	110	108	106	104	102	100	100	102	105	110	110	115	115
14	122	130	128	125	122	120	118	118	120	120	120	122	122	125
15	100	110	108	105	103	100	100	100	112	115	115	115	118	120
16	125	132	130	128	125	122	120	120	120	122	125	124	126	130
17	117	124	122	120	118	116	115	115	118	118	120	122	125	125
18	125	132	130	128	125	122	120	120	120	122	122	125	125	128
19	107	113	112	110	107	105	103	103	107	110	110	110	115	115
20	116	122	120	117	115	113	111	111	113	113	115	115	120	120
21	121	129	125	123	120	118	115	115	118	118	120	120	122	125
22	106	110	108	105	103	103	100	100	102	103	105	105	110	110
23	110	119	116	113	110	108	107	105	105	110	110	112	115	115
24	123	130	127	125	124	122	120	120	120	125	125	128	130	130
25	117	125	123	120	117	115	115	115	118	115	116	119	121	121
26	116	121	119	116	114	112	110	110	111	115	115	115	120	120
27	105	112	110	108	105	102	102	100	100	103	103	105	108	108
28	123	128	125	122	120	118	118	115	115	118	120	120	120	130
29	118	123	120	118	115	114	112	110	110	114	116	113	117	120
30	122	126	124	122	110	110	109	110	110	112	112	115	115	118
31	107	115	113	110	108	106	105	105	108	108	110	115	115	120
32	115	120	123	120	118	115	112	112	115	115	115	120	120	120
33	109	114	112	110	108	105	103	102	105	108	110	110	115	115
34	120	125	123	122	120	118	115	113	115	113	115	117	118	120
35	114	118	115	112	110	108	108	105	105	110	110	115	115	118
36	121	125	122	120	116	114	112	112	115	115	118	120	120	122
37	117	122	120	118	115	113	112	110	110	114	115	120	120	123
38	108	114	112	110	108	108	107	107	110	110	112	115	114	118
39	119	125	123	122	120	118	115	115	115	118	120	120	123	125
40	115	121	119	117	115	113	112	112	115	110	110	110	110	115
41	105	110	108	105	102	102	102	102	105	106	108	110	110	115
42	120	125	123	121	120	118	116	115	115	118	115	119	120	120
43	123	130	127	125	122	120	118	115	115	118	118	122	125	124
44	118	123	120	118	115	113	110	110	110	114	116	118	120	120
45	118	123	120	117	115	113	109	109	110	110	110	120	120	122
46	127	133	130	128	125	122	120	120	125	125	125	130	130	134
47	110	115	113	110	108	105	105	105	108	108	110	115	115	115
48	107	112	110	108	105	103	100	101	105	106	110	110	110	120
49	121	126	123	120	119	117	115	113	116	118	120	122	125	125
50	113	116	114	112	110	108	106	104	105	110	110	115	115	120

S.NO.	DIASTOLIC BLOODPRESSURE PREOP	IND	INTU	1MIN AIT	3MIN AIT	5MIN AIT	8MIN AIT	10MIN AIT	30MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT
1	77	81	77	74	74	76	74	74	75	75	75	75	78	80
2	65	70	68	65	65	64	66	64	65	65	68	70	70	70
3	68	71	67	64	64	64	64	64	65	68	68	70	70	70
