COMPARATIVE EVALUATION OF DEXMEDETOMIDINE AND ESMOLOL FOR ATTENUATION OF INTUBATION STRESS RESPONSE IN WELL CONTROLLED HYPERTENSIVE PATIENTS – A DOUBLE BLIND RANDOMIZED CONTROL STUDY

A STUDY OF 60 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

APRIL 2017

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

CHENNAI

CERTIFICATE

This is to certify that the dissertation entitled **"COMPARATIVE EVALUATION OF DEXMEDETOMIDINE AND ESMOLOL FOR ATTENUATION OF INTUBATION STRESS RESPONSE IN WELL CONTROLLED HYPERTENSIVE PATIENTS – A DOUBLE BLIND RANDOMIZED CONTROL STUDY"** submitted by**Dr.M.SUKUMARAN**,**REGISTER NO. 201420303**in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by The TamilnaduDr.M.G.R. Medical University, Chennai, this is a bonafide original research work done by him in The Department of Anaesthesiology and Critical Care, Tirunelveli Medical College Hospital, under the guidance and supervision of **Prof.Dr.A.BALAKRISHNAN, M.D.,D.A** during the academic year 2014-2017.

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Date :

Place : TIRUNELVELI **Dr.M.SUKUMARAN**.

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Last, but not least, I thank all the patients for willingly submitting themselves for this study.

LIST OF ABBREVIATIONS

1.	ASA	American Society of Anaesthesiologists
2.	AR	Adrenoreceptor
3.	CAD	Coronary Artery Disease
4.	COPD	Chronic Obstructive Pulmonary Disease
5.	CNS	Central Nervous System
6.	CT	Computerized Tomography
7.	CVA	Cereberovascular accident
8.	CVS	Cardio vascular system
9.	DAP	Diastolic Arterial Pressure
10.	DM	Diabetes Mellitus
11.	ECG	Electrocardiogram
12.	FDA	Food and Drug Administration
13.	FRC	Functional Residual Capacity
14.	GA	General Anaesthesia
15.	GIT	Gastrointestinal Tract
16.	HR	Heart Rate
17.	ICU	Intensive Care Unit
18.	IV	Intravenous

19. IVRA	Intravenous Regional Anaesthesia
20. MAC	Minimum Alveolar Concentration
21. MAP	Mean Arterial Pressure
22. MRI	Magnetic Resonance Imaging
23. PICU	Paediatric Intensive Care Unit
24. RBC	Red Blood Cell
25. RS	Respiratory System
26. SAP	Systolic Arterial Pressure
27. SHT	Systemic Hypertension
28. SPO2	Peripheral Oxygen Saturation
29. SVT	Supraventricular Tachycardia
30. WHO	World Health Organization

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PROTOCOL TITLE: COMPARITIVE EVALUATION OF DEXMEDETOMIDINE AND ESMOLOL FOR ATTENTVATION OF INTUBATION STRESS RESPONSE IN WELL CONTROLLED HYPERTENSIVE PATIENTS – A DOUBLE BLIND RANDOMIZED CONTROL STUDY

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DESIGNATION OF PRINCIPAL INVESTIGATOR POST GRADUATE IN ANAESTHESIOLOGY
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Dear , Dr.M.Sukumaran, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.12.15.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
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   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
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   g. Any deviation/violation/waiver in the protocol must be informed.

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1. INTRODUCTION

The hemodynamic responses to laryngoscopy and endotracheal intubation have been recognized since 1951. Though these pressor responses have been observed frequently they have been interpreted differently by many authors. The induction of anaesthesia, laryngoscopy, endotracheal intubation and surgical stimulation often evoke cardiovascular responses characterized by alterations in systemic blood pressure, heart rate and cardiac rhythm. The response following laryngoscopy and intubation peaks at 1-2 min and returns to baseline within 5-10 mins.

These sympathoadrenergic responses are probably of little clinical consequence in healthy patients. Complications like myocardial ischemia, left ventricular failure, and cerebral haemorrhage have been attributed to sudden rise in systemic arterial blood pressure and increase in heart rate. These complications are more likely to occur in patients with pre existing hypertension, coronary heart disease, cerebral vascular disease, intracranial pathology and hyperactive airways. In such cases, reflex circulatory responses such as increase in heart rate, systemic arterial blood pressure and disturbances in cardiac rhythm need to be suppressed.

Prof. Ward and King[1] in their combined study documented myocardial ischemic changes due to reflex sympathoadrenal response immediately following laryngoscopy and endotracheal intubation with a mean increase in systemic pressure of 40mmHg even in normotensive patients.

Prys Roberts et al[2] showed an exaggerated form of this response in hypertensive patients. Anti hypertensive drugs modify the response but do not inhibit it completely.

The cardiovascular responses during laryngoscopy and endotracheal intubation should be abolished to balance the myocardial oxygen supply and demand which is a key note in the safe conduct of Anaesthesia.

Attempts to reduce these untoward haemodynamic responses during laryngoscopy and endotracheal intubation lead to the trial of various systemic as well as topical agents.

The present concept of a definitive sympathetic overactivity during laryngeal intubation clearly shows that a more protection against vagal overactivity and the use of anticholinergic drugs alone may not be sufficient. Those techniques which require prior laryngoscopy to administer the local anaesthetic solution are likely to be of limited value.

The common strategies adapted are narcotics, vasodilators, Beta blockers, calcium channel blockers, lidocaine and other sympatholytics.

The inclusion of a rapid onset, short duration, water soluble, cardio selective β blocker, Esmolol to the armamentarium of the anaesthesiologist to control periods of intense sympathetic stimulation, namely laryngoscopy and endotracheal intubation adds on to the safety of anaesthesia.

Dexmedetomidine is an imidazole derivative, highly selective alpha 2 receptor agonist. It decreases central noradrenergic activity of locus ceruleus. It decreases systemic adrenaline and noradrenaline production. It has negative chronotropic and ionotropic effect and can decrease anesthetic doses. It may be alternative antiadrenergic therapy for cardiovscular response to laryngoscopy and tracheal intubation.

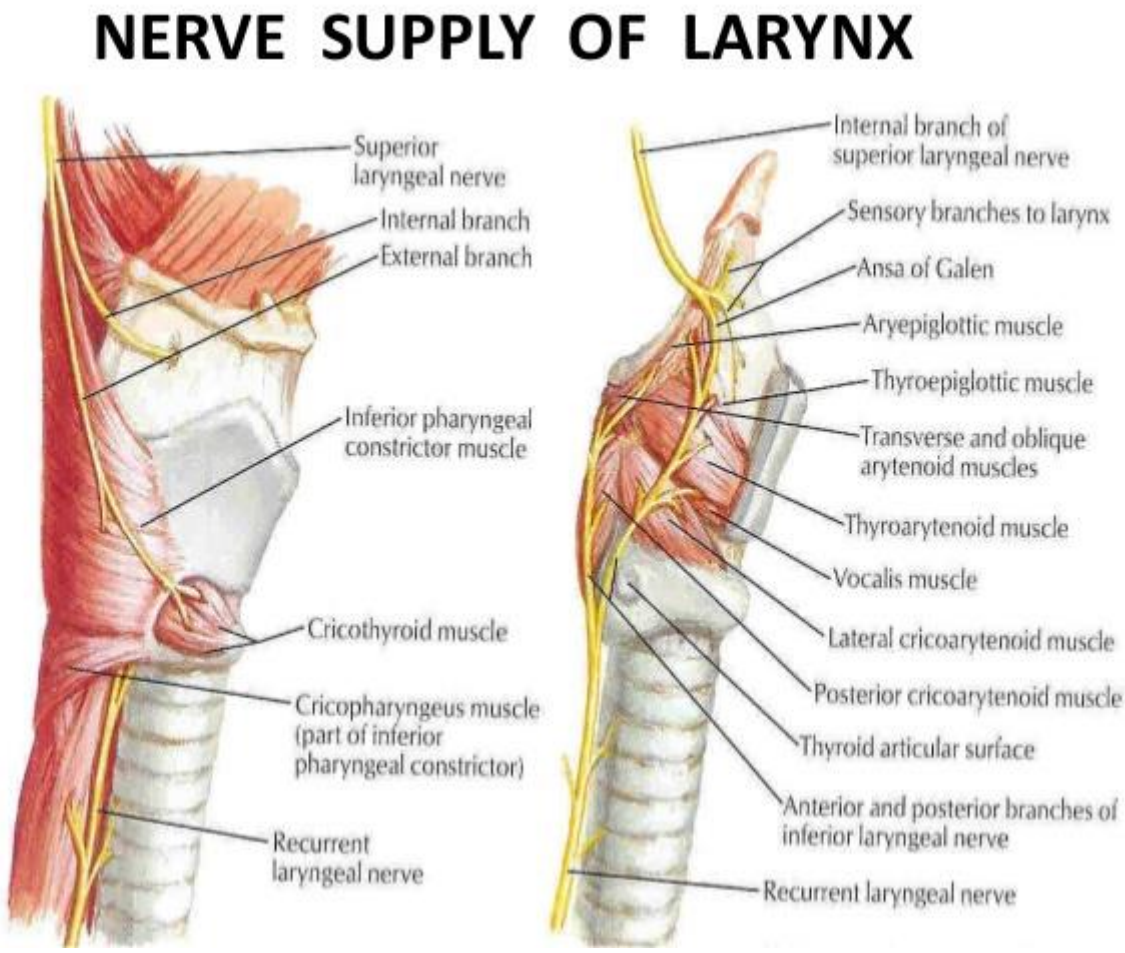
In our study, we have compared the efficacy IV Dexmedetomidine and IV Esmolol to attenuate cardiovascular response during laryngoscopy and endotracheal intubation in controlled hypertensive patients.

2. AIM OF THE STUDY

This study was done to compare the efficacy of IV Dexmedetomidine and IV Esmolol in attenuating the cardiovascular stress responses accompanying laryngoscopy and endotracheal intubation in controlled hypertensive patients by measuring heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

3. NERVE SUPPLY OF LARYNX

Figure 1: Nerve Supply of Larynx



The larynx is supplied by the branches of vagus viz Superior and Recurrent laryngeal. Superior laryngeal nerve divides into a small external branch and a large internal branch, where it is deep to both internal and external carotid arteries.

External branch supplies cricothyroid muscle

Internal branch after piercing the thyrohyoid membrane, supplies the interior of larynx upto the vocal cords.

Recurrent laryngeal nerve:

As the vagus on the right side crosses the subclavian artery, it gives right recurrent laryngeal nerve. It ascends to the larynx after making a loop under the artery and lies in the groove between oesophagus and trachea.

As the vagus on the left side crosses the aortic arch, it gives left recurrent laryngeal nerve. It ascends to the larynx after making a loop under the aortic arch and lies in the groove between oesophagus and trachea.

Once it reaches the neck both side have same relationship. Intrinsic muscles of the larynx except the cricothyroid is supplied by the recurrent laryngeal nerve. It also has a sensory branch which supplies laryngeal mucosa below the vocal cords.

4. NERVE SUPPLY OF TRACHEA

Motor supply:

All muscles of trachea including trachealis supplied by recurrent laryngeal nerve.

Sensory supply:

By Recurrent laryngeal nerve

Sympathetic supply:

From middle cervical ganglion

Connections with recurrent laryngeal nerve

5. PHYSIOLOGIC AND PATHOPHYSIOLOGIC RESPONSES TO DIRECT LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Intubation of trachea alters respiratory and cardiovascular physiology both via, reflex responses and by the physical presence of endotracheal tube. Although the reflex responses are generally of shorter duration and of little consequences in the majority of patients, they may produce profound disturbance in patients with underlying abnormalities such as hypertension, coronary artery disease, reactive airways and intracranial pathology.

Cardiovascular Responses:

The cardiovascular responses to laryngoscopy and intubation are

1. Bradycardia
2. Tachycardia
3. Hypertension

Autonomic nervous system are responsible for these effects. During laryngoscopy and intubation, Bradycardia is often seen in infants and small children and very rarely in adults. An increase in vagal tone at the SA node is responsible for the bradycardia. It is virtually a monosynaptic response to a noxious stimulus in the airway.

The more common response to endotracheal intubation is hypertension and tachycardia. Sympathetic efferents mediates this response via the Cardioaccelerator nerves and sympathetic chain ganglia. The polysynaptic pathways from the vagal and glossopharyngeal afferents to the sympathetic nervous system via the brain stem and spinal cord results in a diffuse autonomic response. This includes widespread release of nor-epinephrine from adrenergic nerve terminals and secretion of epinephrine from the adrenal medulla. Activation of the renin angiotensin system also produces hypertensive response to tracheal intubation, with the release of renin from the renal juxtaglomerular apparatus, which is an end organ innervated by beta adrenergic nerve terminals.

Central Nervous System:

In addition to activation of the autonomic nervous system, endotracheal intubation also stimulates CNS activity. This is evidenced by increasing electroencephalographic activity, cerebral blood flow, and cerebral metabolic oxygen requirement.

Respiratory system:

The effect of endotracheal intubation on the pulmonary vasculature is probably less well studied than the responses elicited in the systemic circulation.

6. AIRWAY-EFFECTS OF ENDOTRACHEAL INTUBATION

1. Upper Airway Reflex: Laryngospasm

Afferent pathway:

1. Glossopharyngeal nerve

   From airway superior to the anterior surface of the epiglottis

2 .Vagus nerve

   Airway from the level of posterior epiglottis down into the lower airway.

Laryngospasm is a monosynaptic reflex primarily elicited under light general anesthesia when vagally innervated nerve endings are stimulated in the upper airway and this reflex cannot be overrided by conscious respiratory efforts.

2. Dead Space:

Normal extra thoracic anatomical dead space of 75 ml which on intubation is reduced by 60 ml.

3. Upper Airway Resistance:

As endotracheal tube decreases airway caliber and increases resistance to breathing, it provides fixed upper airway resistance which produces mechanical burden for spontaneously breathing patient.

4. Lower Airway Resistance:

Bronchospasm and increased airway resistance may occur. Large airway constriction distal to the tube may occur due to stimulation of receptors in the larynx and upper trachea which can extend to the smaller peripheral airways. Following airway instrumentation, parasympathetic activation of airway smooth muscle can cause rapid changes in airway caliber. Cholinergically induced broncho constriction is a normal airway response to intubation in anaesthetized patients.

5. Endotracheal tube Resistance and Exhalation :

Full exhalation does not occur, as endotracheal tube may limit expiratory flow.

6. Functional residual capacity (FRC) :

Presence of endotracheal tube tends to reduce the FRC.

7. Cough :

Whenever an endotracheal tube is in place, Efficiency of cough is reduced.

8. The gases must be warmed and humidified When the upper airway is bypassed following intubation.

7. INTUBATION AND CARDIOVASCULAR DISEASES

In patients with coronary insufficiency, myocardial ischemia is the most common cardiovascular problem following tracheal intubation. Because two of the major determinants of O_2 consumption namely heart rate and blood pressure are markedly increased during intubation. Transmural pressure is the main determinant of the integrity of cerebral and aortic aneurysms. Accordingly sudden increase in BP may produce rupture of the vessels and deterioration of the patient.

Intubation in neurological disorders can cause dangerous increase in intracranial pressure and transient impairment of cerebral perfusion.

Before the advent of neuromuscular blocking drugs, intubation was performed under deep levels of anaesthesia. So that little cardiovascular responses generated.

8. METHODS TO ATTENUATE CIRCULATORY RESPONSES DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

The sympathoadrenal responses should be abolished as maintenance of delicate balance between myocardial oxygen supply and demand forms the keynote in the safe conduct of anaesthesia.

Various methods tried by various workers are

I. Deepening of General Anaesthesia :

Inhalational anaesthetic agents – High dose of volatile agent was required to block haemodynamic response to endotracheal intubation. This deep level of anaesthesia achieved by inhalational agents results in profound cardiovascular depression prior to endotracheal intubation. Various agents used are Halothane, Isoflurane and Sevoflurane.

II. Lignocaine :

a) Lignocaine gargle for Oropharyngeal anaesthesia
b) Aerosol for intratracheal anaesthesia
c) Topical spray for vocal cords
d) Regional nerve blocks – superior laryngeal nerve, glossopharyngeal nerve
e) Intravenous administration.

Topical anaesthesia of upper airway is less effective than lignocaine systemic administration.

Mechanism :

1. By increasing the depth of general anaesthesia,
2. Potentiation of effects of nitrous oxide anaesthesia and reduction of MAC for halothane by 10-28%.
3. Direct myocardial depression,
4. Peripheral vasodilatation
5. Anti arrhythmic properties
6. Suppression of cough reflex

III. Vasodilators:

Hydralazine

Sodium Nitroprusside

Nitroglycerin.

