“COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL”

By

REG NO. BA0122016

Dissertation

Submitted to the KLE Academy of Higher Education and Research, Belagavi, Karnataka
In Partial Fulfilment
of the Requirements for the Degree of

M. D.

in

ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELAGAVI, KARNATAKA

SEPTEMBER - OCTOBER 2025

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitles "**COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL**" is a Bonafide research work done by **REG NO. BA0122016**

DR. RAJESH MANE MD, DNB
Professor and Head,
Department of Anaesthesiology,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date: 24|03|2025
Place: Belagavi

Dr. N.S. Mahantshetti MD (paed) Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10
PRINCIPAL
Jawaharlal Nehru Medical College
BELAGAVI

Date:
Place: Belagavi

KLE Academy of Higher Education & Research (Deemed to be University), Belagavi, Karnataka

UNDERTAKING

I, **Reg No BA0122016,** hereby declare that the information and data mentioned in my dissertation **'COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL'** belongs to me and is original. I am aware of the definition of *Plagiarism* as detailed below:

- An act or an instance of using or closely imitating the language and thoughts of another author without authorization and the representation of that author's work as one's own, as by not crediting the original author.
- A piece of writing or other work reflecting such unauthorized work or imitation.
- The deliberate or reckless representation of another's words, thoughts or ideas as one's own without attribution in connection with submission of academic work, whether graded or otherwise.

I hereby declare that the presentation prepared by me is an original one and does not involve plagiarism anywhere. In case at a later stage, it is found that I have indulged in plagiarism, then, I am solely responsible for the same and the institution is at liberty to take any disciplinary action against me including cancellation of dissertation or any other penalties imposed by the university.

Date: 25|3|25

Place: Belagavi

Reg No: BA0122016

PLAGIARISM CERTIFICATE

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be-University)

(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 – 2471350 0831 – 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/

Date: 21-03-2025

"ACCEPTANCE LETTER"

The softcopy of thesis entitled: **"COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL"** has been submitted for anti-plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **07%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Nagogati

Guide.

KAHER J. N. MEDICAL COLLEGE BELAGAVI

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BA0122016
Postgraduate Student,
2022-23 Batch,
Department of Anaesthesiology
J. N. Medical College, Belagavi.

ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)

JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

DHR Reg. No. EC/NEW/INST/2024/KA/0548

Ref No.MDC/JNMCIEC/ 469.

Date: 07/10/2024

To,
BA0122016
PG Student in Anaesthesiology
J. N. Medical College,
BELAGAVI.

Sub : Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"EVALUATION OF ACROMIO-AXILLO-SUPRASTERNAL NOTCH INDEX AS A PREDICTOR OF DIFFICULT LARYNGOSCOPY IN ADULTS UNDERGOING ELECTIVE SURGERY UNDER GENERAL ANESTHESIA- A ONE- YEAR HOSPITAL BASED OBSERVATIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

LIST OF ABBREVIATIONS

- AAG – Alpha 1 acid glycoprotein
- ABG – Arterial blood gas
- ACLS - Advanced Cardiac Life Support
- ASA – American Society of Anesthesiologists
- bpm – beats per minute
- β - beta
- cc – cubic centimetres
- CNS – Central nervous system
- CTRI - Clinical Trials Registry India
- DBP – Diastolic Blood Pressure
- ECG – Electrocardiogram
- HR – Heart Rate
- IV – Intravenous
- L/kg/hr – litre / kilogram / hour
- MAP – Mean Arterial Pressure
- mcg – microgram
- mcg/kg/min – microgram / kilogram / minute
- mg – milligram
- min – Minutes
- ml/kg – millilitre/kilogram

- mL/kg/min – millilitre / kilogram / minute
- mm Hg – millimetres of mercury
- NMDA receptor - N-Methyl-D-Aspartate receptor
- PaCo2 – Partial pressure of carbon dioxide in arterial blood
- PONV – Post operative nausea and vomiting
- RR – Respiratory rate
- SBP – Systolic Blood Pressure
- secs – seconds
- SpO2 – Percentage of oxygen saturation
- α – alpha

ABSTRACT

Background: Endotracheal extubation is an unpredictable and tricky part of anaesthetic management and can be associated with detrimental airway and hemodynamic responses. Elevation in blood pressure and heart rate during extubation is brief but may have detrimental effects. Hence there should be an effective means of attenuating sympathetic responses to extubation. Many drugs have been used to attenuate extubation response such as IV diltiazem, propofol, verapamil, dexmedetomidine. However, there has been no study comparing the effects of IV esmolol and IV preservative free lignocaine in attenuating the stressor response during extubation.

Methods:

A randomized, single blinded study was conducted on 84 ASA I or II adult patients undergoing elective surgery under general anesthesia. Patients were randomly divided into two groups. Patients in Group 1 (n = 42) were administered 0.5 mg/kg of IV Esmolol and Group 2 (n = 42) were given 1.5 mg/kg of IV preservative free Lignocaine 1 minute after administering the reversal agent. The hemodynamic variables (i.e., heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation) were recorded before administration of the reversal agent (baseline value), post-administration of reversal agent(TR), post-administration of study drug (T0- after 1 minute of administering reversal agent), then for every minute for the first 5 min post-administration of study drug (T1 to T5), 7 minutes after administering study drug (T7) and finally at 10 minutes (T10). Time of extubation was also noted.

Results: There was a statistical significance noted in Heart rate, Systolic, Diastolic and Mean arterial pressure in Group 1. However, in the control group, although a decreasing trend was noted in Heart rate, Diastolic blood pressure and Mean arterial pressure, the changes were not consistently significant at all time points. No statistical significance in SpO_2 was noted in study group, while the comparison was not possible in control group due to similar values at all time points.

0.5mg/kg IV Esmolol was a better intervention as compared to 1.5mg/kg of preservative free lidocaine in attenuating Heart rate, Diastolic blood pressure and Mean arterial pressure effectively. No statistical significance was noted between the two groups with respect to SpO_2 .

Discussion: This study supports the use of Intravenous Esmolol as a superior agent in controlling hemodynamic instability during extubation compared to preservative-free Lidocaine. Its ability to attenuate the sympathetic response effectively and contribute towards a more controlled and predictable extubation process makes it a valuable option.

Conclusions: 0.5 mg/kg IV Esmolol is better for attenuation of hemodynamic responses when compared with 1.5 mg/kg IV preservative free lignocaine during extubation.