4	73	78	75	72	70	69	68	68	70	70	70	70	75	75
5	62	65	63	61	60	60	60	60	60	60	60	60	60	65
6	75	79	77	74	72	72	71	70	70	70	73	73	75	75
7	73	77	74	71	68	65	64	62	65	65	65	70	70	70
8	63	67	64	62	61	60	58	58	60	60	60	63	63	65
9	71	75	73	72	70	69	68	68	70	70	70	75	75	75
10	65	69	67	66	63	62	60	60	60	60	60	65	65	65
11	72	75	73	71	70	68	69	67	70	70	70	70	72	75
12	80	85	83	82	81	80	78	78	80	80	80	80	85	85
13	67	72	70	68	65	64	63	63	65	65	65	65	65	70
14	72	76	74	72	71	70	68	68	70	70	70	72	72	75
15	75	78	75	73	72	70	69	68	70	70	70	70	75	75
16	68	73	72	71	70	69	68	67	70	70	70	70	70	70
17	61	65	63	62	61	60	60	60	60	60	63	65	65	68
18	68	73	72	71	70	68	67	67	69	71	71	75	75	76
19	63	67	66	64	63	61	60	60	60	60	60	65	65	65
20	72	76	74	73	72	70	68	68	65	70	70	70	75	78
21	73	77	75	73	73	72	71	70	70	73	73	75	77	77
22	61	65	64	63	62	61	60	60	60	60	60	60	65	65
23	79	83	81	79	76	75	74	72	72	75	75	75	75	78
24	75	78	76	75	73	72	70	69	69	70	72	72	75	75
25	74	77	76	74	72	70	70	70	70	70	70	76	76	76
26	79	83	81	80	79	75	73	72	75	75	75	75	80	80
27	67	69	67	65	64	62	60	60	60	60	60	60	60	65
28	73	77	75	74	73	71	70	69	70	70	70	73	74	77
29	65	69	67	64	62	61	61	60	60	63	65	65	67	70
30	65	69	67	66	64	62	60	60	60	60	60	65	65	68
31	73	77	74	72	71	70	69	68	70	70	70	75	75	75
32	78	82	80	79	77	75	73	73	73	75	75	75	75	75
33	65	68	66	64	62	60	61	60	60	62	63	65	65	67
34	71	75	74	72	70	69	68	68	68	70	70	70	70	76
35	64	67	65	63	61	60	60	60	65	65	65	65	70	70
36	80	85	83	82	81	79	77	77	77	79	80	80	80	81
37	72	76	74	73	71	70	70	70	72	72	75	75	78	80
38	62	68	66	64	62	61	60	60	62	62	65	65	68	70
39	72	77	74	72	71	70	69	69	70	72	75	75	75	80
40	62	66	64	62	61	60	59	59	60	60	62	65	65	68
41	63	67	64	62	60	59	59	60	60	63	65	65	65	67
42	70	72	70	68	67	67	67	67	70	70	70	73	75	75
43	67	70	69	68	67	66	64	64	65	65	67	69	70	70
44	72	77	74	72	70	69	68	68	70	70	70	72	72	72
45	65	69	67	66	64	63	63	63	65	65	65	69	69	69
46	79	83	82	80	78	76	74	73	75	75	75	76	78	78
47	72	77	74	72	74	71	70	70	70	75	75	75	75	80
48	64	69	64	62	60	60	60	60	60	60	65	65	65	68
49	74	77	75	72	70	69	67	67	69	69	70	70	70	70
50	67	73	71	70	68	65	61	63	65	65	68	70	70	70

S.NO.	MEAN BLOOD PRESSURE PREOP	IND	INTU	1MIN AIT	3MIN AIT	5MIN AIT	8MIN AIT	10MIN AIT	30MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT
1	91.66	96.33	93	90.33	90.33	91.33	89.33	89.33	90	91	91.7	91.7	93.7	95
2	82.33	88.33	86.33	83.67	83.67	82.33	83.33	81.33	81.7	81.7	84.7	86	86.7	86.7
3	86.33	90.67	86.66	84	83.67	83	82.33	82.33	83.3	85.3	85.3	87.7	87.7	88.3