IV. Narcotics

Fentanyl

Alfentanil

Sufentanil

Morphine

Pethidine

Fentanyl is most commonly used narcotic agent.

a) Potent analgesic
b) Has short duration of action
c) Does not increase intracranial tension during controlled ventilation
d) Minimal circulatory changes

Mechanism:

1. The nociceptive stimulation caused by the intubation suppressed by analgesic effect of Fentanyl
2. Decrease in the centrally mediated sympathetic tone.
3. Activation of vagal tone

V. Adrenergic Blockers:

Long acting: Metoprolol, phentolamine, Propranolol, labetalol

Short acting: Esmolol

Of these, Esmolol is most commonly used agent because of its ultra short action.

It reduces resting heart rate, systolic blood pressure, Ejection fraction and cardiac index but it maintains coronary perfusion pressure.

VI. Calcium channel blockers:

Nifedipine

Nicardipine

Diltiazem

Verapamil

Nicardipine has got superior action

VII. Alpha 2 agonist:

Clonidine & Dexmedetomidine

Suppresses the increase in sympathetic activity evoked by the intubation.

VIII. Midazolam:

Sedation and anxiolytic

IX. Magnesium Sulphate:

Sedation and anxiolytic

9.PHYSIOLOGY OF BETA – RECEPTORS

Autonomic nervous system regulates body's ongoing physiological function automatically by a dual function.

First by maintaining an internal environment, and secondly by preparing and enabling the body to undertake extra efforts in situations of threat to the body's well being.

Parasympathetic cholinergic system is a restorative system. Sympathetic adrenergic is primarily stimulatory preparing the body for fight or flight.

In cardiovascular system sympathetic and parasympathetic system are in constant opposition, and the state of the system depends on which system predominates.

AHLQUIST (1960) characterized sympathetic stimulation as being predominantly mediated through alpha or beta receptor effects. Lands et al (1961) observed that beta receptor activity is due to two forms, beta 1 and beta 2 receptor stimulation and is responsible for the effect of sympathetic nervous activation on the heart, smooth muscle relaxation in vascular and respiratory systems, renin release, tissue lipolysis and glycogenolysis.

Beta 1 receptor is primarily involved in cardiac effects. In special circumstances like chronic cardiac failure beta 2 receptors may also mediate cardiac activity.

In congestive cardiac failure beta 1 density decreases without changes in beta 2 receptor accounting for higher inotropic response by isoproterenol.

Beta agonist posses higher affinity for coupled activator forms of the receptor, whereas beta antagonists have affinity for both active and inactive forms with no cellular activity. In addition antagonists maintain the receptors in a relatively inactive form so that considerably more agonists are required to unbalance the equilibrium.

Table 1: Characteristics of Beta Adrenergic Receptors

Receptor	Agonists	Tissue	Responses	Molecular mechanism
Beta 1	Iso > Epi = NE Dobutamine	a. Heart b. Juxta glomerular cells	Force and rate of contraction and AV nodal conduction velocity. Renin secretion	Activation of adenylcyclase and Calcium channels
Beta 2	Iso > Epi = NE Terbutaline	a. smooth muscles (vascular, bronchial, GIT and genitourinary) b. Skeletal muscle c. Liver	Relaxation Glycogenolysis Uptake of potassium Glycogenolysis gluconeogenesis	Activation of adenyl cyclase
Beta 3	Iso=NE>EPi	Adipose tissue	Lipolysis	Activation of adenyl cyclase

Iso - Isoproterenol Epi - Epinephrine NE - Norepinephrine

Table 2: Site of β 1 Receptors and responses of Effector organs to autonomic nerve impulse.

Effector organs	Receptor Type	Adrenergic responses	Cholinergic responses
A. HEART			
SA Node, Atria	β1	↑ H.R. ++ ↑ Contractility and Conduction velocity ++	↓ H.R. Vagal arrest +++
AV Node	β1	↑ Automaticity and conduction velocity ++	↓Contractility and shortened AP duration ++ ↓ Conduction velocity AV block +++
His-Purkinje system	β1	↑ Automaticity and conduction velocity ++	
Ventricle	β1	↑ Contractility, conduction velocity, automaticity and rate of idioventricular pace makers +++	Little effect
B. RENAL Arterioles	β1 + β2	↑Constriction /dilatation ++	
C. INTESTINE Motility and tone	β1 + β2	Decrease	Increase
D. KIDNEY Renin secretion	α 1 + β1	Decrease +	Increase ++

10. BETA RECEPTOR ANTAGONISTS

Most of the currently available β–blocking drugs are propranolamines. The commercial formulation is a racemic mixture, in which the "L" form is the active ingredient.

INDICATIONS

a) Cardiac arrhythmias which are principally due to sympathetic stimulation as in phaeochromocytoma, myocardial infarction and arrhythmias associated with anaesthesia.
b) Ischemic heart disease – improves Oxygen supply – demand ratio.
c) Hypertensive cardiovascular disease – associated with a high plasma renin activity.
d) Thyrotoxicosis
e) Obstructive cardiomyopathy
f) Phaeochromocytoma, Hereditory Tremors, Anxiety neurosis, Schizophrenia, Drug addiction and Migraine

Adverse Reactions:

a. Bronchoconstriction.
b. Cardiac Failure
c. Peripheral vascular insufficiency
d. Hypoglycemia
e. Drug interaction. e.g., antidiabetics.

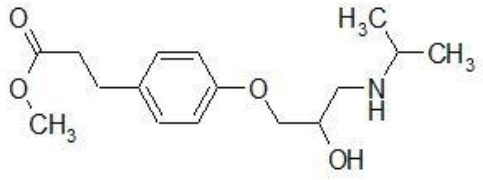
Table 3: BETA ADRENERGIC BLOCKING DRUGS

Drugs	Potency proprano lol=1	Beta selective	Intrinsic sympatho mimetic	Membrane Stabilizing activity	Lipid solubility	Hepatic meta bolism
Propranolol	1	-	-	+	High	99
Timolol	6	-	-	-	Moderate	80
Nadolol	0.8	-	-	-	Low	27
Metoprolol	1	+ +	-	-	Moderate	97
Atenolol	1	+ +	-	-	Low	< 10
Pindolol	6	-	+ ++	+	Mod/Low	60
Oxeprenolol	1	-	+ +	+	Moderate	97
Acebutolol	0.3	+	+	+	High	80
Labetalol	0.3	-	-	-	Mod/High	90+
Esmolol	0.5	+ + +	-	-	Low	0-10

11.PHARMACOLOGY OF ESMOLOL

The concept of an ultrashort acting β-adrenergic blocker was described by ZAROSLINSKI in 1982. From this work, esmolol which is a cardioselective β- blocker and has an extremely short duration of action was subsequently identified and characterized.

Chemistry :



Esmolol is chemically Methyl p- [2-hydroxy -3 (isopropylamino) propoxy] hydrocinnamate hydrochloride, a molecular structure characteristic of second generation β -blockers. The presence and location of an ester in the para position of phenyl ring is of fundamental importance in the determination of Esmolol's cardioselectivity and its ultrashort action.

Esmolol has the empirical formula C16 H26 NO4 C1 and a molecular weight of 331.8. It exists as an enantiomeric pair and has one asymmetric centre.

Esmolol hydrochloride is a white to off-white crystalline powder. It is a relatively hydrophilic compound. It is freely soluble in alcohol and very soluble in water.

Clinical Pharmacology:

Esmolol hydrochloride is a β 1–selective aderenergic receptor (cardioselective) blocking agent with rapid onset, a very short duration of action and no significant membrane stabilizing activity or intrinsic sympathomimetic at therapeutic dose. Esmolol inhibits the β1 receptors located mainly in cardiac muscle, but their preferential effect is not absolute. It inhibits β2- receptors located in the bronchial and vascular musculature at higher doses. Esmolol is 43 fold more potent at β receptors in atria (β 1) than in Trachea (β2). Blockade of vascular β–receptors required a dose several – fold greater than that required for cardiac β–blockade. Esmolol does not have any effect on peripheral vascular resistance.

Pharmacokinetics and Metabolism :

Rapid metabolism of Esmolol is due to hydrolysis of ester linkage, mainly by esterase in the cytosol of RBCs and not by plasma cholinesterase or RBC membrane acetylcholinesterase. Total body clearance of 20L/kg/hr is greater than cardiac output. Thus the metabolism

is not affected by the rate of blood flow to the metabolizing tissues such as the kidney and liver. It has a 2 minutes rapid distribution half-life and an9 minutes elimination half-life.

Steady state Esmolol blood levels are obtained within 5 minutes after an appropriate loading dose and within 30 minutes without loading dose. Blood levels of Esmolol is maintained in steady state during infusion, but after termination of the infusion, it rapidly falls (20 minutes). Since it has a short half-life, blood levels can be altered by changing the infusion rate.

Metabolism of Esmolol results in the formation of an acid metabolite (ASL-8123) phenyl propionic acid and methanol. The acid metabolite has 1/1500th the activity of Esmolol and its blood levels do not correspond to the level of β – blockade. Acid metabolite has an elimination half life of about 3.7 hrs and is excreted in the urine with a clearance approximately equal to the glomerular filtration rate. Elimination of acid metabolite is significantly decreased in patients with renal disease with the elimination half-life increased to ten-fold that of normal. Esmolol is unaffected by plasma cholinesterase. For full enzymatic activity, the Esmolol esterase in RBC cytosol requires a heat–labile high molecular weight plasma component. The enzyme is not inhibited to any significant degree of cholinesterase inhibitor such as

physostigmine or echothiophate, but is totally inhibited by sodium fluoride. No metabolic interactions have been observed between Esmolol and other ester containing molecules of clinical relevance. It does not modify the magnitude or duration of neuromuscular blockade in response to succinylcholine (Richard J.Gorzynski). Esmolol is 55% bound to human plasma protein while acid metabolite is only 10% bound.

In human electrophysiological studies, Esmolol effects that are typical of a β – blocker ; increase in sinus cycle length, decrease in heart rate, and prolongation of sinus node recovery time.

1. Esmolol produces reduction in heart rate, systolic blood pressure, rate pressure product and right ventricular ejection fraction and cardiac index at rest and during exercise, similar in magnitude to propranolol, but produces significantly lower fall in systolic blood pressure ; Esmolol also produces small, clinically insignificant increase in left ventricular end-diastolic pressure and pulmonary capillary wedge pressure. 30 minutes after discontinuation of infusion all the haemodynamic parameters return to pretreatment levels.
2. In asthmatic patients, Esmolol infusion is cardioselective of without significant increase in specific airway resistance Unlike Esmolol, propranolol produces significant bronchospasm requiring bronchodilator

therapy. In COPD patients, Esmolol shows no adverse pulmonary effects.

3. Esmolol is very effective in the management of atrial fibrillation, atrial flutter and supraventricular tachycardia.

There is significant decrease in blood pressure compared to propranolol but was rapidly reversible with decreased infusion rates or on discontinuation. Hypotension was less frequent in those patients receiving concomitant digoxin.

Drug Interactions:

Catecholamine depleting drugs (eg. Reserpine) may have an additive effect when given with Esmolol. So patients should be observed for hypotension or marked bradycardia.

Esmolol concentrations were higher when given with warfarin but this is of no clinical importance. When given with digoxin blood levels of digoxin were high and when given with morphine blood levels of Esmolol were high.

Indications :

For rapid control of ventricular rate as in atrial flutter or fibrillation. For short term control of ventricular rate when short acting agents are

desirable as in (SVT, unstable angina, myocardial infarction) and to control perioperative tachycardia.

Contraindications:

In patients with sinus bradycardia, heart block, cardiogenic shock and overt cardiac failure, diabetics and end stage renal disease.

Adverse Reactions :

CVS – Symptomatic hypotension occurs in 12% of patients. Asymptomatic hypotension in 25% of patients. Hypotension gets resolved on discontinuation of treatment. Very rarely bradycardia, chest pain, syncope, sinus pause and asystole occur all reversible with discontinuation of treatment.

CNS : Dizziness, Headache, agitation and fatigue.

RS : Bronchospasm, nasal congestion – relatively less.

GIT : Nausea, vomiting, constipation, Diarrhoea, Drymouth.

Skin : Inflammation, and induration at the site of infusion, Oedema, skin discolouration, thrombophlebitis and local skin necrosis.

Acute Toxicity:

Accidental massive overdose when it occurs is due to an error in dilution. It can cause hypotension, bronchospasm, drowsiness, bradycardia and loss of consciousness. These are resolved within ten minutes of discontinuation or with administration of a pressor agent.

Compatibility :

Compatible with commonly used intravenous fluids except sodium bicarbonate injection.

Preparations Available :

100 mg	-	10 ml vial
2.5 g	-	10 ml amp

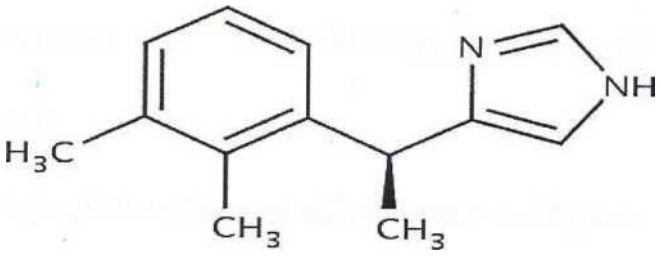
Dosage :

To attenuate the sympathoadrenal response during laryngoscopy and intubation, the dosage is 1.5 mg/kg as bolus or as an infusion at the rate of 500 mcg/kg/minute for 2 minutes as loading dose followed by a maintenance dose of 100 mcg/kg/minute.

To initiate treatment of a patient with supraventricular tachycardia, a loading dose of 500 mcg/kg/minute for 1 minute followed by

maintenance infusion of 50 mcg/kg/minute for 4 minutes. If an adequate therapeutic effect is not observed within 5 minutes, the same loading dose can be repeated and followed with a maintenance infusion increased to 100 mcg/kg/min, therapeutic plasma level being 400-1200 nano gm/ml. The time to 100% recovery is 30 minutes.

12.PHARMACOLOGY OF DEXMEDETOMIDINE



Dexmedetomidine is an a_2- agonist that received FDA approval in 1999. It is indicated for short-term(less than 24 hrs) sedative analgesic especially in the ICU[3]. Clonidine is the prototype of alpha 2 agonists. It is widely used as an anaesthetic adjuvant and in pain medicine but little as a sedative. Dexmedetomidine is a highly selective α_2- adrenoceptor agonist than clonidine and hence it can be used in high doses for sedation and analgesia without the unwanted side effects from the activation of α_1- receptors[4]. Dexmedetomidine is a shorter acting drug than clonidine. The sedative effect of dexmedetomidine can be reversed by Atipamezole. It is used in perioperative period as a sedative, premedication agent, as an adjuvant for general and regional anaesthesia and also for postoperative sedation and analgesia.

PHYSIOLOGY OF α_2 ADRENORECEPTORS

α_2 - adrenoceptors were found in central and peripheral nervous systems, also in effector organs like kidney, liver, pancreas, vascular smooth muscles, eye and platelets.

They are divided into 3 subtypes.

α_2A – predominant subtypes in CNS, this is responsible for the sedative, analgesic and sympatholytic effect. Dexmedetomidine is 8 to 10 times more selective a_2 AR agonist than Clonidine.

α_2B – found in the peripheral vasculature, and is responsible for the short term hypertensive response.

α_2C – found in the CNS, Which is responsible for the anxiolytic effect.

All these subtype act at the cell level by signalling through a G-Protein which couples to effector mechanisms, and the coupling differs depending on receptor sub-type and location. The a_2 A-Subtype appears to couple in an inhibitory manner to the calcium ion channel in the locus ceruleus of the brain stem.

In the vasculature, the α_2 B subtype couple in an excitatory fashion to the same effector mechanism.

MECHANISM OF ACTION OF DEXMEDETOMIDINE

Dexmedetomidine possess unique properties and it differs from other sedative drugs. α_2 - adrenoceptors are found in many sites throughout the CNS, but the highest densities are found in the locus ceruleus, the important noradrenergic nuclei of the brainstem which is an important modulator of vigilance[5]. Presynaptic activation of α_2 A adrenoceptor in the locus ceruleus inhibits nor epinephrine (NE) release and results in sedative and hypnotic effects.

The important modulator for nocioceptive neurotransmission is the descending medullospinal noradrenergic pathway and it originates from locus ceruleus of brainstem. Stimulation of the α_2 -adrenoceptors in this area terminates mainly the propagation of pain signals leading to analgesia. In the CNS, post synaptic activation of α_2 –adrenoceptors may produce hypotension and bradycardia because of decrease in sympathetic activity. Also cardiac vagal activity is augmented and all the effects together produce sedation, analgesia, and anxiolysis.