Keywords : Extubation , Esmolol , Preservative free lignocaine, Hemodynamic response

CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

INTRODUCTION

Endotracheal extubation is a routine procedure performed during general anesthesia.

During extubation, common occurrences include tachycardia and hypertension. These reactions, may be well tolerated in ASA I patients but have deleterious effects on patients with history of cardiac diseases, cerebrovascular accident[1,2]. Such patients are at a risk of myocardial ischemia, heart failure, arrhythmia, cerebrovascular hemorrhage, and pulmonary edema. Although these variations are short-lived, it is essential to mitigate these hemodynamic responses during extubation.

Tracheal extubation causes a 10% to 30% rise in arterial pressure, also causes a rise in pulse rate for 5 to 15 minutes duration[1].

The hemodynamic response to extubation can be attenuated by non-pharmacological methods such as extubation in deep plane of anesthesia, extubation in prone position as well as pharmacological methods[3,4,5]. Several articles have highlighted the effectiveness of various drugs, including verapamil, dexmedetomidine, propofol, lidocaine and esmolol in managing hemodynamic parameters during extubation. However, there are certain limitations associated with the above mentioned drugs. Dexmedetomidine and propofol were associated with a higher sedation score which is a disadvantage especially during extubation. Lidocaine resulted in an initial rise in blood pressure. Verapamil on the other hand, showed a delayed onset and peak effect. Studies have been conducted using IV esmolol at a dose of 1.5 mg/kg. Nevertheless, a comparative study between 0.5 mg/kg of IV esmolol and preservative-free lidocaine in mitigating these parameters during extubation has not yet been conducted.

Hence the present research was aimed to evaluate the impact of IV esmolol versus IV preservative-free lidocaine on hemodynamic variables such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO2) during extubation.

AIMS AND OBJECTIVES OF THE STUDY

AIM:

Evaluating the impact of intravenous esmolol and preservative free lidocaine on various hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation) during the process of extubation.

OBJECTIVE OF THE STUDY :

- **Primary objective:** Comparing IV esmolol versus IV lidocaine on hemodynamic variables(HR,SBP,DBP,MAP,SpO_2) during extubation.

- **Secondary objective:** Assessing the possible adverse to the study drugs.

REVIEW OF LITERATURE

Tracheal extubation following general anesthesia demands skill and judgment that are developed through experience. It is often linked with a rise in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. Several approaches have been explored to reduce the stress response, including non-pharmacological methods like performing extubation at deeper levels of anesthesia or in the prone position, as well as pharmacological methods such as pre-treatment with beta blockers, lidocaine, calcium channel blockers, propofol, dexmedetomidine.

Study conducted by “Bindu B, Pasupuleti S, Gowd UP, Gorre V, Murthy RR, Laxmi MB, et al., titled A double-blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation," was carried out in 2013[6]. The study involved 50 ASA grade I or II patients, of 20-45 years old, scheduled for non-emergency surgeries. They were assigned one of the groups by randomization: Group A was administered dexmedetomidine (0.75 mcg/kg) via IV infusion, while Group B was administered a placebo. Both infusions were delivered over 15 minutes prior to the expected conclusion of procedure in a double-blind fashion. The study focused on evaluating the impact of dexmedetomidine on hemodynamic regulation during extubation. The results showed that a pre-extubation dose of 0.75 mcg/kg of dexmedetomidine, given 15 minutes earlier, helped maintain stable hemodynamics and promoted seamless extubation.. However, Group A experienced higher incidences of bradycardia and hypotension, along with noticeable sedation.

A study titled “Comparative study of the effect of two different doses of intravenous labetalol on the cardiovascular response to endotracheal extubation was conducted in 2023 by Hamidreza Shetabi, Behzad Nazemroaya, Hosein Mahjobipoor, and Sanaz Majidi” [7]. In this study, 72 patients were distributed into three groups, where they received an IV administration of either 0.1 mg/kg labetalol, 0.2 mg/kg labetalol, or NS, 10 minutes ahead of extubation. Hemodynamic variables such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2) were documented before anesthesia was administered, as well as at 1, 3, 5, and 10 minutes following extubation. They concluded that labetalol, at both administered doses, helped reduce the hemodynamic response during extubation, with the 0.2 mg/kg dose offering better mitigation than the 0.1 mg/kg dose.

In 2018, "H. S. Prajwal Patel, M. R. Shashank, and B. T. Shivaramu conducted a study titled Attenuation of Hemodynamic Response to Tracheal Extubation: A Comparative Study between Esmolol and Labetalol" [1] . The study involved 60 patients listed for elective surgical procedures, were randomly split in groups. Group I was given 1.5 mg/kg of esmolol, whereas Group II received 0.25 mg/kg of labetalol, both injected two minutes prior to extubation as part of a standardized perioperative anesthetic protocol. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were documented at baseline, after reversal, after the study drug, , one minute later, at extubation, and at 1, 2, 3, 4, 5, and 15 minutes post-extubation. The study concluded that both drugs reduced the hemodynamic parameters with Esmolol showing superior efficacy during and immediately after extubation. Labetalol is considered the better option for tachycardia at extubation, while esmolol is a better choice when managing elevated blood pressure to blunt the response.

In 2016, "Tuhin Mistry, Shobha Purohit, Gunjan Arora, Nitesh Gill, and Jaya Sharma conducted a study titled Attenuation of Extubation Responses: Comparison of Prior Treatment with Verapamil and Dexmedetomidine" [8]. The study included thirty ASA Grade I and II subjects undergoing spine surgeries, who were randomly assigned a group. After surgery, once spontaneous breathing resumed, (Group V received 0.1 mg/kg verapamil, while Group D received 0.3 mcg/kg dexmedetomidine, both administered as IV boluses during a minute time-frame. The researchers recorded heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) at several time intervals: just before the medication (T0), 2 minutes after administration (TM), after oral suction (TS), immediately post-extubation (TE), and at 1, 3, 5, and 10 minutes post-extubation (E1, E3, E5, E10). The study also measured emergence time, extubation quality, RASS score, and the duration taken to obtain a modified Aldrete score of ≥9. The findings showed that dexmedetomidine (0.3 mcg/kg) was significantly superior to verapamil (0.1 mg/kg) in suppressing circulatory and airway responses.