4	87	93.33	90	87.33	85.33	84	83.33	83.33	85	85	85	85	90	90
5	78	82.67	80.33	78.33	76.67	75.67	75.67	75	75	76	76.7	76.7	76.7	81.7
6	91	95.33	93	89.33	87.33	86.33	85.67	85	85	85	88.7	89.3	91.7	91.7
7	87	92.33	88.67	85.33	82.67	80	79.33	78	80	81.7	81.7	85	86	86.7
8	83.33	88	85	83	81.33	79.33	77	77	78.3	79.3	79.3	82	82	83.3
9	83.66	86.67	84.66	83	81.67	79.33	78.67	78.67	80	80	81.7	85	86.7	86.7
10	82.67	87.33	85.33	84	81.33	79.67	77.33	77.33	77.3	78.3	78.3	81.7	83.3	83.3
11	83.67	88.33	86.33	84.67	83.33	81.33	81.66	81	82.7	83.3	84	85	86.3	88.3
12	93.33	98.67	96.33	94.66	93.67	92.33	90.33	90.33	91.7	91.7	93.3	94	98	98.7
13	80	84.67	82.67	80.67	78	76.67	75.33	75.33	77.3	78.3	80	80	81.7	85
14	88.67	94	92	89.66	88	86.67	84.67	84.67	86.7	86.7	86.7	88.7	88.7	91.7
15	83.33	88.67	86	83.7	83.3	80	79.3	78.7	84	85	85	85	89.3	90
16	87	92.7	91.3	90	88.3	86.7	85.3	84.7	86.7	87.3	88.3	88	88.7	90
17	79.7	84.7	82.7	81.3	81	78.7	78.3	78.3	79.3	79.3	82	84	85	87
18	87	92.7	91.3	90	88.3	86	84.7	84.7	86.7	88	88	91.7	91.7	93.3
19	77.7	82.3	81.3	79.3	77.7	75.7	74.3	74.3	75.7	76.7	76.7	80	81.7	81.7
20	86.7	91.3	89.3	87.7	86.3	84.3	82.3	82.3	81	84.3	85	85	90	92
21	89	94.3	91.7	89.7	88.7	87.3	85.7	85	86	88	88.7	90	92.3	93
22	76	80	78.7	77	67.5	75	73.3	73.3	74	74.3	75	75	80	80
23	89.3	95	92.7	90.3	87.3	86	85	83	83	86.7	86.7	87.3	88.3	90.3
24	91	95.3	93	91.7	90	88.7	86.7	86	86	88.3	89.7	90.7	93.3	93.3
25	88.3	93	91.7	89.3	87	85	85	85	86	85	85.3	90.3	91	91
26	91.3	95.7	93.7	92	90.7	87.3	85.3	84.7	87	88.3	88.3	88.3	93.3	93.3
27	79.7	83.3	81.3	79.3	77.7	75.3	74	73.3	73.3	74.3	74.3	75	76	79.3
28	89.7	94	91.7	90	88.7	86.7	86	84.3	85	86	86.7	88.7	89.3	94.7
29	82.7	87	84.7	82	79.7	78.7	78	76.7	76.7	80	82	81	83.7	86.7
30	84	81.3	80.7	79	78	78	76.3	76.7	76.7	77.3	77.3	81.7	81.7	84.7
31	84.3	89.7	87	84.7	83.3	82	81	80.3	82.7	82.7	83.3	88.3	88.3	90
32	90.3	94.7	94.3	92.7	90.7	88.3	86	86	87	88.3	88.3	90	90	90
33	79.7	83.3	81.3	79.3	77.3	75	75	74	75	77.3	78.7	80	81.7	83
34	87.3	91.7	90.3	88.7	86.7	85.3	83.7	83	83.7	84.3	85	85.7	86	90.7
35	80.7	84	81.7	79.3	77.3	76	76	75	78.3	80	80	81.7	85	86
36	93.7	98.3	96	94.7	92.7	90.7	88.7	88.7	89.7	91	92.7	93.3	93.3	94.7
37	87	91.3	89.3	88	85.7	84.3	84	83.3	84.7	86	88.3	90	92	94.3
38	77.3	83.3	81.3	79.3	77.3	76.7	75.7	75.7	78	78	80.7	81.7	83.3	86
39	87.7	93	90.3	88.7	87.3	86	84.3	84.3	85	87.3	90	90	91	95
40	79.7	84.3	82.3	80.3	79	77.7	76.7	76.7	78.3	76.7	78	80	80	83.7
41	77	81.3	78.7	76.3	74	73.3	73.3	74	75	77.3	79.3	80	80	83
42	86.7	89.7	87.7	85.7	84.7	84	83.3	83	85	86	85	88.3	90	90