Activation of α_2 -receptors at the substantia gelatinosa of dorsal horn at the spinal cord causes inhibition of the nociceptive neurons firing and also inhibition of substance P release. The peripheral α_2 adrenoceptors also have anti nocioception action by preventing NE release at the nerve endings resulting in analgesia. The spinal action is

the principal mechanism for the analgesia, but evidence exists for both supraspinal and peripheral sites of action.

α_2 – receptors located on blood vessels mediates vasoconstriction whereas those located on sympathetic terminals inhibit NE release. In other areas these adrenoceptors cause contraction of vascular and other smooth muscles, decrease in salivation, decrease in secretion and motility of bowel in the gastrointestinal tract. It also causes inhibition of renin release leading to increase in glomerular filtration, increase in secretion of sodium and water by the kidney. α_2 - adrenoceptors activation also causes decrease in insulin release from pancreas, decrease in intraocular pressure, decrease in platelet aggregation and decrease in the shivering threshold by 2°C.[6]

PHARMACOKINETICS, ABSORPTION AND DISTRIBUTION

Dexmedetomidine, is the active d-isomer of medetomidine. It is an imidazole derivative. Dexmedetomidine in doses between 0.2 to 0.7 mcg/kg /hr exhibits linear pharmacokinetics and it is administered as intravenous infusion upto 24 hours. It has 6 minutes half life of distribution and 2 hours half life for elimination, Because it has the rapid distribution phase.

The steady-state volume of distribution is 118L. Average protein binding is 94%. Context- sensitive half life ranges from 4 minutes to 250 minutes for infusion duration of 10-minutes to 8-hours. Because of its extensive first-pass metabolism, its oral bioavailability is poor.

The bioavailability of sublingual route is high (84%) and it offers a potential role in paediatric sedation and premedication[7] .

The pka of dexmedetomidine is 7.1 and is freely soluble in water. For sedation, it has to be given as a loading dose of 1µg/kg i.v over 10 minutes and maintenance dose by an infusion of 0.2 - 0.7µg/kg/hr.

METABOLISM AND EXCRETION

Dexmedetomidine undergoes biotransformation into its inactive metabolites through direct N- glucuronidation and cytochrome P-450 (CYP 2A6) mediated aliphatic hydroxylation. Metabolites are excreted in urine (95%) and in the faeces (4%). Dose has to be reduced in patients with hepatic failure and renal failure.

PHARMACODYNAMICS OF DEXMEDETOMIDINE

α_2 - adrenoceptor agonists have different a_2 / a_1 selectivity. a_2/ a_1 selectivity of dexmedetomidine is 1620:1 whereas it is low for clonidine (220:1) and hence dexmedetomidine is 8 times more specific a_2 - adrenoceptor agonist than clonidine.

CARDIOVASCULAR SYSTEM

Dexmedetomidine does not have any direct action on the heart. It causes a dose dependent increase in the coronary vascular resistance and oxygen extraction, leading to alteration in the supply / demand ratio. It exhibits a biphasic response in blood pressure with short hypertensive phase followed by subsequent hypotension.

RESPIRATORY SYSTEM

Dexmedetomidine does not produce respiratory depression even at high doses[8] . It can be used in spontaneously breathing ICU patients and after surgery. It maintains sedation without cardiovascular instability or respiratory drive depression. Hence it is used during weaning and extubation in surgical ICU /trauma patients in whom previous weaning attempts have failed because of agitation associated with hyperdynamic cardio pulmonary response[9] .

CENTRAL NERVOUS SYSTEM

Cerebral blood flow and cerebral metabolic requirement of oxygen are reduced by Dexmedetomidine. Dexmedetomidine enhances cumulative performance and also possess sedative, analgesic and anxiolytic action through α_2 –AR[10] . Brain and circulating catecholamines levels are reduced, thus balancing the ratio between cerebral oxygen supplies and reduces excitotoxicity. Hence it improves the perfusion in the ischemic penumbra, and possess excellent neuroprotective action. In subarachnoid haemorrhage it reduces the levels of glutamate which is responsible for cellular brain injury.

ENDOCRINE AND RENAL EFFECTS

Dexmedetomidine activates peripheral presynaptic α_2 -AR, thus catacholamine release is reduced and hence sympathetic response to surgery is also reduced. It is an imidazole agent but does not inhibit steroidogenesis when used as an infusion for short term sedation[11] .

ADVERSE EFFECTS

1. Hypotension & hypertension
2. Bradycardia & atrial fibrillation
3. Dry mouth
4. Nausea & vomiting
5. Pulmonary edema
6. Pleural effusion & atelectasis
7. Pyrexia & chills
8. Hyperglycemia & hypocalcaemia
9. Acidosis, etc.,

Transient hypertension is produced when dexmedetomidine infusion is rapidly administered (Loading dose of 1µg/Kg / hr given in less than 10 minutes) and this is mediated by vasoconstriction on action at peripheral α 2B-AR[12] .

The occurrence of hypotension and bradycardia is mediated by central α_2A-AR[13] , causing decrease of noradrenaline release from the sympathetic nervous system. Supersensitization and up regulation of receptors occur during long term use, hence abrupt discontinuation not advised. Withdrawal syndrome, nervousness, headache, hypertensive crisis, and agitation occur during abrupt discontinuation.

USES OF DEXMEDETOMIDINE

PREMEDICATION

Dexmedetomidine is used as an adjuvant for premedication since this drug possess sedative, analgesic, anxiolytic, sympatholytic, and stable hemodynamic profile. It potentiates the anaesthetic effects of all intraoperatively used anesthetics (intravenous, volatile or regional block). In a study by Bohrei et al, preoperative administration of dexmedetomidine either intravenous or intramuscular resulted in a decrease in the induction dose of thiopentone by upto 30%[14] .

Dexmedetomidine can also be used as a premedication in paediatric anaesthesia either orally or nasally[15] . Dexmedetomidine in a dose of 1 µg/kg intramuscularly used as a premedication in outpatient ophthalmic surgery resulted in sedation, and decrease in intraocular pressure without significant bradycardia or hypotension[16]. Dexmedetomidine as a premedication reduces oxygen consumption intraoperatively by 8% and in post operative period by 17%[17] .

AS AN ADJUVANT TO GENERAL ANASTHESIA

Intraoperatively dexmedetomidine produces hemodynamic stability by attenuating the haemodynamic response to intubation, during surgery, during extubation and emergence from anaesthesia[18] . It reduces the maintenance concentration of various inhalational anaesthetic agents and also produces intraoperative and postoperative opioid sparing effect. It reduces the shivering threshold and can be used to prevent and treat shivering.

USE OF DEXMEDETOMIDINE IN REGIONAL ANAESTHESIA

Dexmedetomidine seems to be promising adjuvant in the field of regional anaesthesia. It is used as an effective adjuvant in central neuraxial blocks, minor and major peripheral nerve blocks. Highly lipophilic nature of dexmedetomidine facilitates rapid absorption into the cerebrospinal fluid. It binds to a_2 - AR of spinal cord for its analgesic action[19] . Sensory and motor block produced by local anaesthetics is prolonged. It is also used in brachial plexus block, intravenous regional anaesthesia (IVRA), and intraarticularly. It is also given through intraarticular route in arthroscopic knee surgeries to improve the duration of postoperative analgesia[20] .

SEDATION IN ICU

Dexmedetomidine produce cooperative sedation. It does not interfere with the respiratory drive hence it facilitates early weaning from ventilator, thus reducing ICU stay costs[21] . Many studies have recommended their use for longer than 24 hrs. Other beneficial effects are analgesic sparing effects, minimal respiratory depression, reduced delirium and agitation, and desirable cardio vascular effects.

MONITORED ANAESTHESIA CARE

Dexmedetomidine is used for short term procedural sedation like transesophageal echocardiography[22] , shockwave lithotripsy[23] , colonoscopy[24] , awake carotid endarterectomy[25] , paediatric MRI[26] , and elective awake fiberoptic intubation[27] . The dose is 1 µg/kg which is followed by an infusion of 0.2µg/kg/h.

CONTROLLED HYPOTENSION

Spinal fusion surgery for idiopathic scoliosis[28] , tympanoplasty and septoplasty operations[29] and maxillofacial surgery[30] have been done with dexmedetomidine induced hypotension.

ANALGESIA

Dexmedetomidine activates a_2 -AR in the spinal cord, resulting in a reduced transmission of nocioceptive signals. It possesses significant opioid sparing effect.

CARDIAC SURGERY

Dexmedetomidine reduces the extent of myocardial ischemia during cardiac surgery[31] . Its other uses are in the management of pulmonary hypertension in patients undergoing mitral valve replacement[12] .

NEUROSURGERY

Dexmedetomidine possess neuroprotective effect. It also attenuates delirium and agitation, so that postoperative neurological evaluation will be easier. It has a role in functional neurosurgery like awake craniotomy surgeries and implantation of deep brain stimulators for Parkinson's disease[32] .

OBESITY

In morbidly obese patients this drug does not cause respiratory depression in the dose of 0.7µg /kg intra operatively.

OBSTETRICS

Intravenous dexmedetomidine is used as an adjuvant along with systemic opioids for labour analgesia[33] . Because of its high lipophilicity, it is retained in the placenta and less readily enters the fetal circulation than clonidine. Thus the chance of fetal bradycardia is less.

PAEDIATRICS

Recently it is used in paediatric patients for sedation during non-invasive procedures in radiology like CT scan and MRI[34] . It is also used for sedation in PICU settings, various invasive surgical procedures like upper GI scopy, colonoscopy, fiberoptic intubation[35] . Dexmedetomidine is also used in paediatric open heart surgeries to attenuate the hemodynamic and neuroendocrine stress response to surgical trauma and cardiopulmonary bypass[36].

OTHER USES

Used as an anti-shivering agent. Also used in the treatment of withdrawal from opioids, benzodiazepines, and alcohol.

13.REVIEW OF LITERATURE

Though laryngoscopy and intubation were performed with ease in earlier years, the Anaesthesiologists had to struggle to combat or subdue the circulatory or cardio vascular effects of the said procedure in patients with compromised circulatory system.

RIED&BRACE[37] (1940) postulated that reflex circulatory responses to laryngeal instrumentation were mediated through the vagus nerve and they named it as "Vaso Vagal Reflex".

KING et al[38] (1951) used deep Ether anaesthesia to abolish the reflex circulatory response to tracheal intubation.

KING and his associates[38] (1960) believed the reflex mechanisms to be essentially non-specific in character. They stated that the impulses initiating the reflex arc are probably carried over the vagus, while the effector system is less clearly defined and may be due to decreased parasympathetic or increased sympathetic adrenal activity.

WYCOFF C.C.[39] (1960) in his study stated that topical anaesthesia of the pharynx along with Superior laryngeal nerve blocks reduced the increase in mean arterial pressure after intubation.

FORBES and DALLY[40] (1970) observed that laryngoscopy and endotracheal intubation is immediately associated with an average increase in mean arterial pressure of 25mm of Hg in all 22 normotensive patients. These responses were interpreted as due to reflex sympathetic adrenal stimulation.

PRY ROBERT et al[41] (1971) found that the increases in heart rate and blood pressure are much more exaggerated in hypertensive patients

They observed

i. Inotropic failure

ii. Ischemic arrhythmias

iii. CerebrovascularAccidents

In patients with uncontrolled hypertension who came up for emergency surgery and associated substantial increase in heart rate and blood pressure following laryngoscopy and endotracheal intubation which lasted for several minutes.

DENLINGER J.K and ELLISON N.E.[42] (1974) have used intratracheal lignocaine spray which causes a 50% reduction in the hypertensive response.

VICTORIA FARIA BALNC and NORMAND A.G.[43] (1974) in their article of "Complications of Tracheal Intubation" has classified the neurogenic or reflex mediated complication into three different categories.

i. Laryngo Vagal Reflexes- Which give rise to spasm of the glottis, apnoea, bronchospasm, cardiac dysrhythmias, bradycardia, and arterial hypotension. The mere presence of the tracheal tube seems to be the most common cause of bronchospasm in anaesthetized asthmatic patients.

ii. Laryngo Sympathetic Reflexes which include tachyarrhythmias, tachycardia and acute arterial hypertension as frequent complication. During laryngoscopy, the hypertensive hyperdynamic state may be related to an increased noradrenaline fraction of the total catecholamines.

iii. Laryngo Spinal Reflexes- which include vomiting, coughing, and bucking

J.CURRAN, M.CROWLEY[44] (1980) has studied the use of Droperidol an alpha blocker to attenuate the pressor response. Droperidol administration was found to be associated with an undesirably low mean arterial pressure for a short period in a proportion of patients.

PARNASS SM, KERCHBERGER JP, ROTHENBERG DM, and IVANKOVICH AD[45] (1990) demonstrated that single bolus dose of esmolol blunted tachycardia and hypertensive response to laryngoscopy and endo tracheal intubation.

STEVEN M. HELFMAN, EVERTARD A, MARTIN I GOLD, CLAIRE A. HERRINGTON and DE LESSER (1991)[46] observed that esmolol provides consistent and reliable protection from increase in both heart rate and systolic blood pressure during and after intubation. Where as lignocaine and fentanyl failed to protect against increases in heart rate but provided protection against increase in systolic blood pressure equivalent to that provided by esmolol.

D. R. MILLER and R.J. MARTENEAN[47] (1991) concluded that esmolol 1.5mg/kg is safe and effective in controlling cardiovascular responses during anaesthetic induction.

HELFMAN SM, GOLD MI, DELISSER EA, HERRINGTON CA[48] (1991) demonstrated that only esmolol provided consistent and reliable protection against increase in both heart rate and systolic blood pressure accompanying laryngoscopy and intubation.

FENQ CK, CHAN KH, LOKN, ORCH, LECTY[49](1996), observed that only esmolol could reliably offer protection against increase in both heart rate and systolic blood pressure, low dose fentanyl (3mcg/kg) prevented hypertension but not tachycardia and 2mg/kg lidocaine has no effect to blunt adverse haemodynamic response during layngoscopy and tracheal intubation.

Suman Sharma et al[50] (1996) reported that in treated hypertensive patients, 100mg of Esmolol is safe and convenient method for attenuating haemodynamic response during layngoscopy and tracheal intubation.

Oxorn et al.[51] (1990) reported that 100mg and 200mg of esmolol in bolus doses affects solely increase in heart rate in a significant manner.

Kindler et al.[52] (1996) concluded that administration of esmolol was effective on attenuating increase in heart rate to tracheal intubation, But not effective on attenuating the blood pressure response.

Scheinin et al.[53] (1992) concluded that in healthy individuals dexmedetomidine 0.6 μg/kg decreased, but not totally abolished, the cardiovascular response to tracheal intubation.

Menda et al.[54] (2010) reported that in patients undergoing myocardial revascularization, dexmedetomidine when combined with fentanyl effectively attenuated the hemodynamic response to endotracheal intubation.

Hale Yarkan Uysal et al.[55] (2012) concluded that in hypertensive patients, administration of dexmedetomidine in a single dose before induction of anesthesia was an effectively attenuate the hemodynamic response to tracheal intubation.

14. MATERIALS

METHODOLOGY

A Single centre, Prospective, Randomized, Double blind study

SAMPLE SIZE

Total of 60 controlled hypertensive patients (Diagnosis of SHT according to WHO criteria SAP≥160 mm of Hg or DAP≥90 mm of Hg) undergoing general anaesthesia for elective non cardiac surgery

RANDOMIZATION AND ALLOCATION

60 Patients are randomly divided into 2 groups of 30 patients each by using sealed envelope technique

1. ***Group D (Dexmedetomidine):***

   consisting of 30 patients who received Dexmedetomidine 1µg/kg in 100ml normal saline, 2 minutes prior to intubation.

2. ***Group E (Esmolol):***

   consisting of 30 patients who received 1.5 mg / kg Esmolol, 2 minutes prior to intubation.

INCLUSION CRITERIA

1. **ASA Physical status II**
2. **Well controlled Hypertensive Patients**
3. **Age 30 - 60 years**
4. **Both Gender**

EXCLUSION CRITERIA

1. Patient’s refusal
2. Secondary Hypertension
3. Co-morbidities like DM, CAD, CVA
4. Pregnancy
5. Predicted Difficult Intubation
6. Intubation time >30Secs
7. Intubation in more than one attempt.

Preoperative preparations:

Age

I.P.No

Body weight

Baseline vital parameters

History

Previous anaesthesia and Surgery

Any co-morbidities

Medications

Any allergy

Complete physical examination

Airway assessment

Laboratory investigations

Hb %

Blood Sugar

Serum urea & Creatinine, electrolytes

Bleeding and clotting time

Urine analysis

X ray chest

ECG

Other investigations were obtained on the basis of the condition of the patient.

15.METHODS

After getting institutional ethical committee approval, the procedure was explained to the patients and written informed consent was obtained.