In a 2021 study by "A. Kireeti, Nirmala Jonnavithula, Ayya Syama Sundar, Akhya Kumar Kar, N.V.S.S.K. Prashanth, K. Shiva Priya, and J. Veronica, titled Effect of Pre-Extubation Low-Dose Fentanyl on Attenuation of Hemodynamic Response and Quality of Extubation: A Prospective Randomized Trial," 70 ASA grade I or II patients were enrolled to study the effectiveness of low concentration of fentanyl (0.5 mcg/kg) in reducing the hemodynamic response during extubation following elective laparoscopic cholecystectomy[9]. Patients were randomly categorized into Group-F, which received 0.5 mcg/kg of intravenous fentanyl, and Group-C, that was given same volume of normal saline.The study concluded that administering low-dose fentanyl at extubation effectively facilitated smooth extubation, stabilized hemodynamics, and minimized agitation.

In a 2020 study titled "Attenuation of Hemodynamic Responses to Endotracheal Extubation—Diltiazem versus Lidocaine, conducted by Shaik Umar Farooq, B. Sandhya Rani, and Anand Acharya", 90 patients were evaluated to evaluate the impact of diltiazem and lidocaine in reducing extubation responses [2]. The participants were randomly assigned into three distinct groups. Group I was given NS, Group II was given 0.2 mg/kg intravenous diltiazem two minutes prior to extubation, while Group III was given 1 mg/kg of intravenous lidocaine at the same interval. Post-surgery, vital findings of heart rate, systolic blood pressure, and diastolic blood pressure were measured. The results demonstrated that the impact of diltiazem in mitigating hemodynamic responses was either similar to or more potent than the effect produced by 1 mg/kg intravenous lidocaine.

In a 2021 study titled "Lidocaine versus Propofol Administration on the Attenuation of Hemodynamic Responses During Extubation in Adult Elective Surgical Patients: A Prospective Cohort, conducted by Nigussie E, Aregawi A, Abrar M, Hika A, Aberra B, Tefera B, and Teshome D", aimed at comparing the impact of lidocaine and propofol in suppressing hemodynamic responses at the time of extubation in 72 ASA I patients undergoing elective surgery [10]. Group P was given 0.5 mg/kg of propofol, Group L was given 1.5 mg/kg of lidocaine, both given 2 minutes prior to extubation, while Group C served as the control group for this study. The results showed that propofol (0.5 mg/kg) proved to be efficacious compared to lidocaine (1.5 mg/kg) in preserving heart rate, diastolic blood pressure, and mean arterial pressure for 5 minutes, and BP for 3 minutes post-extubation. However, after 5 minutes post-extubation, lidocaine (1.5 mg/kg) proved to be superior in stabilizing heart rate, diastolic blood pressure, and mean arterial pressure, while lidocaine also maintained systolic blood pressure better than propofol after 3 minutes.

In 2018, a study titled "Alleviating Stress Response to Tracheal Extubation in Neurosurgical Patients: A Comparative Study of Two Infusion Doses of Dexmedetomidine, was conducted by Ankur Luthra, Hemanshu Prabhakar, and Girija Prasad Rath" [11]. This study explored the consequences of two dexmedetomidine doses on hemodynamic and airway responses at the time of extubation in 90 ASA I–II patients undergoing intracranial surgeries. Group D 0.2 received 0.2 mcg/kg/h, Group D0.4 received 0.4 mcg/kg/h, and Group P received placebo. Airway, cardiovascular, and respiratory complications, as well as postsurgical adverse effects like nausea, vomiting, shivering, and intraoperative awareness, were also observed. Results indicated that dexmedetomidine effectively reduced HR and MAP without affecting emergence time or causing major complications.

In 2018, “Ramyavel Thangavelu, Ranjan R Ventakesh, and Kandasamy Ravichandran conducted a study titled Comparison of the Effect of Airway Nebulization with Lidocaine 2% versus Ropivacaine 0.25% on Intubation and Extubation Responses in Patients Undergoing Surgery under General Anesthesia: A Randomized Double-Blind Clinical Trial.” The study enrolled 75 ASA I–II patients, aged 18-60 years posted for general anesthesia [12]. Patients were assigned to be administered 5 ml of normal saline (Group 1), 0.25% ropivacaine (Group 2), or 2% lignocaine (Group 3) via nebulization before induction. Hemodynamic variables and cough response were assessed during intubation, extubation, and post-extubation phases. The study demonstrated that ropivacaine significantly attenuated intubation and extubation responses against NS. However, its effect on extubation response was comparable to that of lignocaine, with no notable difference.

In 2023, “Neha T. Gaidhankar, K. Chandra Mohan, R. Arun Kumar, and Amar Nandha Kumar conducted a study titled Alleviating Hemodynamic Response to Tracheal Extubation: A Comparative Study Between Dexmedetomidine and Lidocaine in Surgical Patients [13].” Sixty patients classified as ASA I and II, planned for non-emergency surgeries expected to last for at least 60 minutes requiring endotracheal intubation, were enlisted. Subjects were equally allocated in a group: Group D was given 0.5 mcg/kg dexmedetomidine, and Group L received 1.5 mg/kg lignocaine. The findings indicated that dexmedetomidine contributed to a greater attenuation of hemodynamic stress response and produced a higher level of sedation than lignocaine

In 2020, “Chetan Gopal Agrawal and Suchita Joshi Khadke conducted a study titled Comparison of IV Magnesium Sulphate and IV Esmolol in Attenuating Hemodynamic Extubation Response After General Anesthesia." The study included 60 patients planned for major surgeries, who were randomly allocated into two groups[14]. Group M was given 40 mg/kg magnesium sulfate, and Group E received 0.6 mg/kg esmolol via IV infusion five minutes prior to extubation. Various parameters, including pulse rate, MAP, pain scores, and sedation scores, were recorded from extubation to 15 minutes following extubation. According to the results, magnesium sulfate was considerably more effective than esmolol in improving hemodynamic response and relieving postoperative pain.

In 2015, "Seyed Mojtaba Marashi, Reza Hassan Nikkhouei, Ali Movafegh, Gita Shoeibi, and Shaqayeq Marashi conducted a study titled Comparison of the Effects of Magnesium Sulfate and Remifentanil on Hemodynamic Responses During Tracheal Extubation After Laparotomy: A Randomized Double-blinded Trial" [15] . This study included 120 patients, divided in three groups. Group R received 1 mcg/kg of remifentanil, Group M was given 50 mg/kg of magnesium sulfate, and Group C (placebo) received normal saline. Hemodynamic variables namely MAP and HR were noted at intervals: preoperatively, during drug administration, immediately preceding and following extubation, and at 3, 5, and 10 minutes post-extubation. The findings showed that both remifentanil and magnesium sulfate effectively suppressed the increase in HR and MAP following extubation, with remifentanil promoting quicker recovery of consciousness and muscle strength.