43	85.7	90	88.3	87	85.3	84	82	81	81.7	82.7	84	86.7	88.3	88
44	87.3	92.3	89.3	87.3	85	83.7	82	82	83.3	83.3	84.7	85.3	87.3	88
45	82.7	87	84.7	83	81	79.7	78.3	78.3	80	80	80	86	86	86.7
46	95	99.7	98	96	93.7	91.3	89.3	88.7	91.7	91.7	91.7	94	95.3	96.7
47	84.7	89.7	87	84.7	85.3	82.3	81.7	81.7	82.7	86	86.7	88.3	88.3	91.7
48	78.3	83.3	79.3	77.3	75	74.3	73.3	73.7	75	75.3	80	80	80	85.3
49	89.7	93.3	91	88	86.3	85	83	82.3	84.7	85.3	86.7	87.3	88.3	88.3
50	82.3	87.3	85.3	84	82	79.3	77.3	76.7	78.3	80	83.7	85	85	86.7

Ivabradine masrter chart

GROUP-II (INTRAVENOUS LIGNOCAINE)

NO.	NAME	AGE/SEX	IP.NO	WT/KGS	HEART RATE												SYSTOLIC BLOOD PRESSURE/MMHG												DIASTOLIC BLOOD PRESSURE/MM HG												MEAN ARTERIAL PRESSURE/MM HG											
					PREOP	AT IND	AT INT	1 MIN AIT	3 MIN AIT	5 MIN AIT	8 MIN AIT	10 MIN AIT	30 MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT	PREOP	AT IND	AT INT	1 MIN AIT	3 MIN AIT	5 MIN AIT	8 MIN AIT	10 MIN AIT	30 MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT	PREOP	AT IND	AT INT	1MIN AIT	3MIN AIT	5 MIN AIT	8 MIN AIT	10 MIN AIT	30 MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT	PRE OP	AT IND	AT INT	1 MIN AIT	3 MIN AIT	5 MIN AIT	8 MIN AIT	10 MIN AIT	30 MIN AIT	1HR AIT	2HR AIT	4HR AIT	6HR AIT	12HR AIT
1	Vignesh Kumar	22/M	1117	57	86	89	92	90	89	86	84	84	83	82	89	95	97	95	125	128	130	127	124	120	118	118	120	120	124	120	120	120	80	83	78	75	73	77	70	70	79	72	73	70	70	70	95	98	95.3	92.3	90	88	86	86	92.7	88	90	86.7	86.7	86.7
2	Saravanan	31/M	2706	56	95	97	95	93	90	90	89	89	87	90	93	96	98	96	120	124	127	124	120	118	117	117	120	123	125	125	120	124	79	85	87	85	83	80	80	80	83	80	80	80	80	80	92.7	98	100	98	95.3	92.7	92.3	92.3	95.3	94.3	95	95	93.3	94.7
3	Jayalakshmi	42/F	3390	54	90	94	91	89	90	86	84	84	88	90	95	95	95	95	118	123	120	118	116	113	115	115	115	118	120	125	125	124	69	75	73	73	71	70	69	69	70	72	72	70	70	70	85.3	91	88.7	88	86	84.3	84.3	84.3	85	87.3	88	88.3	88.3	80
4	Radhunisha	32/F	4513	56	100	97	99	94	92	91	89	88	90	95	98	101	103	105	110	115	113	111	109	107	105	105	110	113	115	115	118	118	62	65	67	66	63	62	60	59	60	65	65	65	65	65	78	81.7	82.3	81	78.3	77	75	74.3	76.7	81	81.7	81.7	82.7	82.7
5	Lingam	40/M	6716	58	89	94	92	90	88	87	86	86	86	89	92	93	92	90	100	105	105	102	100	98	97	97	100	105	110	110	110	115	61	63	63	61	60	59	58	58	60	60	60	62	60	60	74	77	77	74.7	73.3	72	71	71	73.3	75	76.7	78	76.5	78.3