All patients were premedicated with injection Midazolam 0.05 mg/kg and Injection glycopyrrolate 0.2 mg intramuscularly 45 minutes before surgery.

In operating room, IV line was established. Patients were monitored by NIBP,ECG, SpO2 and 0.9% NaCl was started at the rate of volume based on fluid deficit and maintainence fluid according to patients body weight. Baseline Parameters (HR, SAP, DAP, MAP and SpO2) were recorded.

Group D received 1µg/kg of Dexmedetomidine in 100 ml 0.9% NaCl over 10 minutes. Group E received 1.5mg/kg of Esmolol over 1 min. An anaesthesiologist who is not involved in the study, administered the study drug.

After 2 min, Patient induced with thiopentone sodium 5 mg/kg, fentanyl 2 µg/kg and atracurium 0.5mg/kg. All patients were ventilated via face mask. Laryngoscopy and endotracheal intubation is done by appropriate size cuffed endotracheal tube. Anaesthesia was maintained with controlled ventilation with nitrous oxide 66% and oxygen 33%.

HR,SAP,DAP,MAP and SpO2 were recorded Baseline(T1), after drug administration(T2), after induction(T3), 0, 1, 3, 5, 10, 15 min after intubation(T4-T9). No surgical intervention was allowed throughout the study period.

16.STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done by using statistical package for social sciences version 16.

All data were expressed as mean ± 2 SD. Student 't' test and Pearson chi square were used to analyze the nominal data. Paired 't' test was used to compare intra group variation. A 'p' value less than 0.05 is taken to denote significant relationship.

17.OBSERVATION AND RESULTS

60 patients under this study were categorized into 2 groups(Group D & Group E). They comprised both sexes with age ranging from 30-60 years.

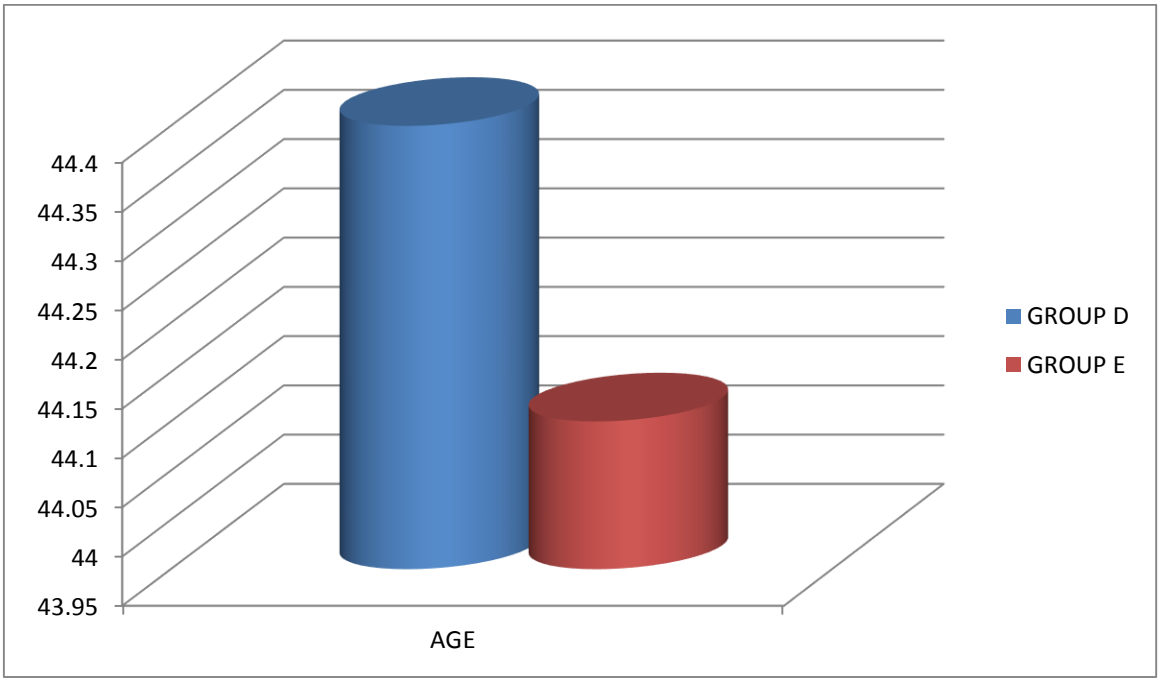
Demographic profile, type of anti hypertensive medications and baseline parameters between two groups were comparable and were not statistically significant (P>0.05).

AGE

Table 4: AGE

	MEAN ±SD	P VALUE
GROUP D	44.4 ±7.2	0.884
GROUP E	44.4 ±8.62	

Figure 2: AGE



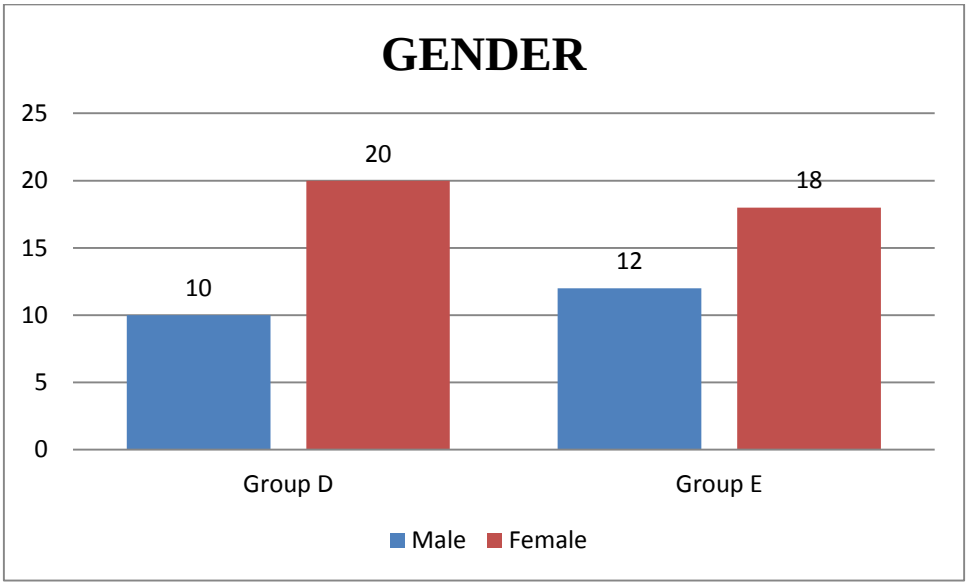
The mean age of the patients is 44.4 in Group D & E. There is no significant difference in the age composition of the cases in the two groups(P 0.884).

SEX

Table 5: SEX

Groups	GENDER		Total	P value
	Male	Female		
Group D	10	20	30	0.592
Group E	12	18	30	
Total	22	38	60	

Figure 3: SEX



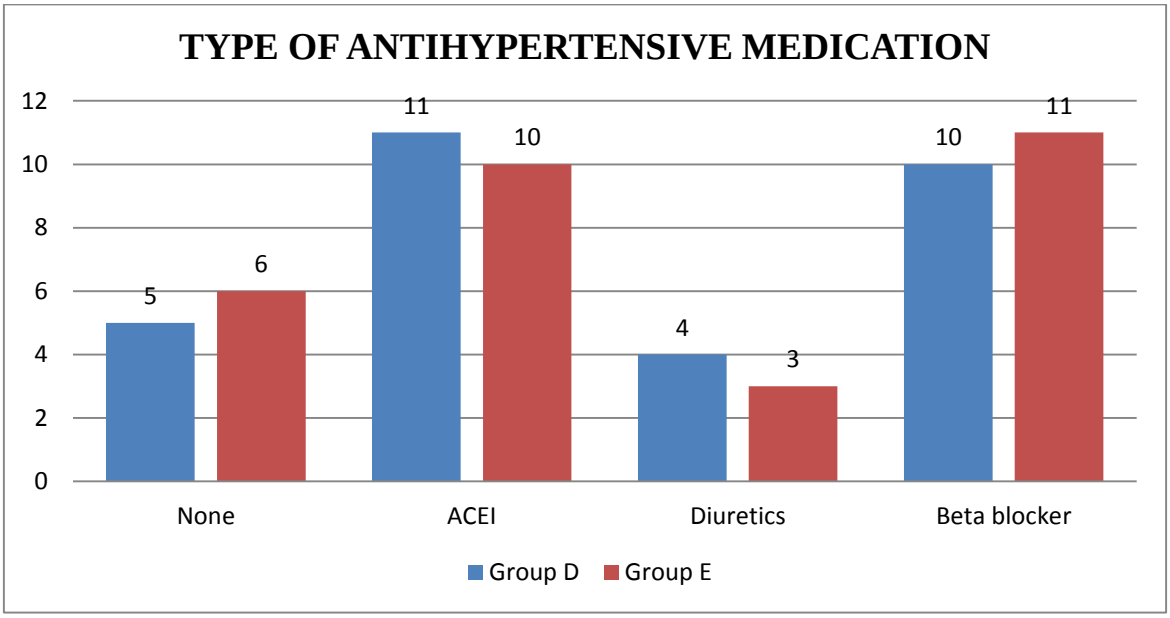
There is no significant difference in the sex composition of the cases in the two groups (P 0.592).

ANTI HYPERTENSIVE MEDICATION

Table 6: ANTI HYPERTENSIVE MEDICATION

Groups	ANTI HYPERTENSIVE DRUGS				Total	P value
	None	ACEI	Diuretics	Beta blocker		
Group D	5	11	4	10	30	0.954
Group E	6	10	3	11	30	
Total	11	21	7	21	60	

Figure 4: ANTI HYPERTENSIVE MEDICATION



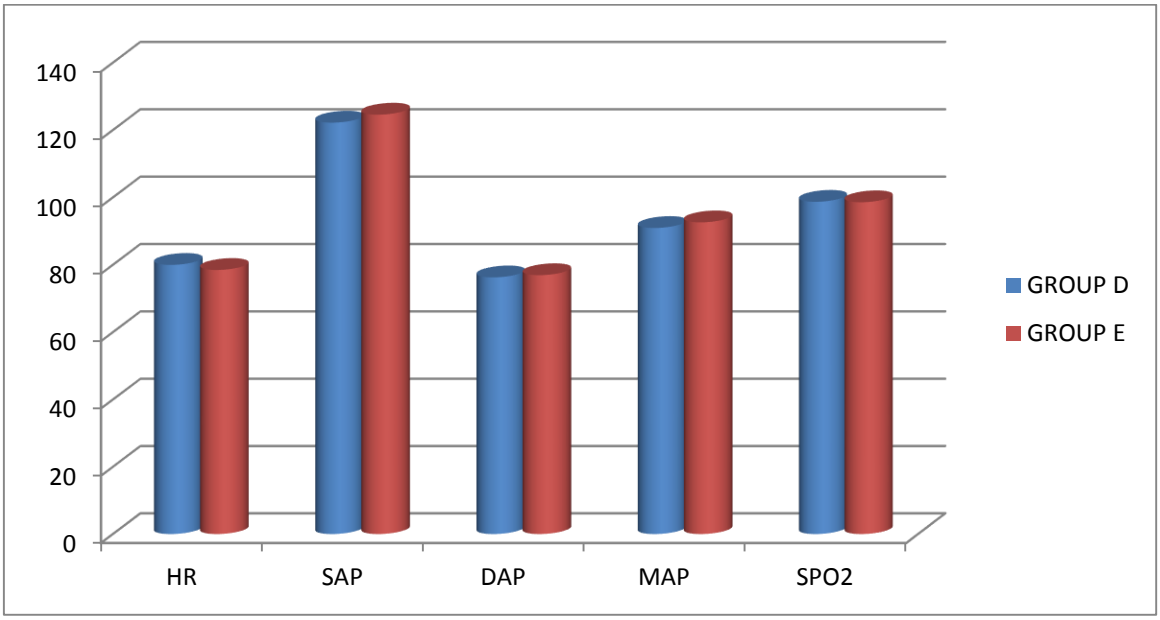
There is no statistical difference in anti hypertensive drugs taken by patients in two groups (P 0.954).

BASELINE PARAMETERS

Table 7: BASELINE PARAMETERS

PARAMETERS	GROUP	Mean	Std. Deviation	t value	P value
HR	D	79.97	5.70	1.02	0.314
	E	78.47	5.74		
SAP	D	122.20	10.55	-0.84	0.402
	E	124.57	11.17		
DAP	D	76.27	8.36	-0.33	0.740
	E	76.93	7.07		
MAP	D	90.93	8.58	-0.79	0.434
	E	92.60	7.77		
SPO2	D	98.70	1.26	-0.76	0.429
	E	98.57	1.33		

Figure 5: BASELINE PARAMETERS



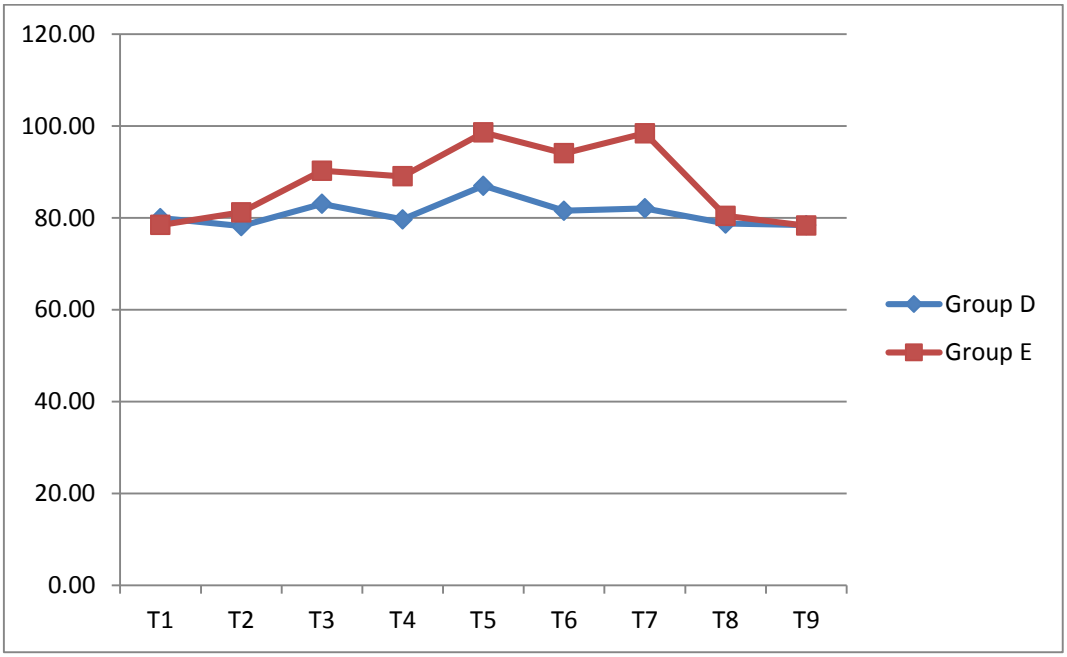
The mean HR, SAP, DAP, MAP & SPO2 of the patients were 79.97, 122.20, 76.27, 90.93 & 98.70 in Group D and 78.47, 124.57, 76.93, 92.60 & 98.57 in Group E respectively. There is no statistical difference in baseline parameters between two groups.

HEART RATE

Table 8: HEART RATE

Time	GROUP	Mean	Standard Deviation	t value	P value
T1	D	79.97	5.70	1.02	0.314
	E	78.47	5.74		
T2	D	78.20	5.91	-2.17	0.034
	E	81.20	4.72		
T3	D	83.07	9.93	-3.20	0.002
	E	90.27	7.29		
T4	D	79.67	6.94	-6.48	<0.0001
	E	89.03	3.81		
T5	D	87.00	11.52	-4.23	<0.0001
	E	98.60	9.62		
T6	D	81.57	8.32	-4.58	<0.0001
	E	94.07	12.43		
T7	D	82.07	8.12	-7.97	<0.0001
	E	98.43	7.78		
T8	D	78.76	7.26	-0.85	0.398
	E	80.43	7.89		
T9	D	78.43	7.13	0.08	0.934
	E	78.30	5.14		

Figure 6: HEART RATE



In Dexmedetomidine group (Group D), the mean basal heart rate was 79.97 beats / minute and reached maximum of 87 beats / minute at 1 min after laryngoscopy and endotracheal intubation and came back to the basal value of 78.6 beats / minute at 10 minutes.

In Esmolol group (Group E), the mean basal heart rate was 78.47 beats / minute which reached maximum of 98.6 beats / minute following laryngoscopy and endotracheal intubation and came back to the basal value of 78.37 beats/minute at 15 minutes following laryngoscopy and intubation.