BASIC SCIENCES

PHARMACOLOGY OF ESMOLOL

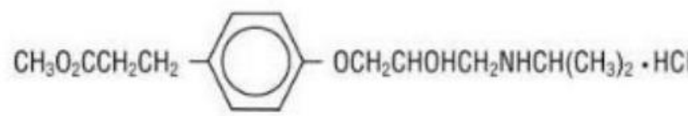


Figure 1[16]: Chemical structure of esmolol

Esmolol hydrochloride, with the chemical formula $C_{16}H_{26}NO_4Cl$ and a molecular weight of 331.8, possesses a single asymmetric center, making it an enantiomeric compound. This substance appears as a white to off-white crystalline powder. Being relatively hydrophilic, it readily dissolves in both water and alcohol. Its octanol-to-water partition coefficient at pH 7.0 is 0.42, significantly lower than the 17.0 value observed for propranolol. The injectable form of esmolol hydrochloride is a sterile, nonpyrogenic, iso-osmotic solution that is clear, colorless, or light yellow in appearance.

Mechanism of action[17]:

Esmolol is a short-acting, cardio-selective β-blocker classified as a class II antiarrhythmic agent. It functions as a competitive inhibitor of β-1-adrenergic receptors, primarily affecting cardiac myocytes. By counteracting the adrenergic effects of epinephrine and norepinephrine, esmolol reduces myocardial contractility (negative inotropic effect), lowers heart rate (negative chronotropic effect), and slows electrical conduction through the heart. Additionally, it prolongs atrioventricular refractory time, decreases myocardial oxygen demand, and slows atrioventricular conduction (negative dromotropic effect). At high intravenous infusion doses, a slight β-2-adrenergic blockade may occur in bronchial and vascular smooth muscle. However, esmolol does not exhibit membrane-stabilizing properties or α-adrenergic blocking activity.

When an appropriate loading dose is administered, steady-state blood concentrations of esmolol hydrochloride are achieved within five minutes for infusion rates ranging from 50 to 300 mcg/kg/min (0.05–0.3 mg/kg/min). Without a loading dose, steady-state levels are typically reached in approximately 30 minutes. Within this dosage range, steady-state blood concentrations increase proportionally, and the drug follows dose-independent elimination kinetics. During continuous infusion, esmolol hydrochloride maintains steady blood levels but declines rapidly once the infusion is stopped. Due to its short half-life, blood concentrations can be quickly adjusted by modifying the infusion rate and rapidly cleared from the system upon discontinuation.

Figure 2 : Esmolol vial

Pharmacokinetics[18]

Absorption: Esmolol is rapidly absorbed, the onset of action is within 60 seconds, and it maintains a steady state within 5 minutes of initiating infusion. A steady state is achieved at 2 minutes if a loading dose is administered. The drug has a 9-minute half-life and rapid renal clearance.

Distribution: Esmolol has plasma protein binding of 55%. The mean apparent volume of distribution is approximately 0.33 to 0.53 L/kg.

Consistent with the high rate of blood-based metabolism of esmolol hydrochloride, less than 2% of the drug is excreted unchanged in the urine. Within 24 hours of the end of infusion, approximately 73-88% of the dosage has been accounted for in the urine as the acid metabolite of esmolol hydrochloride.

Metabolism : Esmolol hydrochloride undergoes rapid metabolism through hydrolysis of its ester bond, primarily by esterases found in the cytosol of red blood cells, rather than by plasma cholinesterases or red cell membrane acetylcholinesterase. This metabolic process results in the formation of an inactive acid metabolite and methanol. The acid metabolite, which is excreted via the kidneys, possesses an activity level that is approximately 1500 times lower than that of esmolol. Methanol concentrations remain within normal physiological ranges. The total body clearance rate is approximately 20 L/kg/hr, exceeding cardiac output. As a result, the metabolism of esmolol hydrochloride is independent of blood flow to metabolic organs such as the liver and is not influenced by hepatic or renal circulation.

Elimination: Esmolol hydrochloride has a rapid distribution half-life of about 2 minutes and an elimination half-life of about 9 minutes. The metabolite has a half-life of 3.7 hours and is excreted via urine. Esmolol has a higher clearance (281 mL/kg/min) in infants than in adults and children

Indications[17,18,19]:

- **Temporary treatment** of supraventricular tachycardia, including rapid ventricular rates in individuals with atrial fibrillation or atrial flutter.
- **A critical emergency option** for managing focal atrial tachycardia, particularly in patients with active bronchospasm.
- **Helps regulate a fast ventricular response** in atrial fibrillation patients who do not have heart failure, hemodynamic instability, or bronchospasm.
- **Proven to be a safe and effective choice** for controlling blood pressure during surgical procedures due to its short duration of action.
- **Used in cases of sinus tachycardia**, where immediate intervention is needed, especially during acute coronary syndrome episodes.
- **Hypertensive emergency:** Loading dose of 500 to 1000 mcg/kg over 1 minute (can be repeated once), followed by infusion of 50 mcg/kg/min until the maximum dose of 200 mcg/kg/min is achieved.

- **Aortic dissection:** Loading dose of 500 mcg/kg over 2 to 5 minutes, followed by 10 mcg/kg infusion to 20 mcg/kg/min.
- **Acute coronary syndrome:** Loading dose of 500 mcg/kg over 1 minute, followed by 50 mcg/kg per minute infusion titrated every 5 to 15 minutes until the maximum dose of 300 mcg/kg/min.
- **Electroconvulsive therapy:** Loading dose of 1000 mcg/kg over 1 minute before administration of anesthesia.
- **Thyrotoxicosis:** 50 to 100 mcg/kg/min.
- **Intubation cholinergic response:** Loading dose of 1000 to 2000 mcg/kg administered 1.5 to 3 min before endotracheal intubation.
- **Ventricular tachycardia, ventricular fibrillation:** Loading dose of 500 mcg/kg bolus, followed by 50 mcg/kg/min.