6	Anitha	22/F	6439	49	91	95	93	90	89	87	85	85	84	87	90	94	97	99	100	106	104	100	99	96	96	99	100	105	114	115	115	60	65	63	62	60	58	59	58	60	62	65	65	65	65	72	94.7	95.3	92.7	90.7	88.7	87.3	86.7	86.7	87.7	88.3	88.7	88.3	88.3	91.3
7	Tamilselvi	22/F	6442	50	85	90	86	83	82	81	80	80	82	84	86	88	87	86	126	130	128	126	124	122	120	120	122	125	126	125	125	130	78	78	75	73	71	70	70	70	70	70	70	70	70	72	91.7	92	89.3	87.3	85.7	85.7	83	83.3	83.3	85.7	86.3	88.3	89.3	89.3
8	Rajeshwari	20/F	7067	45	68	75	76	74	71	70	70	70	74	77	70	84	89	87	115	120	118	116	113	111	109	108	110	113	115	115	118	118	80	78	75	73	72	70	70	68	70	72	72	75	75	75	86.3	91.7	88.3	86.7	85.3	85	84.7	83.3	85	86.7	90	91	90	90
9	Kaladuraichi	27/F	8946	52	93	95	89	85	83	91	80	80	83	85	86	83	90	96	119	125	123	120	118	117	116	114	115	110	120	123	120	120	70	74	73	71	70	69	69	68	70	75	75	75	75	75	79.3	83.3	82	80	77.3	77.3	76	74	75	76	80	80	81.7	81.7
10	Karthikeyan	29/M	8576	57	79	86	86	84	82	80	78	78	80	85	88	92	95	94	108	110	110	108	108	106	104	102	105	108	110	110	115	115	65	70	68	66	63	63	62	60	60	60	65	65	65	65	79.3	83.3	82	80	77.3	77.3	76	74	75	76	80	80	81.7	81.7
11	Sathyapriya	20/F	19436	49	91	93	91	90	88	86	83	83	83	85	88	90	92	94	122	127	125	123	120	118	116	115	115	118	120	120	120	120	65	69	69	65	63	62	62	61	65	69	65	68	68	70	84	88.3	87.7	84.3	82	80.7	80	79	81.7	82.7	83.3	85.3	85.3	86.7
12	Kavitha	20/F	22365	51	88	90	87	87	85	83	81	80	81	84	86	88	91	92	114	118	117	115	112	110	107	105	109	110	116	115	115	120	71	75	74	72	70	68	68	65	65	65	70	70	70	70	85.3	89.3	88.3	86.3	84	82	81	78.3	79.7	80	85.3	85	85	86.7
13	Kalavathy	31/F	23857	54	97	100	101	97	95	93	91	90	92	94	94	97	97	100	119	125	123	120	118	116	115	112	115	115	118	120	120	120	67	73	71	68	66	64	62	60	60	60	65	65	65	65	79.3	83	80	78	76	75.3	74.7	74.7	75	80	80	81.7	81.3	82.7
14	Lokesh	21/M	24630	53	92	95	97	93	91	89	87	85	88	89	90	94	94	92	110	115	112	110	108	106	104	104	105	110	110	115	114	118	64	67	64	62	60	60	60	60	60	65	65	65	65	65	79.3	83	80	78	76	75.3	74.7	74.7	75	80	80	81.7	81.3	82.7
15	Durga	35/F	5732	53	84	88	89	85	84	82	80	80	82	84	87	89	90	91	120	126	124	122	120	118	116	114	116	120	120	120	120	125	80	84	82	80	78	78	77	75	75	75	75	80	80	80	93.3	98	96	94	92	91.3	90	88	88.7	90	90	93.3	93.3	95
16	Anjali	40/F	6271	55	100	102	104	99	96	94	93	92	93	95	98	100	96	96	117	122	120	120	118	115	114	113	115	115	118	119	120	122	65	69	67	64	63	60	60	58	60	60	65	65	58	70	82.3	86.7	84.7	82	80.3	78.3	78	76.3	78.3	82.7	83	85.3	87.3
17	Arunachalam	40/M	6767	57	83	88	85	83	81	80	80	80	81	84	87	89	91	90	125	130	128	126	123	120	118	116	118	120	122	125	125	125	80	83	83	81	80	78	76	75	75	75	75	80	80	80	95	98.7	98	96	94.3	92	90	88.7	89.3	90	90.7	95	95	95