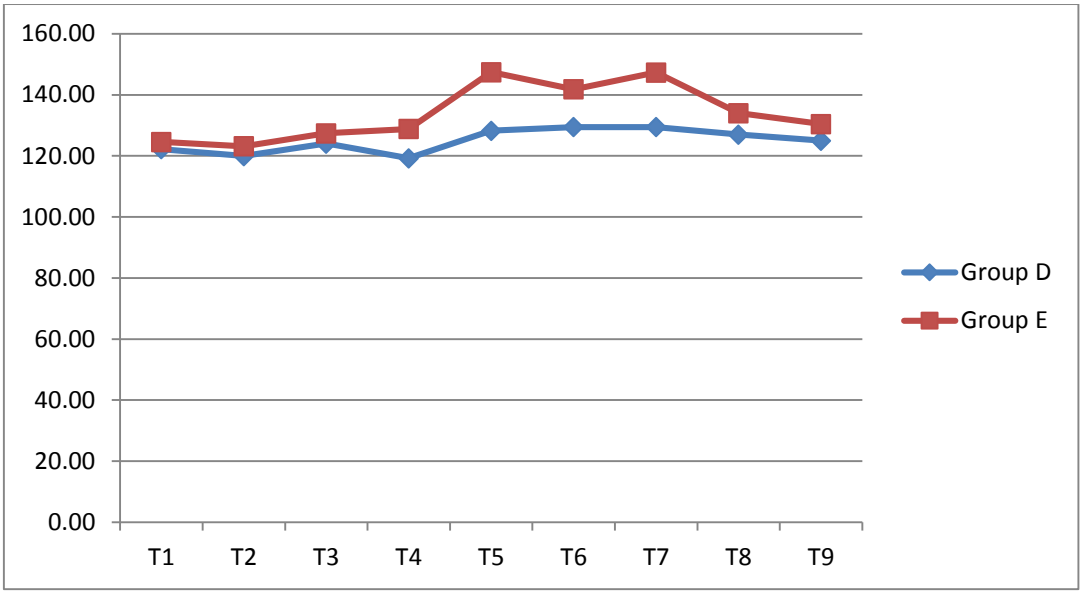
There is statistical significant lower heart rate in group D compared to group E at T3 to T7.

SYSTOLIC ARTERIAL PRESSURE

Table 9: SAP

Time	GROUP	Mean	Standard Deviation	t value	P value
T1	D	122.20	10.55	-0.84	0.402
	E	124.57	11.17		
T2	D	119.97	10.71	-1.20	0.235
	E	123.13	9.72		
T3	D	124.03	17.60	-0.95	0.346
	E	127.40	8.03		
T4	D	119.20	13.01	-3.32	0.002
	E	128.80	9.00		
T5	D	128.27	14.95	-4.93	<0.0001
	E	147.40	15.12		
T6	D	129.43	13.47	-3.09	0.003
	E	141.83	17.38		
T7	D	129.43	12.34	-5.88	<0.0001
	E	147.33	11.20		
T8	D	127.00	10.63	-1.84	0.071
	E	134.03	18.03		
T9	D	124.97	9.91	-1.66	0.102
	E	130.47	15.17		

Figure 7: SAP



In Dexmedetomidine group (Group D), the mean basal systolic blood pressure 122.2 mm of Hg and reached maximum of 129.43 mm of Hg at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 10 minutes.

In Esmolol group (Group E), the mean basal systolic blood pressure was 124.57 mm of Hg and reached maximum of 144.40 mm of Hg at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 15 minutes following intubation.

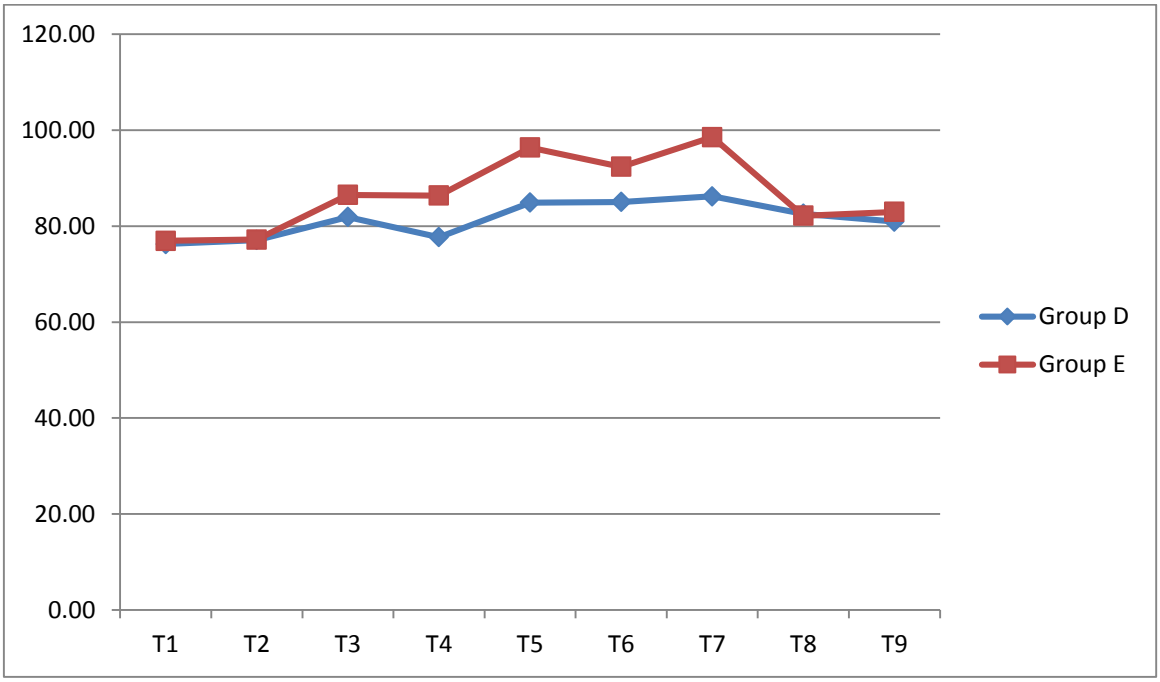
There is statistical significant lower SAP in group D compared to group E at T4 to T7.

DIASTOLIC ARTERIAL PRESSURE

Table 10: DIASTOLIC ARTERIAL PRESSURE

Time	GROUP	Mean	Standard Deviation	t value	P value
T1	D	76.27	8.36	-0.33	0.740
	E	76.93	7.07		
T2	D	77.10	8.23	-0.05	0.960
	E	77.20	7.25		
T3	D	81.90	13.84	-1.50	0.137
	E	86.50	9.36		
T4	D	77.70	9.64	-4.17	<0.0001
	E	86.37	6.04		
T5	D	84.90	15.20	-3.35	0.001
	E	96.37	10.99		
T6	D	85.03	12.89	-2.37	0.021
	E	92.37	11.03		
T7	D	86.20	13.50	-4.35	<0.0001
	E	98.53	7.65		
T8	D	82.56	12.09	0.13	0.890
	E	82.16	10.07		
T9	D	80.93	10.28	-0.77	0.445
	E	82.96	10.17		

Figure 8: DIASTOLIC ARTERIAL PRESSURE



In Dexmedetomidine group (Group D), the mean diastolic blood pressure was 76.27 mm Hg and reached maximum of 86.2 at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 10 minutes following intubation.

In Esmolol group (Group E), the mean diastolic blood pressure was 76.93 mm of Hg and reached maximum of 98.53 mm of Hg at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 15 minutes following intubation.

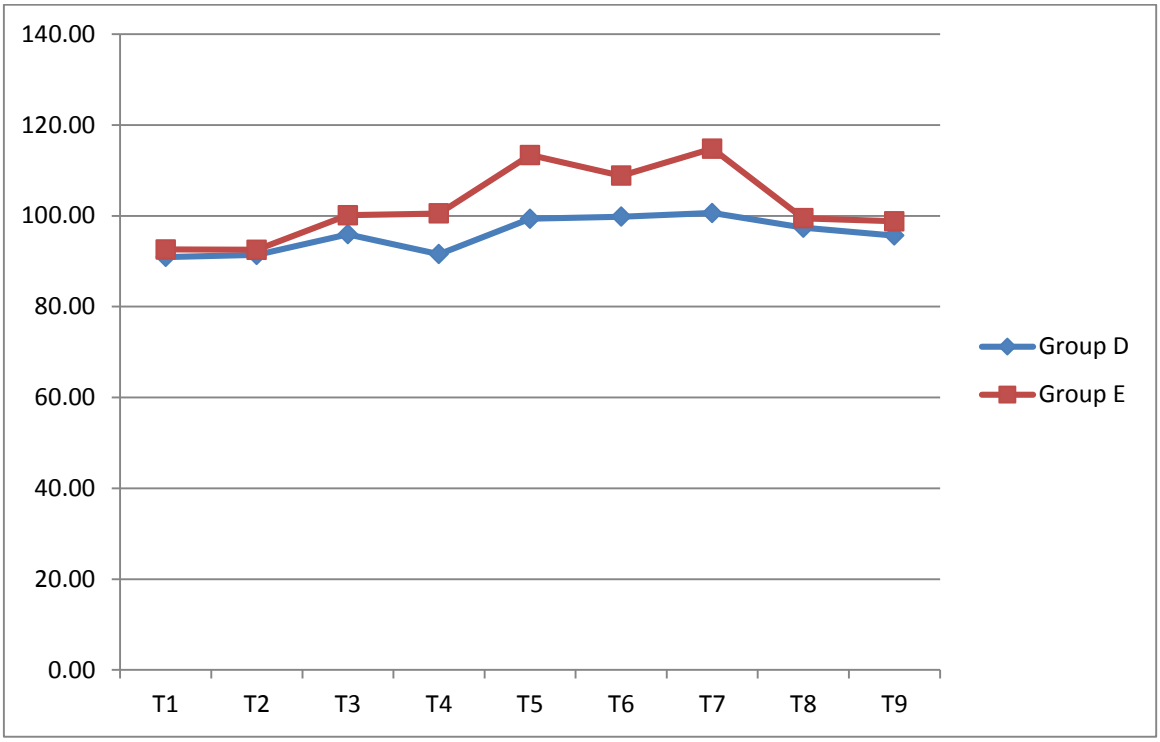
There is statistical significant lower DAP in group D compared to group E at T4 to T7

MEAN ARTERIAL PRESSURE

Table 11: MEAN ARTERIAL PRESSURE

Time	GROUP	Mean	Standard Deviation	t value	P value
T1	D	90.93	8.58	-0.79	0.434
	E	92.60	7.77		
T2	D	91.39	8.43	-0.56	0.579
	E	92.51	7.06		
T3	D	95.94	14.49	-1.36	0.176
	E	100.13	8.40		
T4	D	91.56	10.07	-4.18	<0.0001
	E	100.53	6.07		
T5	D	99.36	14.59	-4.07	<0.0001
	E	113.38	11.94		
T6	D	99.83	12.70	-2.79	0.007
	E	108.86	12.35		
T7	D	100.61	12.66	-5.26	<0.0001
	E	114.80	7.60		
T8	D	97.37	10.80	0.72	0.477
	E	99.45	11.67		
T9	D	95.67	9.21	-1.21	0.228
	E	98.80	10.99		

Figure 9: MEAN ARTERIAL PRESSURE



In Dexmedetomidine group (Group D), the mean MAP was 90.93 mm of Hg and reached maximum of 100.61 mm of Hg at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 10 minutes following intubation.

In Esmolol group (Group E), the mean MAP was 92.6 mm of Hg and reached maximum of 114.8 mm of Hg at 1 minute following laryngoscopy and endotracheal intubation and came back to the basal value at 15 minutes following intubation.

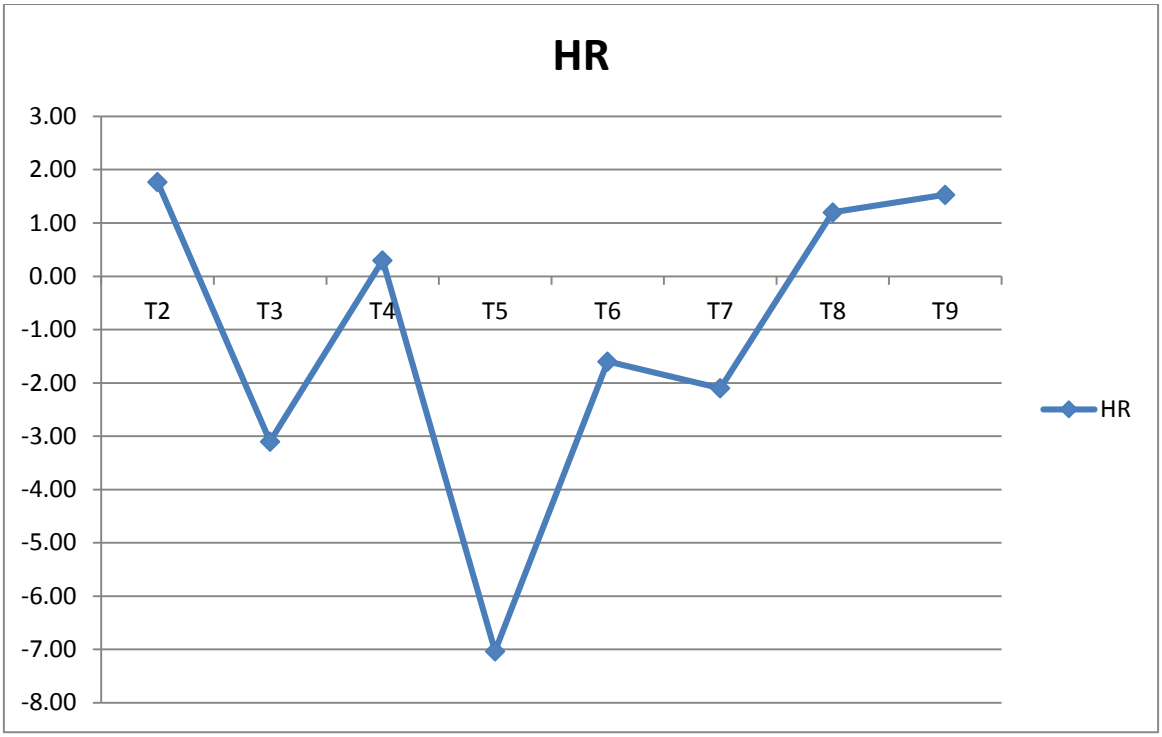
There is statistical significant lower MAP in group D compared to group E at T4 to T7.

COMPARISON OF HEART RATE IN GROUP D

Table 12: COMPARISON OF HEART RATE IN GROUP D

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	1.77	7.76	1.25	0.223
T3	-3.10	12.79	-1.33	0.195
T4	0.30	9.55	0.17	0.865
T5	-7.03	14.62	-2.63	0.013
T6	-1.60	10.30	-0.85	0.402
T7	-2.10	10.11	-1.14	0.265
T8	1.20	9.23	0.71	0.482
T9	1.53	9.09	0.92	0.363

Figure 10: COMPARISON OF HEART RATE IN GROUP D



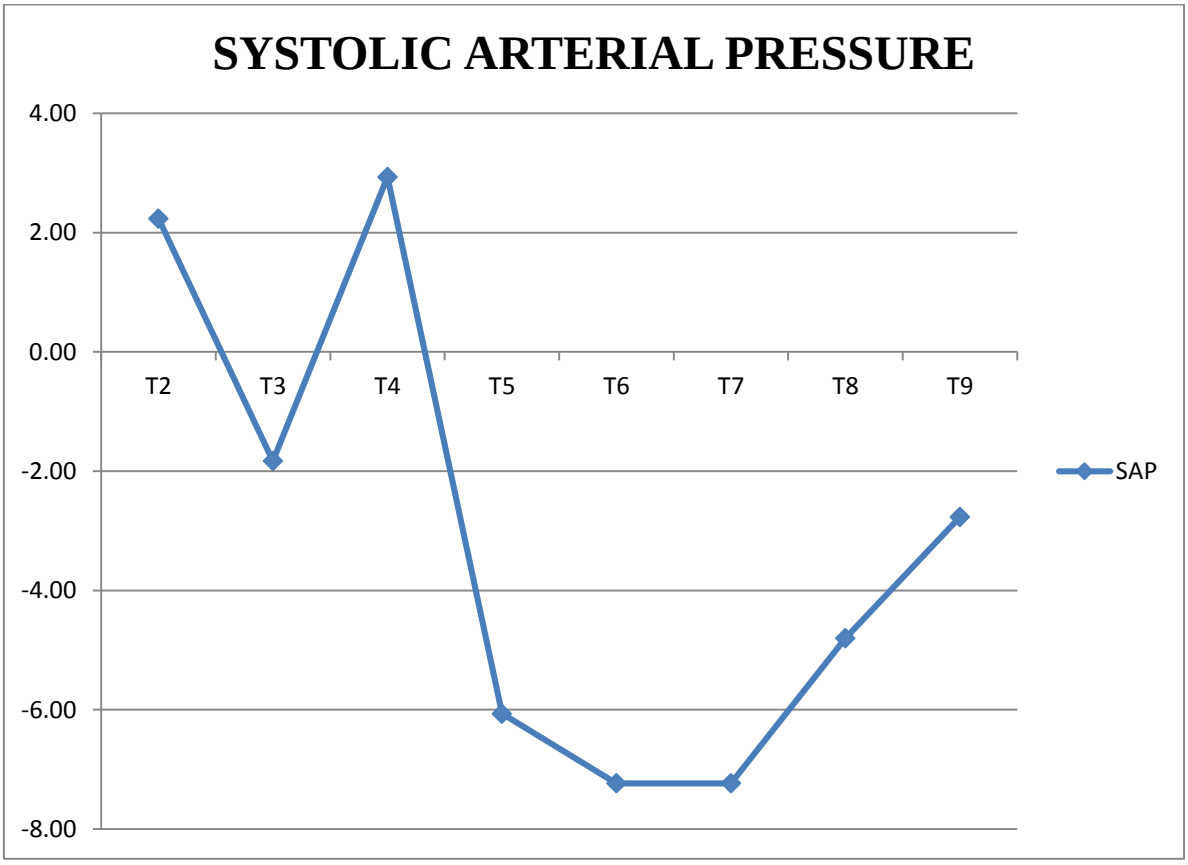
There is no statistical significant change of heart rate compared to baseline in Group D.