Administration

Available Dosage Forms and Strengths

Esmolol is available in multiple formulations, including a 100 mg injection in a 10 mL vial (10 mg/mL), a premixed infusion bag containing 2500 mg in 250 mL (10 mg/mL), and a concentrated premixed infusion bag with 2000 mg in 100 mL (20 mg/mL).

It is administered intravenously, ideally through central venous access, though peripheral infusion is also an option. However, peripheral administration carries the risk of extravasation, which may lead to thrombophlebitis. In case of extravasation, the infusion should be discontinued, gentle aspiration of the line should be performed, and the affected limb should be elevated.

Adult Dosage

Perioperative and postoperative tachycardia and hypertension (2 methods) [17]**:** A 1000 mcg/kg bolus over 30 seconds, followed by 150 mcg/kg per minute infusion, with a maximum dose of 300 mcg/kg per minute.

Or a bolus of 500 mcg/kg over 1 minute, followed by 50 mcg/kg/min infusion for 4 minutes. If the desired therapeutic effect is not achieved, the esmolol dose may be increased to 50 mcg/kg/min until the maximum dose of 300 mcg/kg/min.

Supraventricular tachycardia and non-compensatory sinus tachycardia: A bolus loading dose of 500 mcg/kg over 1 minute was followed by a 50 mcg/kg/min infusion for 4 minutes. If the desired effect is not reached, it may increase in 50 mcg/kg per minute increments until the maximum dose of 200 mcg/kg per minute.

Specific Patient Populations[17,18]

Hepatic impairment: Esmolol does not require dosage adjustment for hepatic impairment.

Renal impairment: Esmolol does not require dosage adjustment for renal impairment.

Pregnancy considerations: Esmolol is a category C drug in pregnancy. During trials in third-trimester pregnancy and labor, Esmolol causes fetal bradycardia, which persisted after the drug infusion was discontinued.

Breastfeeding considerations: Esmolol has 55% plasma protein binding, < 1% renal excretion, and a short half-life of <10 minutes; hence, infants have no risk of accumulation. There is inconclusive data regarding milk excretion; however, it should not be used in breastfeeding mothers due to the serious potential for adverse effects.

Pediatric patients: The safety and effectiveness of esmolol are unestablished in pediatric patients. However, esmolol is used off-label for supraventricular tachycardia.

Older patients: The initiation of esmolol dosage in older patients is usually recommended at the lower end of the range due to a higher prevalence of reduced renal or cardiac function and increased occurrences of concurrent diseases or concomitant drug therapies.

Adverse effects:

- Most common , hemodynamic compromise
- Dose dependent hypotension

- Dizziness (3%), peripheral ischemia (1%), and infusion site reaction (8%), such as blistering, necrosis, or thrombophlebitis.
- Rare adverse drug reactions (less than 1% of patients without comorbidities) include bradycardia, decompensated heart failure, cardiac arrest, and heart block.
- In the setting of a patient with pheochromocytoma, esmolol is given with an α-blocker to avoid β-blockage without opposed alpha. Patients with a history of hyperthyroidism should be closely monitored after discontinuation of esmolol as it may exacerbate hyperthyroidism. Esmolol may also aggravate arterial insufficiency in patients with a history of significant peripheral vascular disease.
- Esmolol is reported to exacerbate coronary vasospasms, such as Prinzmetal's Angina.

Drug-Drug Interactions

Numerous drug-drug interactions exist with esmolol, the most significant being:

- Digoxin: A 10% to 20% increase in digoxin levels may aggravate slow AV conduction and heart rate.

- Anticholinesterases: Prolonged neuromuscular junction blockage and recovery time.

- Calcium channel blockers: Decreases myocardial contractility and may trigger cardiac arrest.

- Vasoconstrictor and inotropic agents: Esmolol should not be used to control heart rate elevation in patients who receive peripheral vascular constrictive agents such as epinephrine, norepinephrine, and dopamine.

Contraindications:

- Sinus bradycardia, sick sinus syndrome, atrioventricular heart block, heart failure
- Cardiogenic shock, pulmonary hypertension,
- History of hypersensitivity reactions to esmolol
- Esmolol and calcium channel blockers should not be administered together, as this may exacerbate hypotension and bradycardia.

- Patients with first-degree heart block and nodal dysfunctions are at an increased risk of progressive heart block, bradycardia, and AV dissociation.
- Patients with preexisting heart failure are at greater risk of decompensated heart failure and cardiogenic shock.

Toxicity:

Signs and Symptoms of Overdose

An overdose of esmolol can lead to various symptoms and complications. Cardiac toxicity may manifest as bradycardia, atrioventricular (AV) block of any degree, complete AV dissociation, reduced contractility, cardiogenic shock, asystole, and pulseless electrical activity. Neurological effects may include irregular breathing, seizures, coma, and psychiatric disturbances.

Management of Overdose[18]

Due to esmolol's extremely short half-life, the primary approach to toxicity management is stopping the infusion. Acute toxicity is typically self-limiting and managed with supportive care. Bradycardia is addressed using atropine, cardiac pacing, or other anticholinergic medications. Cardiogenic shock is treated with inotropic agents such as dopamine, dobutamine, or isoproterenol. Although uncommon, bronchospasm can be managed with β-2 agonists like albuterol. Pulseless electrical activity and cardiac arrest should be managed following ACLS guidelines. Similar to other β-blocker overdoses, calcium chloride may be administered to counteract esmolol's metabolic effects.

PHARMACOLOGY OF PRESERVATIVE FREE LIDOCAINE

Figure 3[20]: Preservative free lidocaine

Mechanism of action[21,22,23]:

Lidocaine exerts its effects by targeting sodium ion channels on the inner surface of nerve cell membranes. It first diffuses as a neutral, uncharged molecule through the neural sheaths into the axoplasm. Once inside, it becomes ionized by combining with hydrogen ions. The resulting lidocaine cations then bind to sodium channels from within, keeping them in an open state that inhibits nerve depolarization. With sufficient channel blockage, the postsynaptic neuron membrane fails to depolarize, preventing the transmission of an action potential. This mechanism not only disrupts pain signal propagation to the brain but also stops their generation at the source, producing an anesthetic effect.

Beyond its role in blocking nerve conduction in the peripheral nervous system, lidocaine also has significant effects on both the central nervous system and the cardiovascular system. Once absorbed, it can initially stimulate the CNS, followed by a depressive phase. In the cardiovascular system, lidocaine primarily affects the myocardium, leading to reduced electrical excitability, slower conduction rates, and decreased contractile force. Within cardiac myocytes, it delays phase 0 depolarization of the cardiac action potential, effectively increasing the excitation threshold. At elevated blood concentrations, lidocaine may further impact cardiovascular function by lowering cardiac output, reducing total peripheral resistance, and decreasing mean arterial pressure, likely due to its overall depressant effects on the cardiovascular system.