18	Saraswathy	34/F	6708	53	79	80	82	80	78	79	78	78	80	84	88	89	92	92	107	115	112	110	106	105	102	102	105	105	110	115	115	115	61	72	71	70	68	66	68	67	70	70	70	75	75	75	76.3	86.3	84.7	83.3	80.7	79	79.3	78.7	81.7	81.7	83.3	88.3	88.3	88.3
19	Anandaraj	38/M	8118	57	88	90	89	85	84	83	82	81	82	84	88	89	92	90	113	116	113	110	108	106	103	100	105	110	114	120	124	125	72	75	76	73	70	69	67	66	70	70	73	75	75	75	85.7	88.7	88.3	85.3	82.7	81.3	79	77.3	81.7	83.3	86.7	90	91.3	91.7
20	Vinothkumar	23/M	8010	56	93	93	95	90	89	86	85	85	86	87	87	89	90	90	110	115	113	110	108	106	104	104	105	110	114	115	118	120	60	65	65	63	61	59	58	58	60	60	60	65	65	65	76.7	81.7	81	78.3	76.7	74.7	73.3	72.3	75	77.7	80	80	80
21	Selvam	32/M	7998	54	86	89	90	86	84	83	81	80	81	83	85	88	87	85	106	110	109	105	104	104	103	101	100	105	105	110	110	110	60	65	62	61	60	60	58	58	60	60	64	65	65	65	75.3	80	77.7	75.7	74.7	74.7	73	72.3	73.3	75	77.7	80	80	80
22	saranya	20/F	8494	56	69	72	71	70	69	67	66	66	68	70	74	77	79	82	122	126	124	123	122	119	117	115	115	118	120	122	125	125	73	78	75	73	71	70	69	69	70	70	75	75	75	75	89.3	94	91.3	89.7	88	86.3	85	84.3	85	86	90	90.7	91.7	91.7
23	Deivanayagi	45/F	7749	56	92	95	94	91	90	87	86	85	86	88	90	92	91	91	120	125	123	123	119	117	116	115	115	118	120	120	125	125	62	65	63	61	60	58	58	57	60	60	60	65	65	65	81.3	85	83	81.7	79.7	77.7	77.3	76.3	78.3	79.3	80	83.3	85	85
24	Sharmila	27/F	8303	57	89	91	90	90	97	87	86	85	88	89	91	93	93	95	108	114	112	108	106	106	104	104	105	108	110	115	115	115	80	85	83	81	79	76	75	75	75	75	78	80	80	80	89.3	94.7	92.7	90	88	86	84.7	84.7	85	86	88.7	91.7	91.7	91.7
25	Chitra	30/F	8772	54	85	88	86	85	83	81	80	80	82	83	86	88	89	90	115	123	120	119	116	116	113	112	115	118	120	120	122	122	67	69	67	64	63	62	61	60	60	60	63	63	65	65	83	87	84.7	82.3	80.7	80	78.3	77.3	78.3	79.3	82	82	84	84
26	Gomathy	25/F	10423	52	94	97	97	96	95	92	91	90	92	93	95	97	98	99	124	131	128	126	124	120	118	116	120	122	125	125	125	125	67	70	70	69	67	67	65	64	65	65	65	65	70	70	86	90.3	89.3	88	86	84.7	82.7	81.3	83.3	84	85	85	88.3	88.3
27	Mathavi	30/F	11003	54	88	90	88	89	85	83	81	80	80	82	85	88	89	87	110	116	114	112	112	108	107	105	108	110	115	120	120	120	70	75	73	72	70	68	68	65	70	70	70	70	70	70	83.3	88.7	85.7	85.3	84	81.3	81	78.3	82.7	83.3	85	86.7	86.7	86.7
28	Amsa	32/F	9517	57	69	72	71	70	69	69	68	68	70	71	73	75	77	74	120	124	122	120	117	115	115	113	115	118	120	120	120	120	67	72	71	70	68	68	66	66	70	70	70	75	75	75	84.7	89.3	88	86.7	84.3	83.7	82.3	81.7	85	86	86.7	90	90	90