COMPARISON OF SYSTOLIC ARTERIAL PRESSURE IN GROUP D

Table 13: COMPARISON OF SYSTOLIC ARTERIAL PRESSURE IN GROUP D

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	2.23	5.59	2.19	0.037
T3	-1.83	14.89	-0.67	0.506
T4	2.93	11.29	1.42	0.165
T5	-6.07	13.19	-2.52	0.078
T6	-7.23	11.71	-3.38	0.062
T7	-7.23	11.15	-3.55	0.062
T8	-4.80	9.64	-2.73	0.081
T9	-2.77	8.65	-1.75	0.090

Figure 11: COMPARISON OF SYSTOLIC ARTERIAL PRESSURE IN GROUP D



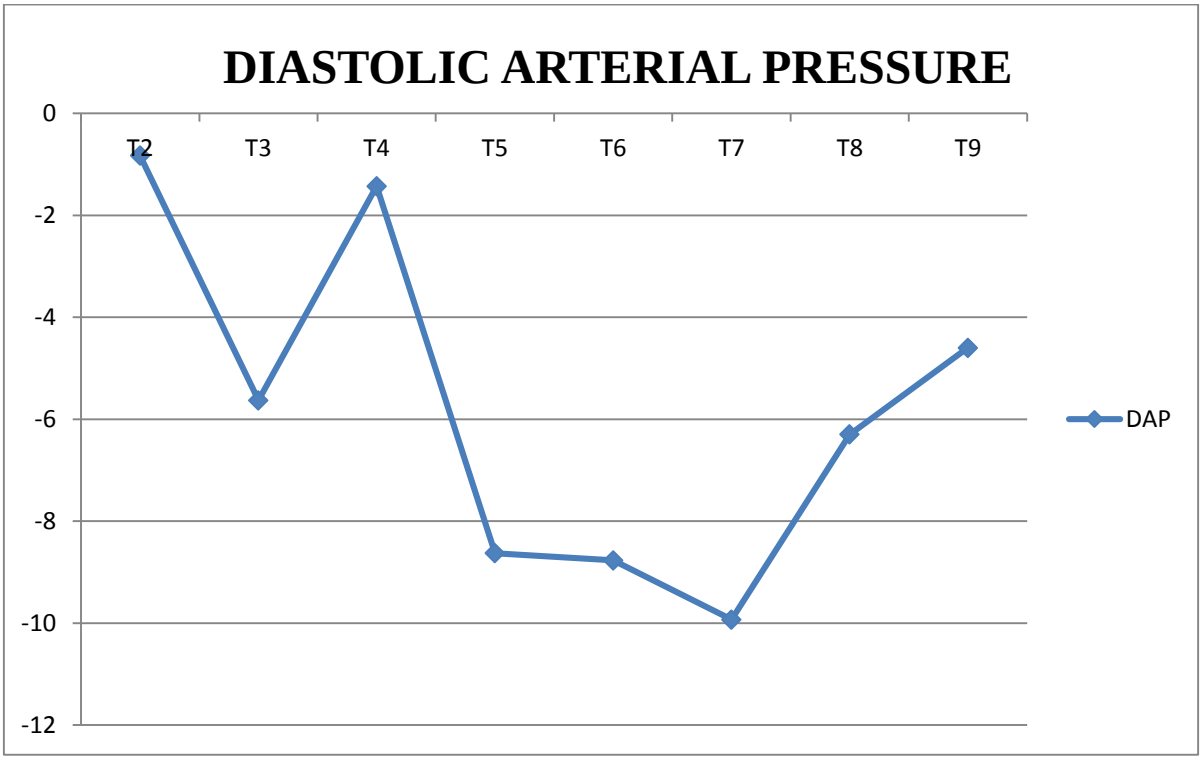
There is no statistical significant change of SAP compared to baseline in Group D.

COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP D

Table 14: COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP D

TIME	Paired Differences Mean	Std. Deviation	t value	P value
T2	-0.83	4.81	-0.95	0.350
T3	-5.63	11.16	-2.76	0.070
T4	-1.43	6.38	-1.23	0.229
T5	-8.63	13.01	-3.64	0.061
T6	-8.77	10.46	-4.59	0.058
T7	-9.93	11.57	-4.70	0.051
T8	-6.30	9.23	-3.73	0.067
T9	-4.60	7.66	-3.33	0.082

Figure 12: COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP D



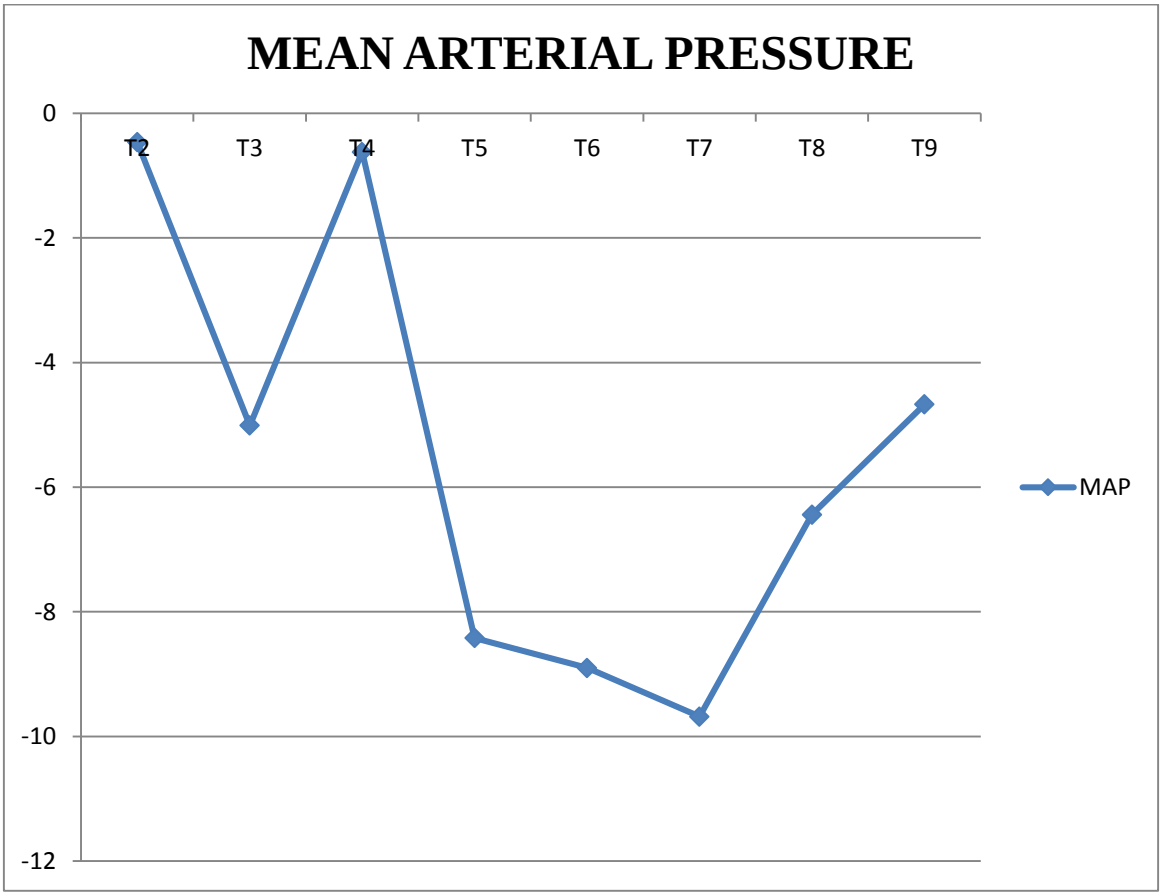
There is no statistical significant change of DAP compared to baseline in Group D.

COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP D

TABLE 15: COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP D

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	-0.46	4.20	-0.59	0.557
T3	-5.01	11.56	-2.37	0.025
T4	-0.62	7.20	-0.47	0.639
T5	-8.42	12.07	-3.82	0.052
T6	-8.90	10.11	-4.82	0.058
T7	-9.68	10.45	-5.07	0.057
T8	-6.44	8.06	-4.37	0.064
T9	-4.67	6.76	-3.78	0.054

Figure 13: COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP D



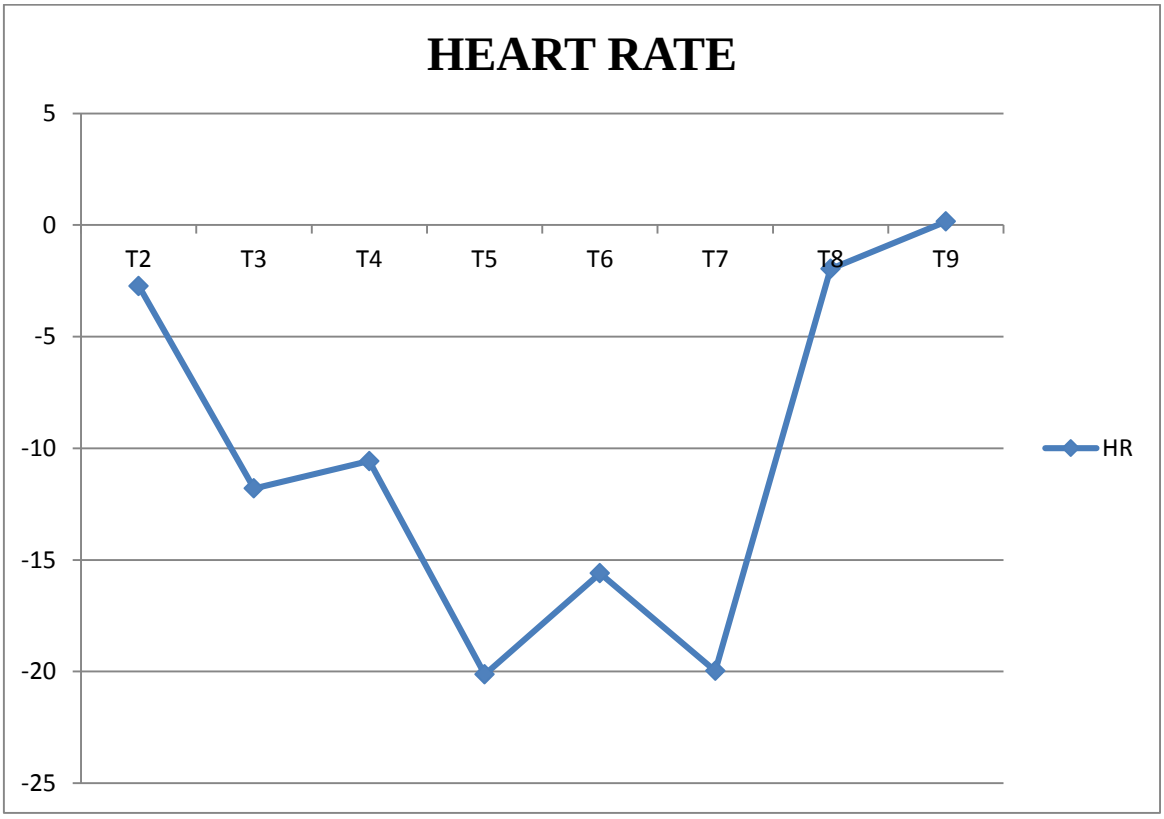
There is no statistical significant change of MAP compared to baseline in Group D.

COMPARISON OF HEART RATE IN GROUP E

Table 16: COMPARISON OF HEART RATE IN GROUP E

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	-2.73	2.77	-5.41	<0.0001
T3	-11.80	6.49	-9.96	<0.0001
T4	-10.57	4.99	-11.59	<0.0001
T5	-20.13	9.46	-11.66	<0.0001
T6	-15.60	10.73	-7.96	<0.0001
T7	-19.97	9.26	-11.81	<0.0001
T8	-1.96	7.49	-1.43	0.162
T9	0.16	6.61	0.14	0.891

Figure 14: COMPARISON OF HEART RATE IN GROUP E



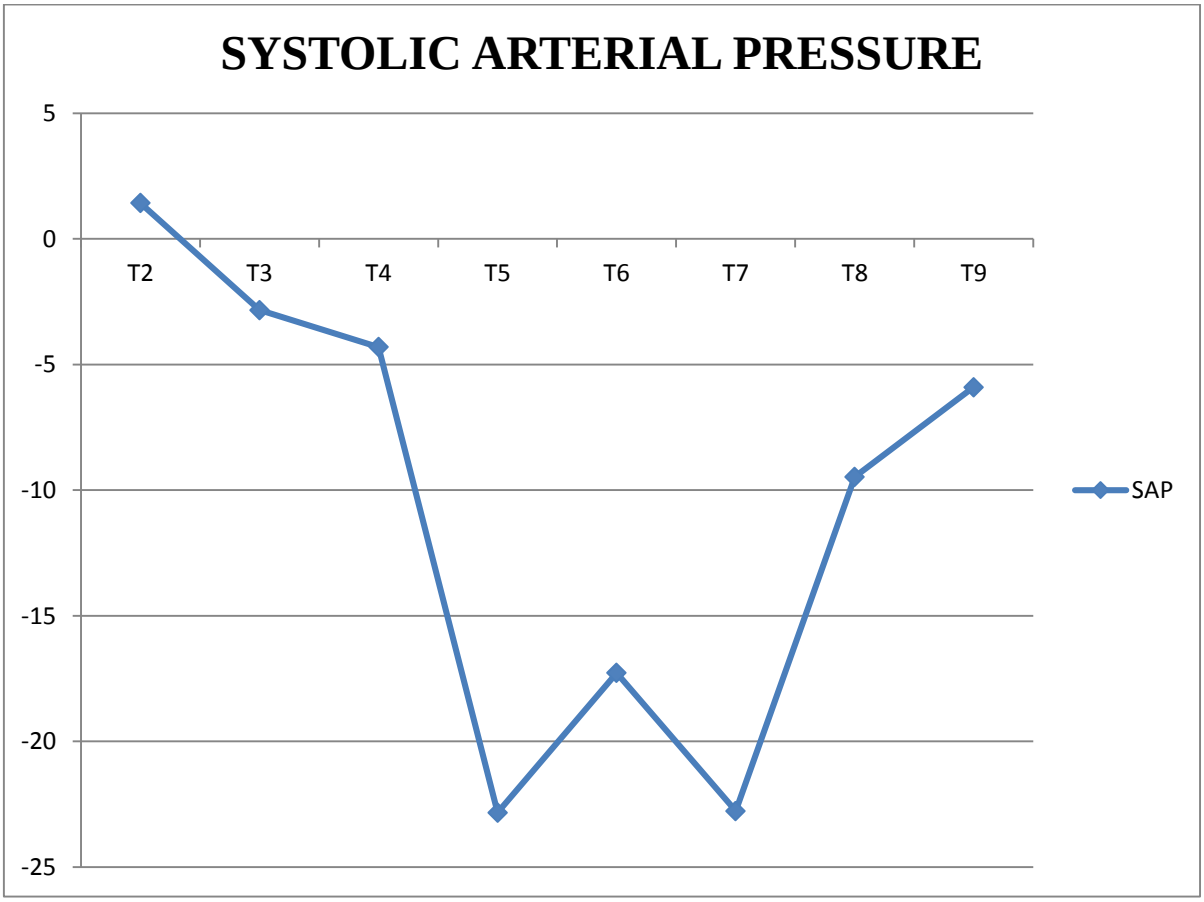
There is statistical significant (Higher) change of HR compared to baseline in Group E at T2 to T7.