Lidocaine's effectiveness is reduced in inflamed tissues. This may be due to factors such as acidosis, which lowers the proportion of uncharged molecules available for diffusion, increased blood flow that accelerates the clearance of lidocaine from the affected area, or inflammatory mediators like peroxynitrite that directly interact with sodium channels. Furthermore, lidocaine's ability to act as an NMDA receptor antagonist presents a potential therapeutic benefit in treating complex pain conditions, including mixed nociceptive and neuropathic pain or cases of central sensitization.

Indications[21,22] **:**

- Lidocaine is commonly used for local anesthesia and is often combined with epinephrine (which extends lidocaine's duration of action by opposing the local vasodilatory effects of lidocaine).
- Lidocaine can also be administered intravenously during tracheal intubation, obtunding the hypertensive response to laryngoscopy and potentially reducing the incidence of myalgia and hyperkalemia after succinylcholine is given.
- As a component of ACLS interventions for patients experiencing cardiac arrest due to polymorphic ventricular tachycardia or ventricular fibrillation.
- Amiodarone or lidocaine may be considered for patients with ventricular fibrillation or pulseless ventricular tachycardia that does not respond to defibrillation.
- Intravenous lidocaine for adults undergoing open and laparoscopic abdominal surgeries, provided there are no contraindications.
- Intravenous lidocaine has been assessed as part of a multimodal analgesia approach.
- Lidocaine demonstrates significant efficacy as an adjunctive therapy for chronic post-surgical pain.
- Epidural analgesia with fentanyl and lidocaine is equivalent to intrathecal fentanyl for pain relief during early labor, with similar efficacy, duration, and patient satisfaction.

Pharmacokinetics[22,23] **:**

Absorption: Lidocaine administered as an intravenous bolus exhibits a very rapid onset of action.

Distribution: About 65% of lidocaine in the plasma binds to proteins, primarily albumin and α1-acid glycoprotein, giving it a moderate duration of action compared to other local anesthetics. Its relatively lower lipid solubility limits its potency. The drug's volume of distribution ranges between 0.7 and 1.5 L/kg.

Metabolism: Lidocaine is metabolized in the liver by the enzymes CYP1A2 and CYP3A4, producing both active and inactive metabolites. The primary active metabolites are monoethylglycylxylidide (MEGX) and glycylxylidide (GX).

Elimination: Lidocaine has a half-life of approximately 1.5 to 2 hours, which can be extended in individuals with hepatic impairment or congestive heart failure. Around 90% of the drug is eliminated via the urine.

Available Dosage Forms and Strengths[21,22]

Lidocaine is available as solutions, aqueous gels, and ointments of various strengths. Additionally, lidocaine may be combined with epinephrine or another local anesthetic (eg, prilocaine). Lidocaine is also a component of other products, including medicated plasters designed to treat chronic postherpetic neuralgia. Various administration routes require different preparations of lidocaine.

- **Aqueous formulations** ranging from 0.5% to 2% are available in plain solutions or combined with epinephrine at a ratio of 1:200,000. In dentistry, stronger concentrations, such as 1:100,000 or higher, are sometimes used. These solutions may contain preservatives or be preservative-free.
- **Diluted solutions (0.05% to 0.1%)** can be injected subcutaneously in large volumes to achieve tumescent local anesthesia, causing localized swelling and firmness, which can be beneficial for specific surgical procedures.
- **Intermediate concentrations (0.25% to 0.5%)** are commonly used for intravenous regional anesthesia (Bier's block) or for infiltration into subcutaneous tissue.
- **Higher concentrations (1% to 2%)** are used for epidural anesthesia and regional nerve blocks and are also available as intravenous preparations for treating cardiac arrhythmias.

- **Aqueous gels (1% to 2%)** often contain antiseptics such as chlorhexidine and are applied to the urethra for lubrication and anesthesia before procedures like Foley catheterization.
- **Topical solutions (4%)** are used to anesthetize the mucous membranes of the airway, including the mouth, throat, and respiratory tract. These solutions are applied via gargling, spraying, or atomization.
- **Ointments (5%)** typically include lidocaine mixed with hydrocortisone and are applied to mucous membranes such as the skin or rectum for localized relief.
- **Stronger topical solutions (10%)** are administered through a metered-dose atomizer for airway anesthesia.
- **Eutectic mixtures of lidocaine and prilocaine (EMLA)** combine both local anesthetics to penetrate the skin effectively, providing cutaneous anesthesia. EMLA is widely used to minimize pain during needle punctures.

Adult Dosage

The appropriate lidocaine dosage for infiltrative or regional anesthesia depends on the specific nerve block being administered. To suppress airway reflexes, a dose ranging from 1 to 2 mg/kg is given approximately 2 to 5 minutes before intubation. For treating cardiac dysrhythmias, an initial intravenous dose of 1 to 1.5 mg/kg may be administered, with the option of a continuous infusion if required. During awake intubation, ensuring effective topical application is essential. The maximum recommended dose should not exceed 9 mg/kg of lean body weight. To minimize the likelihood of laryngospasm, clinicians may opt for nebulized lidocaine and lower concentrations.

Specific Patient Populations

Hepatic impairment: A lidocaine patch can be used for pain relief in patients with decompensated cirrhosis; however, it should be used with caution.

Renal impairment: Dosage adjustments are generally unnecessary for patients with renal impairment, as topical lidocaine demonstrates limited absorption.

Pregnancy considerations: Lidocaine is thought to cross the placenta by passive diffusion. The maximum recommended dose of lidocaine is 4.5 mg/kg (300 mg) for plain formulations and 7 mg/kg (500 mg) when used with epinephrine. Current evidence indicates that in utero, exposure to anesthetic or sedative drugs does not appear to affect fetal brain development.

Breastfeeding considerations: Lidocaine concentrations in breast milk are low following continuous intravenous infusion, epidural administration, or high-dose local anesthesia, placing breastfeeding infants at minimal risk of exposure. Therefore, lidocaine is unlikely to cause adverse effects in breastfed infants, and no special precautions are necessary.