29	Savitha	20/F	9836	48	79	82	80	81	79	77	75	75	77	78	80	83	85	88	103	108	106	105	103	102	100	100	106	110	115	115	118	120	60	65	63	62	61	59	59	58	60	65	65	65	65	68	74.3	79.3	77.3	76.3	75	73.3	72.7	72	75.3	80	81.7	81.7	82.7	85.3
30	Alamelu	38/F	10877	52	89	91	90	88	88	87	86	85	86	87	89	90	90	91	112	119	117	116	114	112	110	108	110	112	115	118	120	125	71	75	73	71	70	68	67	67	70	70	70	70	75	75	84.7	89.7	87.7	85	84.7	82.7	81.3	80.7	83.3	84	85	86	90	93.7
31	Parameshwaran	38/M	11788	54	90	94	93	92	90	89	88	85	85	87	89	88	90	92	123	129	127	126	123	120	118	116	120	120	120	125	125	125	64	70	69	68	66	65	65	64	65	65	70	70	70	70	83.7	88	86.7	84.7	83.3	82.7	81	81	83.3	85	85	83.3	86.7	86.7
32	Selvi	39/M	11176	53	91	94	93	92	90	89	87	87	89	88	86	90	93	92	109	114	112	110	108	108	105	105	110	115	115	120	120	120	71	75	74	72	71	70	69	69	70	70	70	70	70	70	83.7	88	86.7	84.7	83.3	82.7	81	81	83.3	85	85	83.3	86.7	86.7
33	Shobana	42/F	12149	56	95	97	96	95	93	90	89	88	89	90	92	95	99	100	118	124	122	120	118	118	115	115	118	120	122	125	125	125	65	68	67	65	64	64	63	63	65	65	70	70	70	70	82.7	86.7	85.3	83.3	82	82	80.3	80.3	82.7	83.3	86.7	88.3	88.3	89.3
34	Prabhakaran	25/M	11117	56	87	91	90	89	86	85	85	86	87	89	92	92	94	96	124	130	128	125	123	120	120	119	120	123	125	125	125	125	71	76	74	72	71	70	68	67	70	70	70	70	75	75	89.3	94	92	89.7	88.3	86.7	85.3	84.3	86.7	87.7	88.3	91.7	91.7
35	Jayanthi	35/F	11846	49	99	103	100	99	98	95	95	93	95	96	95	97	99	100	106	112	110	108	106	105	105	104	105	110	112	112	115	118	60	65	63	62	60	60	59	58	60	60	60	65	65	65	75.3	80.7	78.7	77.3	75.3	75	74.3	73.3	75	76.7	77.3	80.7	81.7	82.7
36	Prema	45/F	11874	58	87	90	90	90	89	86	85	85	83	83	85	88	89	92	95	116	120	120	118	116	114	112	110	112	115	115	118	120	65	71	70	68	68	66	65	65	65	65	68	70	70	70	75	82	87.3	85.7	84.7	84	82	80.7	80	80.7	83.7	85	86	86.7	90.7
37	Nandakumar	25/M	13280	50	95	98	97	96	95	93	92	92	93	95	97	99	100	102	108	114	112	110	109	107	105	104	105	110	115	115	118	120	59	66	65	63	62	61	60	60	60	60	65	65	65	70	75.3	82	80.7	78.7	77.7	76.3	75	74.7	75	80	81.7	81.7	86	86.7
38	Ragavi	20/F	13280	46	87	91	90	89	88	86	85	82	83	85	86	89	90	92	121	125	123	121	120	118	116	115	115	118	120	120	125	125	80	87	84	82	81	80	78	77	80	80	80	82	82	80	93.7	99.7	97	95	94	92.7	90.7	89.7	91.7	92.7	93.3	94.7	96.3	97
39	Kala	45/F	13316	50	94	97	95	93	91	90	89	88	90	92	92	95	97	97	111	115	113	111	108	107	107	105	105	110	115	115	115	115	67	70	70	68	66	65	65	64	65	65	70	70	70	70	81.7	85	84.3	82.3	80	79	79	77.7	78.3	80	85	85	85	85