COMPARISON OF SYSTOLIC ARTERIAL PRESURE IN GROUP E

Table 17: COMPARISON OF SYSTOLIC ARTERIAL PRESSURE IN GROUP E

TIME	Paired Differences Mean	Std. Deviation	t value	P value
T2	1.43	9.53	0.82	0.417
T3	-2.83	10.89	-1.45	0.165
T4	-4.30	13.29	-1.77	0.087
T5	-22.83	15.74	-7.95	<0.0001
T6	-17.27	18.66	-5.07	<0.0001
T7	-22.77	17.73	-7.03	<0.0001
T8	-9.47	17.47	-2.97	0.006
T9	-5.90	15.14	-2.13	0.041

Figure 15: COMPARISON OF SYSTOLIC ARTERIAL PRESSURE IN GROUP E



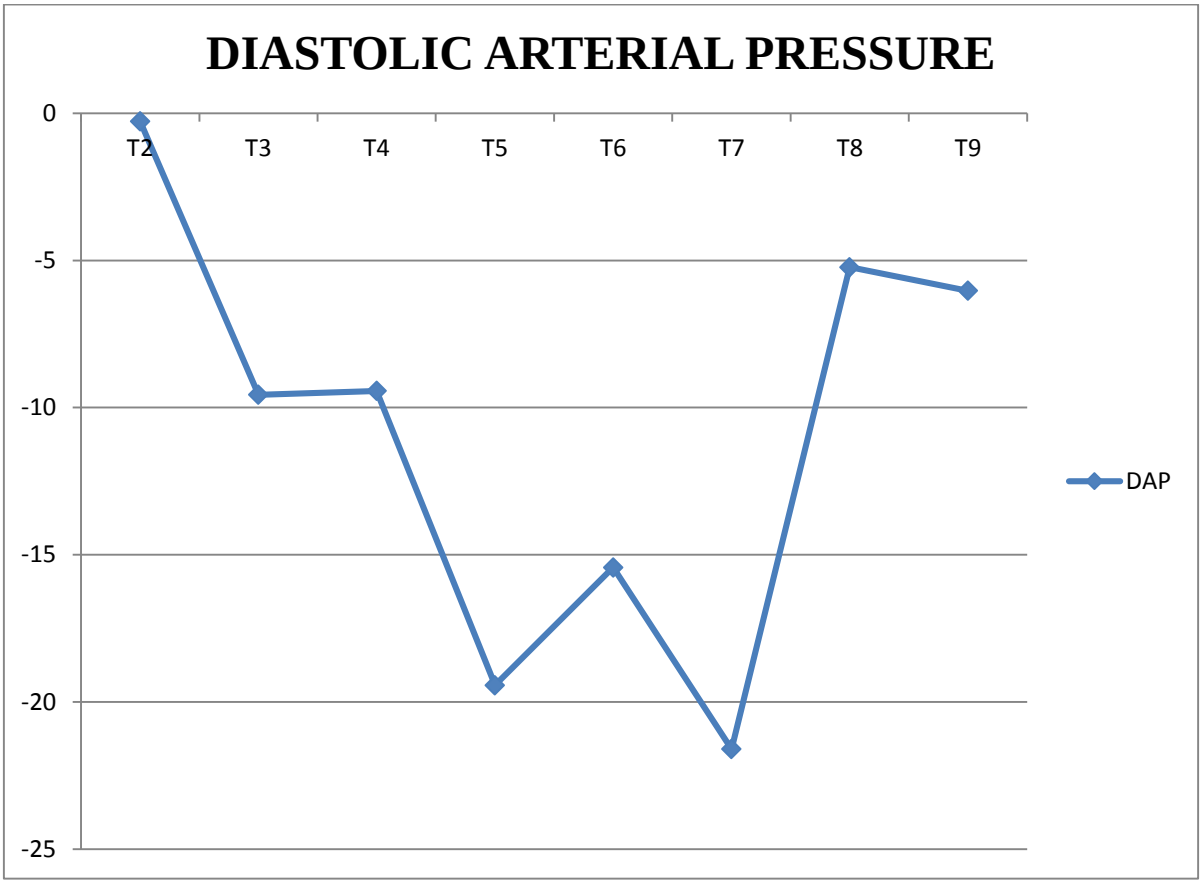
There is statistical significant (Higher) change of SAP compared to baseline in Group E at T5 to T8.

COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP E

Table 18: COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP E

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	-0.27	7.72	-0.19	0.851
T3	-9.56	10.39	-5.04	<0.0001
T4	-9.43	8.95	-5.78	<0.0001
T5	-19.43	12.64	-8.42	<0.0001
T6	-15.43	12.75	-6.63	<0.0001
T7	-21.60	11.18	-10.58	<0.0001
T8	-5.23	11.27	-2.54	0.017
T9	-6.03	11.50	-2.87	0.008

Figure 16: COMPARISON OF DIASTOLIC ARTERIAL PRESSURE IN GROUP E



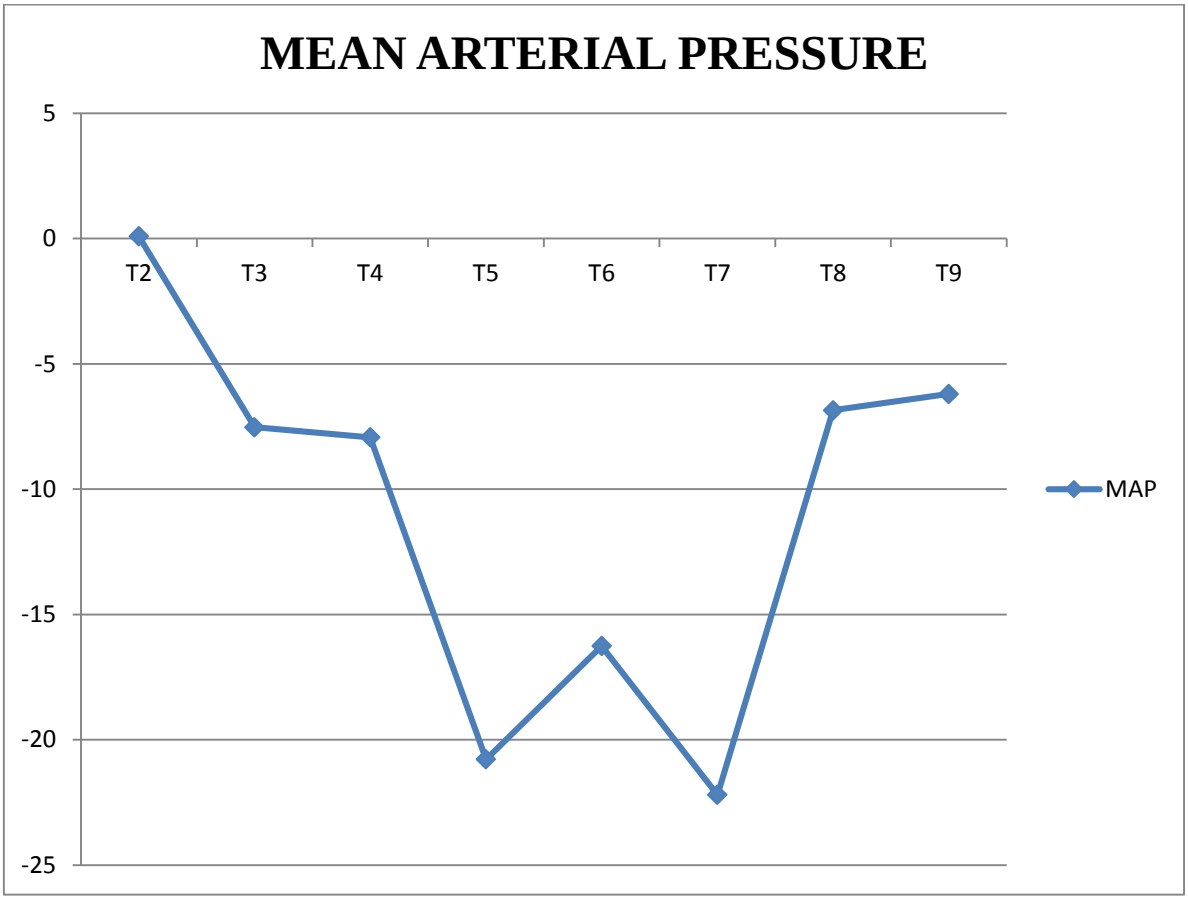
There is statistical significant (Higher) change of DAP compared to baseline in Group E at T3 to T8.

COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP E

Table 19: COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP E

TIME	Paired Differences Mean	Standard Deviation	t value	P value
T2	0.09	7.06	0.07	0.945
T3	-7.53	9.79	-4.21	<0.0001
T4	-7.93	9.42	-4.61	<0.0001
T5	-20.78	12.92	-8.81	<0.0001
T6	-16.26	13.48	-6.60	<0.0001
T7	-22.20	11.92	-10.20	<0.0001
T8	-6.85	12.26	-3.06	0.005
T9	-6.20	11.41	-2.97	0.006

Figure 17: COMPARISON OF MEAN ARTERIAL PRESSURE IN GROUP E



There is statistical significant (Higher) change of MAP compared to baseline in Group E at T2 to T9.

18.DISCUSSION

In this study, Dexmedetomidine (1mcg/kg) infusion 2 minutes prior to induction of anaesthesia attenuated the rise in heart rate and blood pressure following laryngoscopy and tracheal intubation in hypertensive patients, whereas Esmolol (1.5mg/kg) bolus injection 2 minutes prior to induction of anaesthesia, failed to protect the cardiovascular response following laryngoscopy and tracheal intubation in hypertensive patients.

Esmolol,

- Is Cardioselective β antagonist
- Has Rapid onset of action
- Has Short elimination half-life

  For attenuation of the cardiovascular response to laryngoscopy and tracheal intubation, Esmolol seems to be an appropriate selection.

Miller et al.[56] (1989) concluded that the cardiovascular response to tracheal intubation was effectively attenuated by administration of 100 mg bolus of esmolol in a Canadian multicentre trial.

Sharma et al.[50](1996) concluded that in hypertensive patients, the cardiovascular response to tracheal intubation was suppressed by 100 mg esmolol.

Oxorn et al.[51] (1990) reported that esmolol 100 mg and 200 mg in bolus doses significantly affects heart rate response to tracheal intubation.

Kindler et al. [52] (1996) concluded that heart rate response to tracheal intubation was controlled by esmolol administration before laryngoscopy, but it did not affect SAP.

Hale Yarkan Uysal et al. [55] (2012) reported that in hypertensive patients, esmolol was not effectively attenuating the blood pressure response but it attenuate the heart rate response to tracheal intubation.

In our study, esmolol 1.5mg/kg was not effective in attenuating cardiovascular response to laryngscopy and tracheal intubation in controlled hypertensive patients.

Alpha-2 adrenoceptor agonists – Clonidine and dexmedetomidine

- Had significant effects on the anesthetic requirements.
- Had significant effects on the sympathoadrenal and hemodynamic responses induced by tracheal intubation, anaesthesia and surgery.

Scheinin et al.[53] (1992) concluded that in healthy individuals dexmedetomidine 0.6 μg/kg decreased, but not totally abolished, the cardiovascular response to laryngscopy and tracheal intubation.

Menda et al.[54] (2010) reported that dexmedetomidine when combined with fentanyl effectively attenuated the cardiovascular response to endotracheal intubation in patients undergoing myocardial revascularization.

Hale Yarkan Uysal et al.[55] (2012) reported that in hypertensive patients, there are no significant differences in HR and blood pressure between baseline value and after intubation value in dexmedetomidine group. But the mean percentage variation analysis showed an absence of increase in HR, SAP and DAP in dexmedetomidine group. Dexmedetomidine is as an effective agent for blunting the cardiovascular response to tracheal intubation in hypertensive patients.

Our study demonstrated that there is no significant difference in HR, SAP, DAP and MAP between baseline and after intubation in dexmedetomidine group and also significant difference in HR, SAP, DAP and MAP after intubation between dexmedetomidine group and esmolol group in controlled hypertensive patients.

Bradycardia and hypotension have been reported as adverse effect of dexmedetomidine in previous studies on the effect of dexmedetomidine in perioperative hemodynamics.

Hale Yarkan Uysal et al.[55] (2012) did not observe any bradycardia or hypotension contrast to the previously mentioned studies. We also did not observe any adverse effect in our study.

No control group is the limitation of our study. However, we decided that withdrawing any medication would cause detrimental effect in hypertensive patients.

19.SUMMARY

Dexmedetomidine (1mcg/kg) infusion given 2 minutes prior to induction of anaesthesia provided consistent and reliable protection against increases in mean heart rate and mean systolic, diastolic and mean blood pressure during laryngoscopy and endotracheal intubation and thereafter, compared to Esmolol group.

In Dexmedetomidine group, rise in HR, SAP, DAP and MAP following intubation returns to baseline after 10 minutes. But, in Esmolol group, rise in HR, SAP, DAP and MAP following intubation returns to baseline after 15 minutes.

In this study, Dexmedetomidine attenuated the rise in heart rate and blood pressure following laryngoscopy and tracheal intubation in hypertensive patients, whereas, Esmolol failed to protect the cardiovascular response following laryngoscopy and tracheal intubation in hypertensive patients.

20.CONCLUSION

Dexmedetomidine (1mcg/kg) infusion 2 minutes prior to induction of anaesthesia attenuated the rise in heart rate and blood pressure following laryngoscopy and tracheal intubation in hypertensive patients, whereas, Esmolol (1.5mg/kg) bolus injection 2 minutes prior to induction of anaesthesia, failed to protect the cardiovascular response following laryngoscopy and tracheal intubation.

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22.CONSENT FORM

ஆராய்ச்சி ஒப்புதல் படிவம்

அறுவை சிகிச்சைக்காக முழுமயக்கம் கொடுக்கும் போது லாரிங்காஸ்கோபி மற்றும் எண்டோட்றக்யல் இண்டுபேசன் செய்யும் போது ஏற்படும் அதிக இருதய துடிப்பு மற்றும் இரத்த அழுதத்தை குறைப்பதற்காக பயன்படும் இரு மயக்க மருந்துகளின் விளைவுகள் பற்றி ஆய்வு.

பெயர் :

வயது :

இனம் :

உள்நோயாளி எண்:

வார்டு :

நோய் :

அறுவை சிகிச்சை :

விளக்கம்:

அறுவை சிகிச்சைக்காக முழுமயக்கம் கொடுக்கும் போது லாரிங்காஸ்கோபி மற்றும் எண்டோட்றக்யல் இண்டுபேசன் செய்யும் போது ஏற்படும் அதிக இருதய துடிப்பு மற்றும் இரத்த அழுதத்தை குறைப்பதற்காக பல்வேறு மருந்துகள் உபயோகபடுத்தபடுகின்றன. அவற்றில் இரண்டு மருந்துகளாகிய டெக்ஸ்மெடிட்டோமெடின் மற்றும் எஸ்மொலால் மருந்துகளை நரம்பு மூலம் உடலில் செலுத்தி அறுவை சிகிச்சை செய்வதால் ஏற்படும் பயன்கள்இ விளைவுகள்இ பக்கவிளைவுகள் அனைத்தும் எனக்கு நன்கு புரிகின்ற வகையில் எனது தாய் மொழியில் தெளிவாக விளக்கி கூறப்பட்டது.

என்னுடைய அடையாளம் எந்த வகையிலும் இந்த அராய்ச்சி மூலம் வெளியே தெரியாது என்பதை அறிவேன். இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் விலகலாம் என்பதையும் அதனால் எந்த பாதிப்பு ஏற்படாது என்பதையும் அறிவேன்.