Pediatric patients: Neonates have an immature metabolic clearance physiology, which increases their risk of drug and metabolite accumulation. Additionally, the α1-acid glycoprotein levels in neonates and infants are lower, with AAG at birth about half that of adults. This results in a higher unbound fraction of lidocaine, an extended elimination half-life, and an increased risk of accumulation, particularly with continuous infusions.

Older patients: Local anesthesia should be prioritized for surgical procedures in older adults. The lowest effective volume and concentration should be administered to reduce the risk of systemic toxicity. For lidocaine, the recommended concentration is 10 mg/mL, and dosing should not exceed 5 mg/kg. This approach provides effective local anesthesia for many surgical procedures while reducing the risk of postoperative complications.

Drug-Drug Interactions[22,23]

- The administration of lidocaine with propranolol significantly increases lidocaine serum concentration.
- Caution is advised when administering lidocaine hydrochloride in patients with digitalis toxicity and atrioventricular block.
- Lidocaine is a substrate of CYP1A2, CYP2B6, and CYP2D6 and exerts an inhibitory effect on CYP1A2. Caution is advised when co-administering lidocaine with fluvoxamine.
- Patients may be at increased risk of developing methemoglobinemia if co-administered local anesthetics (eg, lidocaine) and other drugs, including nitrates, nitric oxide, hydroxyurea, dapsone, sulfonamides, chloroquine, phenobarbital, and phenytoin. Methemoglobinemia can also occur due to lidocaine metabolism to O-toluidine. This metabolite is more likely to be present when very high doses are given, but it may also occur with lower doses

when the patient is taking other medications that can precipitate methemoglobinemia or have a hemoglobinopathy or another cause of anemia.

Contraindications:

- Methemoglobinemia is possible in patients with hemoglobinopathy or another cause of anemia.
- Lidocaine should not be used as an antiarrhythmic if the dysrhythmia may be secondary to local anesthetic toxicity.

Monitoring :

Lidocaine has a **narrow therapeutic window**, making plasma-level monitoring essential for patients with **hepatic impairment** who require prolonged infusions. To prevent excessively high plasma concentrations, dosage calculations should be based on **ideal body weight** rather than actual body weight, with an absolute infusion limit of **120 mg per hour**. Continuous monitoring of **vital signs and ECG** is necessary.

Toxicity :

Mild toxic effects typically emerge at plasma levels exceeding 5 mcg/mL, presenting symptoms such as slurred speech, tinnitus, circumoral numbness, and dizziness. At concentrations above 10 µg/mL, patients may experience seizures or loss of consciousness. Further depression of the myocardium and central nervous system occurs at 15 mcg/mL, progressing to cardiac arrhythmias, respiratory failure, and cardiac arrest beyond 20 mcg/ml .

Compared to other local anesthetics, lidocaine has a higher cardiovascular collapse-to-CNS toxicity (CC/CNS) ratio, with bupivacaine's ratio estimated at 2.0. In cases of toxic overdose in conscious patients, lidocaine is generally less prone than other anesthetics to cause sudden cardiovascular collapse following neurological symptoms. However, if the patient is under sedation or general anesthesia, neurological warning signs may be masked, making cardiovascular instability or arrhythmias the first detectable indicators of toxicity.

Management of Overdose

- If toxicity or overdose is suspected, lidocaine administration must be discontinued immediately.
- In the event of cardiorespiratory collapse, ensuring airway management and respiratory support is crucial to prevent respiratory acidosis, which can worsen toxicity and amplify lidocaine's depressant effects on heart rate and contractility.
- Supportive care should include oxygen administration, intravenous fluids, and inotropic agents if necessary.
- Intravenous lipid emulsion therapy is recommended as a rescue treatment, particularly in cases where cardiovascular collapse does not respond to conventional interventions.

Extubation is removing an endotracheal tube .

Problems associated with extubation, recovery, and emergence are quite common .Endotracheal extubation causes transient hemodynamic stimulation leading to increase in heart rate (HR) and blood pressure (BP) due to increase in sympathoadrenergic activity caused by epipharyngeal and laryngopharyngeal stimulation.

Most patients tolerate hypertension and tachycardia without any significant consequences, but some show an exaggerated response which is poorly tolerated and may lead to myocardial ischemia, cardiac decompensation, pulmonary edema, and cerebral hemorrhage. Respiratory complications include cough, sore throat, laryngospasm, and bronchospasm which leads to hypoxemia.

Bucking occurring during extubation can mimic Valsalva maneuver physiologically[24]. It can cause negative pressure pulmonary edema if lung volumes are less than vital capacity. It can also cause abrupt increase in intracavitary pressures (intraocular, intrathoracic, intra-abdominal, and intracranial) which could put patient at high risk.

EQUIPMENTS TO BE KEPT READY DURING EXTUBATION[25]

- Appropriate sized mask
- Guedel’s airway
- Working laryngoscope and blade
- Endotracheal tube
- Stylet , bougie
- 10 cc syringe
- Sterile suction catheter
- Self inflating ambu bag
- Bain’s circuit
- Difficult airway cart

[26]**Figure 4 : Goodell's (oropharyngeal) airway, 10 cc syringe , endotracheal tube , laryngoscope and blade (left to right)**

[27]**Figure 5 : Self inflating Ambu bag with face mask**

Criteria for extubation [28]:

Objective criteria :

● $PaCO_2$< 50 mm Hg

● Vital capacity > 10 ml /kg

● Spontaneous tidal volume > 5 ml/kg

● Spontaneous RR < 10 L/ min with satisfactory ABG

● Max insp. Pressure > -30 cm H_20 in 20 secs

Subjective criteria :

- Follows commands
- Clear oropharynx/hypopharynx(bleeding,secretions)
- Intact gag reflex
- Sustained head lift for 5 secs, hand grasp
- Adequate analgesia

Procedure of extubation [29]:

- Cut off the inhalational agents and provide 100% oxygen for a few minutes before extubation to prevent desaturation.
- Perform oral and endotracheal suctioning to clear secretions.
- Place the patient in a semi-upright to optimize airway patency.
- Change the ventilator settings from mechanical ventilation to manual ventilation to check how much tidal volume is generated.
- Deflate the endotracheal tube cuff while observing for secretions or leaks.
- Instruct the patient to take a deep breath.
- After having met the objective and subjective criteria for extubation, remove the tube swiftly while suctioning if necessary to reduce aspiration risk.