40	Suganya	20/F	13159	49	87	91	90	89	87	85	86	84	89	90	92	95	92	96	105	110	108	106	105	104	103	103	105	110	112	115	115	120	60	65	64	62	61	60	58	58	60	60	60	65	65	65	75	80	78.7	76.7	75.7	74.7	73	73	75	76.7	77.3	78.3	78.3	78.3
41	Ajithkumar	20/M	15243	56	96	100	99	97	95	93	91	90	90	93	95	95	98	98	120	124	122	120	118	115	114	114	115	120	123	124	125	125	71	77	75	74	72	71	69	68	70	70	70	75	75	75	87.3	92.7	90.7	89.3	87.3	85.7	84	83.3	85	86.7	87.7	91.3	91.7	91.7
42	Sundari	20/F	15201	54	90	95	94	92	90	88	86	86	86	88	89	90	91	94	111	115	114	112	110	108	106	105	108	110	115	115	118	120	60	65	64	63	61	60	60	60	60	65	65	65	65	65	77	81.7	80.7	79.3	77.3	76	75.3	75	75	79.3	80	81.7	82.7	83.7
43	Madiga	40/F	13012	56	86	90	88	86	85	84	82	80	82	82	84	86	87	90	102	107	105	102	100	99	97	96	100	110	115	115	118	118	60	64	64	62	63	61	61	60	60	60	60	65	65	65	74	78.3	77.7	76	74	73.7	73	72.7	73.3	76.7	78.3	81.7	82.7	83.7
44	Malarvizhi	36/F	15204	50	94	97	95	95	93	90	90	91	93	94	96	98	98	98	114	118	115	114	112	110	108	106	110	110	118	120	120	122	73	77	75	73	72	71	70	69	70	70	74	75	75	75	86.7	90.7	88.3	86.7	85.3	84	82.7	81.3	83.3	85.3	88.7	90	90.7	91.7
45	Mythili	35/F	16244	52	90	93	92	90	89	88	86	86	86	88	89	90	92	94	123	126	123	120	118	115	113	110	113	115	118	120	124	125	80	85	84	82	80	79	78	77	80	80	80	80	80	80	94.3	98.7	97	94.7	92.7	91	89.7	88	90.7	91.7	92.7	93.3	94.3	95
46	Banupriya	24/F	14006	47	89	93	92	90	88	86	85	84	85	86	87	89	90	90	100	105	107	106	104	102	100	99	102	108	110	113	115	115	60	66	64	63	62	60	59	58	60	60	65	65	65	65	73.3	80.3	78.3	76.3	76	74	72.9	71.7	74	75	79	80	81.7	82.7
47	Chinnapponnu	45/F	15197	58	85	90	88	85	84	85	83	80	83	85	87	89	87	90	106	110	109	107	105	103	101	100	103	110	115	115	118	118	62	67	65	64	62	60	59	58	60	60	65	65	65	65	76.7	81.3	79.3	78.3	76.3	74.3	73.7	72	74	75	80	81.7	82.7	83.7
48	Karunakaran	32/M	14578	62	79	84	82	81	79	77	76	74	74	75	76	78	80	82	130	134	132	130	128	126	124	122	125	130	135	140	140	140	80	86	85	84	82	80	80	78	80	80	80	82	82	85	96.7	102	101	99.3	97.3	96	95.3	94	95	96.7	98.7	100	100	100
49	Karthika	44/F	14603	57	89	91	90	89	87	87	85	85	88	89	91	92	92	92	124	127	126	124	122	120	118	118	120	120	120	120	125	125	78	84	83	81	80	78	77	77	80	80	80	82	82	85	93.3	98.3	97.3	95.3	94	92	90.7	90.7	93.3	93.3	94.7	96.7	98.3	98.3
																															76	80	80	78	78	77	76	76	80	80	80	80	80	80	88.3	92.7	92	90.3	89.3	88	86.7	86.7	90	90.7	91.7	92.7	93.7	93.7