நான் யாருடைய நிர்பந்தமுமின்றி என் சொந்த விருப்பத்தின் பேரில் சுய நினைவுடன் இந்த ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

இடம் :

தேதி : நோயாளியின் கையொப்பம்

23.PROFORMA

COMPARATIVE EVALUATION OF DEXMEDETOMIDINE AND ESMOLOL FOR ATTENTUATION OF INTUBATION STRESS RESPONSE IN WELL CONTROLLED HYPERTENSIVE PATIENTS – A DOUBLE BLIND RANDOMIZED CONTROL STUDY

Name: **Age :** **Sex :** **Date :**

Type of surgery: **Anaesthesia:**

Pre anaesthetic Assessment:

Height: Weight: PR: BP:

CVS: RS: PA: CNS:

Airway

ASA

Investigations:

Hb %

Urine: Sugar Albumin

Blood: Sugar Urea Creatinine

Premedication:

Drug	Dose	Route	Time

Time	Heart Rate	SAP	DAP	MAP	SPO2
Baseline(T1)					
After drug administration(T2)					
After Induction(T3)					
After Intubation(T4)					
1Minute (T5)					
3Minute (T6)					
5Minute (T7)					
10Minute (T8)					
15Minute(T9)					

Intra operative complications :

Recovery room condition :

Post operative visit :

Sl. No	Age	Sex	Group (D/E)	BASELINE					HEART RATE								SYSTOLIC ARTERIAL PRESSURE							
				HR	SBP	DBP	MAP	SpO 2	After Drug Admin	After Induction	After Intubation	1 min	3 min	5 min	10 min	15 min	After Drug Admin	After Induction	After Intubation	1 min	3 min	5 min	10 min	15 min
1	35	F	D	88	120	74	89	100	71	74	72	77	71	77	68	66	110	108	106	112	116	118	115	116
2	37	F	D	82	132	81	97	100	79	80	80	83	87	89	80	82	129	110	110	126	126	128	130	132
3	48	F	D	79	113	69	83	97	77	81	79	80	85	85	70	72	117	120	118	122	120	124	126	124
4	43	F	D	77	120	70	86	98	71	74	72	77	71	72	74	70	118	116	110	117	118	120	122	120
5	44	M	D	80	112	70	83	98	73	75	70	76	73	73	74	72	114	112	110	114	120	122	114	116
6	49	M	D	84	130	84	99	99	72	75	75	74	70	72	68	66	120	120	120	126	130	132	132	132
7	39	F	D	83	142	91	107	99	80	82	82	89	80	80	80	82	139	146	140	142	140	137	140	142
8	46	F	D	79	123	79	93	100	78	80	80	82	74	74	72	70	130	132	130	132	134	132	130	128
9	45	M	D	78	130	80	96	99	72	77	75	78	70	70	70	71	128	132	126	136	130	132	136	136
10	48	F	D	79	122	80	93	96	74	80	76	81	76	76	73	72	124	122	122	124	130	132	134	126
11	38	M	D	84	110	64	79	98	89	92	90	95	87	87	83	80	100	99	98	110	110	112	112	112
12	48	F	D	68	122	71	87	99	74	76	76	78	72	70	70	71	119	126	120	116	126	122	120	122
13	36	F	D	86	110	59	75	100	80	84	80	88	89	82	82	80	114	117	120	130	132	132	132	130
14	38	F	D	76	110	60	76	100	82	82	80	84	81	82	82	80	108	100	100	107	108	110	112	110
15	44	M	D	86	120	80	93	100	76	76	74	77	78	78	75	77	110	110	108	120	126	124	122	124
16	50	F	D	85	102	72	81	98	81	82	80	86	88	88	74	73	104	102	102	110	110	110	109	106
17	42	M	D	86	132	78	95	98	74	79	70	78	78	78	77	75	130	130	130	135	132	132	135	131
18	32	F	D	79	114	66	81	98	78	78	78	80	81	82	82	80	115	113	110	112	122	120	116	114
19	43	F	D	89	140	77	98	99	84	86	86	90	90	90	89	90	122	109	110	118	120	120	120	119
20	52	F	D	78	117	83	94	96	74	72	70	78	78	80	80	81	103	100	100	110	112	114	114	110
21	40	M	D	84	110	76	87	100	82	84	84	88	87	89	90	90	110	110	106	120	120	122	122	118
22	32	F	D	86	129	91	102	100	68	70	70	77	77	78	80	82	129	130	124	132	132	130	132	132
23	54	M	D	72	116	68	84	98	83	90	88	95	90	92	80	85	116	142	130	140	145	140	120	118
24	58	F	D	72	140	86	104	99	80	120	80	121	95	95	80	79	140	134	128	142	148	146	142	140
25	60	F	D	80	136	88	104	97	86	92	90	102	98	98	84	82	136	162	140	150	160	156	138	122
26	55	F	D	78	134	81	98	100	92	96	90	98	92	92	80	82	134	154	130	149	145	144	127	130
27	50	M	D	74	110	70	83	100	79	84	80	107	76	77	76	78	110	133	128	144	141	142	138	130
28	44	M	D	86	126	80	95	97	89	92	90	92	80	81	90	92	126	162	148	166	158	158	150	143
29	42	F	D	71	120	78	91	98	74	98	95	111	97	98	100	91	120	128	124	138	132	132	128	128
30	40	F	D	70	124	82	95	100	74	81	78	88	76	77	80	82	124	142	130	148	140	140	142	138

31	46	F	E	76	110	71	83	99	78	98	87	125	120	122	80	83	110	118	122	144	150	152	152	140
32	54	M	E	76	124	83	96	99	78	82	87	105	92	93	70	70	124	122	136	148	162	164	112	114
33	56	F	E	78	116	73	87	100	82	74	85	108	107	92	85	76	116	125	124	124	102	130	102	104
34	60	F	E	76	141	88	106	99	84	86	90	88	80	99	70	80	141	135	118	152	132	136	139	141
35	58	F	E	71	126	82	96	99	75	79	90	86	80	100	82	74	126	135	120	146	138	141	122	124
36	36	M	E	76	109	78	88	97	82	86	85	92	81	103	76	78	109	124	130	136	125	162	110	112
37	37	M	E	81	132	80	97	96	86	86	90	84	81	99	68	70	132	132	122	142	136	144	118	120
38	32	M	E	69	112	70	84	99	73	78	85	75	71	105	70	72	112	124	128	118	110	156	108	110
39	56	F	E	70	126	84	98	100	76	79	90	95	88	98	74	76	126	136	130	142	131	140	120	122
40	44	F	E	73	112	70	84	98	71	83	89	87	70	100	75	77	112	123	130	117	112	160	108	110
41	45	F	E	88	140	86	104	100	88	97	90	98	91	92	78	70	126	118	124	138	130	130	134	128
42	48	F	E	78	140	82	101	100	80	89	85	99	96	99	79	79	110	115	118	132	134	136	140	130
43	42	F	E	86	132	81	97	98	85	94	90	105	109	100	86	87	124	126	120	146	140	141	142	132
44	40	M	E	85	120	70	86	98	87	90	90	100	102	103	88	80	120	134	130	170	160	162	162	150
45	39	F	E	83	110	70	83	99	80	89	85	90	95	99	80	80	118	118	122	138	142	144	146	140
46	45	M	E	78	132	81	97	97	80	95	90	101	108	105	89	80	122	128	128	148	152	156	160	150
47	56	F	E	75	116	68	84	97	78	87	85	97	98	98	88	80	134	127	130	149	145	140	127	130
48	33	F	E	88	136	88	104	100	86	97	90	105	100	100	85	79	120	136	130	160	166	160	150	152
49	36	M	E	79	120	70	86	96	85	90	89	98	88	88	72	74	120	128	136	178	166	154	136	114
50	39	M	E	68	106	71	82	99	74	85	79	100	76	77	78	80	106	109	110	124	118	128	102	104
51	40	F	E	76	132	78	95	99	82	100	95	104	96	98	76	78	132	138	142	154	141	138	136	128
52	49	F	E	82	140	82	101	99	84	90	90	98	87	88	85	77	140	137	142	166	160	158	152	148
53	38	F	E	75	142	84	103	100	79	93	85	92	86	87	65	67	142	142	150	158	131	130	127	129
54	32	F	E	71	118	72	87	98	75	97	90	98	97	98	78	80	118	136	126	164	154	150	124	128
55	42	M	E	78	128	82	97	98	84	100	90	110	107	107	90	87	128	127	132	154	150	146	142	132
56	33	M	E	83	120	74	89	97	85	98	95	108	100	100	88	80	128	126	132	154	148	146	142	138
57	45	M	E	79	113	60	83	100	80	98	90	102	105	106	99	84	130	122	132	152	148	150	150	148
58	38	M	E	85	134	81	98	96	85	98	97	111	110	100	87	80	114	117	120	140	142	144	146	130
59	60	F	E	84	116	68	84	100	86	94	93	99	95	97	85	87	122	136	148	166	170	166	152	146
60	44	F	E	87	134	81	98	100	88	96	95	98	106	100	87	84	132	128	134	162	160	156	160	160

Sl. No	DIASTOLIC ARTERIAL PRESSURE								MEAN ATRERIAL PRESSURE								O2 SATURATION								Remarks
	After Drug Admin	After Induction	After Intubation	1 min	3 min	5 min	10 min	15 min	After Drug Admin	After Induction	After Intubation	1 min	3 min	5 min	10 min	15 min	After Drug Admin	After Induction	After Intubation	1 min	3 min	5 min	10 min	15 min	
1	77	78	77	82	82	84	72	72	88	88	87	92	93	95	86	87	98	100	100	100	100	100	100	100	ACEI
2	82	82	80	86	84	86	86	82	98	91	90	99	98	100	101	99	99	100	100	100	100	100	100	100	ACEI
3	71	72	70	77	77	79	70	72	86	88	86	92	91	94	89	89	100	100	100	100	100	100	100	100	ACEI
4	72	75	71	72	74	77	74	70	87	89	84	87	89	91	90	87	100	100	100	100	100	100	100	100	DIURETICS
5	74	72	72	75	74	75	75	74	87	85	85	88	89	91	88	88	98	100	100	100	100	100	100	100	NONE
6	87	84	80	82	84	88	84	81	98	96	93	97	99	103	100	98	99	100	100	100	100	100	100	100	ACEI
7	92	90	90	92	94	92	94	92	108	109	107	109	109	107	109	109	100	100	100	100	100	100	100	100	β BLOCKER
8	81	80	80	82	84	86	83	82	97	97	97	99	101	101	99	97	100	100	100	100	100	100	100	100	β BLOCKER
9	82	83	80	82	82	80	78	80	97	99	95	100	98	97	97	99	100	100	100	100	100	100	100	100	β BLOCKER
10	84	82	82	80	84	82	82	84	97	95	95	95	99	99	99	98	98	100	100	100	100	100	100	100	β BLOCKER
11	61	62	60	64	71	72	68	69	74	74	73	79	84	85	83	83	97	100	100	100	100	100	100	100	ACEI
12	72	75	70	74	74	74	70	72	88	92	87	88	91	90	87	89	96	100	100	100	100	100	100	100	DIURETICS
13	61	60	60	62	66	66	60	62	79	79	80	85	88	88	84	85	95	100	100	100	100	100	100	100	NONE
14	62	60	61	64	67	68	67	62	77	73	74	78	81	82	82	78	100	100	100	100	100	100	100	100	NONE
15	77	75	77	79	78	78	77	77	88	87	87	93	94	93	92	93	100	100	100	100	100	100	100	100	β BLOCKER
16	75	78	78	76	80	80	82	80	85	86	86	87	90	90	91	89	100	100	100	100	100	100	100	100	β BLOCKER
17	80	80	77	82	83	83	85	79	97	97	95	100	99	99	102	96	98	100	100	100	100	100	100	100	ACEI
18	68	66	65	70	72	72	70	71	84	82	80	84	89	88	85	85	98	100	100	100	100	100	100	100	ACEI
19	83	80	80	85	86	88	86	82	96	90	90	96	97	99	97	94	99	100	100	100	100	100	100	100	β BLOCKER
20	67	65	65	68	70	72	70	71	79	77	77	82	84	86	85	84	97	100	100	100	100	100	100	100	DIURETICS
21	74	74	70	78	78	80	80	79	86	86	82	92	92	94	94	92	97	100	100	100	100	100	100	100	DIURETICS
22	90	92	90	90	92	90	92	90	103	105	101	104	105	103	105	104	100	100	100	100	100	100	100	100	NONE
23	76	101	80	112	100	112	90	88	89	115	97	121	115	121	100	98	100	100	100	100	100	100	100	100	ACEI
24	80	92	86	99	99	100	87	89	100	106	100	113	115	115	105	106	100	100	100	100	100	100	100	100	β BLOCKER
25	86	120	90	122	120	122	110	100	103	134	107	131	133	133	119	107	98	100	100	100	100	100	100	100	ACEI
26	80	90	88	102	96	98	90	88	98	111	102	118	112	113	102	102	99	100	100	100	100	100	100	100	ACEI
27	78	103	88	108	102	100	98	96	89	113	101	120	115	114	111	107	99	100	100	100	100	100	100	100	NONE
28	88	100	90	110	108	110	108	100	101	121	109	129	125	126	122	114	100	100	100	100	100	100	100	100	β BLOCKER
29	71	88	80	92	90	92	90	92	87	101	95	107	104	105	103	104	97	100	100	100	100	100	100	100	β BLOCKER
30	82	98	94	100	100	100	99	92	96	113	106	116	113	113	113	107	96	100	100	100	100	100	100	100	ACEI

31	62	76	76	90	90	92	88	78	78	90	91	108	110	112	109	99	100	100	100	100	100	100	100	100	NONE
32	70	72	80	90	86	88	78	82	88	89	99	109	111	113	89	93	100	100	100	100	100	100	100	100	β BLOCKER
33	79	87	88	88	72	98	72	82	91	100	100	100	82	109	82	89	100	100	100	100	100	100	100	100	β BLOCKER
34	90	95	80	100	92	90	82	95	107	108	93	117	105	105	101	110	96	100	100	100	100	100	100	100	ACEI
35	81	103	92	85	82	92	74	72	96	114	101	105	101	108	90	89	98	100	100	100	100	100	100	100	ACEI
36	78	98	92	92	91	108	70	72	88	107	105	107	102	126	83	85	99	100	100	100	100	100	100	100	ACEI
37	81	92	80	84	78	92	70	68	98	105	94	103	97	109	86	85	99	100	100	100	100	100	100	100	β BLOCKER
38	70	88	86	76	74	104	62	64	84	100	100	90	86	121	77	79	100	100	100	100	100	100	100	100	β BLOCKER
39	82	96	90	86	80	102	72	72	97	109	103	105	97	115	88	89	100	100	100	100	100	100	100	100	ACEI
40	68	80	88	69	70	114	60	68	83	94	102	85	84	129	76	82	99	100	100	100	100	100	100	100	ACEI
41	86	80	88	94	96	98	80	80	99	93	100	109	107	109	98	96	97	100	100	100	100	100	100	100	NONE
42	76	78	80	88	88	90	78	78	87	90	93	103	103	105	99	95	96	100	100	100	100	100	100	100	β BLOCKER
43	88	84	92	96	90	92	82	84	100	98	101	113	107	108	102	100	100	100	100	100	100	100	100	100	β BLOCKER
44	80	88	92	108	110	108	88	90	93	103	105	129	127	126	113	110	100	100	100	100	100	100	100	100	DIURETICS
45	70	80	80	94	91	92	80	89	86	93	94	109	108	109	102	106	99	100	100	100	100	100	100	100	NONE
46	78	84	86	100	102	104	92	94	93	99	100	116	119	121	115	113	96	100	100	100	100	100	100	100	ACEI
47	84	89	90	102	100	102	89	90	101	102	103	118	115	115	102	103	100	100	100	100	100	100	100	100	β BLOCKER
48	80	102	88	108	112	114	102	89	93	113	102	125	130	129	118	110	97	100	100	100	100	100	100	100	ACEI
49	70	96	99	110	104	106	90	64	87	107	111	133	125	122	105	81	98	100	100	100	100	100	100	100	DIURETICS
50	69	70	76	90	81	84	76	67	81	83	87	101	93	99	85	79	99	100	100	100	100	100	100	100	NONE
51	74	94	90	111	99	100	78	90	93	109	107	125	113	113	97	103	100	100	100	100	100	100	100	100	ACEI
52	71	86	90	110	104	102	90	89	94	103	107	129	123	121	111	109	100	100	100	100	100	100	100	100	β BLOCKER
53	84	94	98	112	105	106	92	96	103	110	115	127	114	114	104	107	100	100	100	100	100	100	100	100	ACEI
54	71	102	91	114	100	100	91	92	87	113	103	131	118	117	102	104	96	100	100	100	100	100	100	100	ACEI
55	82	90	90	101	93	92	101	93	97	102	104	119	112	110	115	106	99	100	100	100	100	100	100	100	NONE
56	86	80	82	98	98	99	88	90	100	95	99	117	115	115	106	106	98	100	100	100	100	100	100	100	β BLOCKER
57	70	82	82	96	96	98	80	89	90	95	99	115	113	115	103	109	99	100	100	100	100	100	100	100	β BLOCKER
58	70	70	80	92	90	92	84	88	85	86	93	108	107	109	105	102	100	100	100	100	100	100	100	100	DIURETICS
59	88	80	85	108	105	104	90	94	99	99	106	127	127	125	111	111	100	100	100	100	100	100	100	100	NONE
60	78	79	80	99	92	93	86	90	96	95	98	120	115	114	111	113	99	100	100	100	100	100	100	100	β BLOCKER