- Apply appropriate oxygen therapy (nasal cannula, face mask) as required.
- Monitor for any signs of respiratory distress.

- Assess for complications such as:
    - Respiratory distress
    - Stridor (indicating laryngeal edema)
    - Cyanosis
    - Hypoxia
- Monitor vital signs and maintain continuous pulse oximetry and other vital monitoring.
- Post extubation care:

i. Provide humidified oxygen.
ii. Monitor blood gases if needed.
iii. Administer medications such as corticosteroids or nebulized treatments for airway inflammation if indicated.

METHODOLOGY

Present study titled "Comparison of effect of intravenous esmolol and preservative free lidocaine in attenuation of hemodynamic response to extubation in elective surgeries under general anesthesia – a one year hospital based double blinded Randomized Clinical Trial" was undertaken in the "Department of Anaesthesiology, KLE'S Dr. Prabhakar Kore Hospital, Belagavi" during the period of January 2024 to December 2024.

Source of data:

Patients of both genders, between 18-60 years, categorized as American Society of Anesthesiologists (ASA) grade I or II, undergoing elective surgery under general anesthesia with endotracheal tube at "KLE's Prabhakar Kore Charitable Hospital and KLE's Prabhakar Kore Hospital and Medical Research Centre, Nehru Nagar, Belagavi" between January 2024 to December 2024 were encompassed.

Type of study:

A one year randomized controlled trial.

Study duration:

One year from January 2024 to December 2024

Sample size:

Sample size calculation:

At 95% confidence interval, 95% power and 10% attrition and using :

$$N = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \ (SD_1^{\ 2} + SD_2^{\ 2})}{(X_1 - X_2)^2} \times 1.10$$

Considering mean and standard deviation

Referencing values from the 2020 research conducted by "Chetan Gopal Agrawal and Suchita Joshi Khadke, which examined the effects of IV Magnesium Sulphate and IV Esmolol on hemodynamic responses during extubation" [30]. Where,

$X_1 = 92.86$

$X_2 = 83.26$

$SD_1 = 14.11$

$SD_2 = 11.4$

$Z_{1-\alpha/2} = 1.96$

$Z_{1-\beta} = 1.64$

SD = Standard deviation

Plugging in these values:

$n = [(1.96 + 1.94)^2 * (14.11 + 11.4)^2] / (92.86-83.26)^2 * 1.10 \approx 41.22$

An initial calculation yielded a sample size of 41.22. To enhance the study's validity, the total sample size was adjusted to 84, ensuring that each group contained 42 participants.

Sampling technique and randomization:

Patients who conformed to the eligibility criteria and consented to the study were allocated between two groups through a computer-generated randomization process.

Group 1 - administered 0.5 mg/kg Esmolol

Group 2- administered 1.5 mg/kg preservative- free lidocaine

Inclusion criteria:

- Age 18-60 years
- Either gender
- ASA grade I and II patients

- Patients undergoing elective surgeries under general anesthesia with endotracheal tube.

Exclusion criteria:

- Patients with ASA grade III or more
- Patients on beta blockers
- Patients with allergy to study drug

Methodology :

Approval from ethical committee was acquired from "The institutional Ethical Research Committee, Jawaharlal Nehru Medical College, Belagavi" and CTRI registration was done. 84 patients requiring elective surgeries under general anesthesia with tracheal intubation were enlisted in this study.

Following confirmation of eligibility and receipt of informed consent, participants were divided into groups via a computer-generated randomization sequence.

Group 1: Patients were administered 0.5 mg/kg of IV esmolol

Group 2: Patients were administered 1.5 mg/kg of IV preservative-free lidocaine

A thorough pre-anesthetic evaluation was conducted a day before surgery. They were advised to fast for eight hours before the procedure. On the day of surgery, IV access was established in the preoperative area. Once the patient was shifted to the operating theatre, routine monitoring equipment was attached, and initial vital variables—namely heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2)—were documented.

Patients received premedication with glycopyrrolate at 0.005 mg/kg IV, midazolam at 0.05 mg/kg IV, and fentanyl at 2 mcg/kg IV. Following preoxygenation with 10 liters of oxygen for three minutes using a suitable face mask, general anesthesia was induced with thiopentone administered intravenously at a dose of 3–5 mg/kg until the loss of eyelash reflex was observed. To facilitate endotracheal intubation, succinylcholine at 1–2 mg/kg IV was administered. Anesthesia was sustained using a mixture of oxygen, nitrous oxide, isoflurane, and intermittent IV doses of atracurium, beginning with 0.5 mg/kg as bolus dose, and successive maintenance doses equal to one-fourth of the loading dose. Fluid and blood losses were replaced using intravenous fluids or blood products. For postoperative pain management, intravenous paracetamol 15mg/kg was administered.

Once the surgery was completed, recovery from neuromuscular blockade was achieved by glycopyrrolate at 0.01 mg/kg IV and neostigmine at 0.05 mg/kg IV. One minute later, the study drug was administered. Extubation was carried out after the patient satisfied the required criteria.

Hemodynamic parameters, including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), was measured at specific time points: prior to the administration of the reversal agents (baseline), immediately after the reversal agent (TR), immediately following the study drug administration (T0), one minute after the reversal agent), every minute for the first five minutes after the study drug administration (T1 to T5), at seven minutes (T7), and at ten minutes (T10). Additionally, the time of extubation was documented.

STATISTICAL ANALYSIS

METHODS:

Statistical evaluation was done by SPSS version 27 and Microsoft Excel. Qualitative data were displayed as frequency tables while Quantitative data as Mean ± SD / Median (Min, Max). The Chi-square test was employed to evaluate the relationship between these two. Paired t test was performed to assess intra group and Independent t test was performed to assess inter group. Statistical significance was defined as a p-value ≤ 0.05.

RESULTS

84 patients were divided into 2 groups, 42 in each group.

Group 1- 0.5 mg/kg of esmolol.
Group 2 – 1.5 mg/kg of preservative free lidocaine

The following table gives the demographic details Group 1 and Group 2

Table 1: Age distribution (years)

Group	Mean Age (years)	SD	p value
Group 1	41.29	13.53	0.24
Group 2	44.67	12.65	

The age of participants in Group 2 had a mean of 44.67 ±12.65. In Group 1, the mean age was slightly lower at 41.29 ±13.53.
From Independent t test comparison at 5 % level of significance, the difference in age across the groups was found to be statistically insignificant (p-value=0.24).

Graph 1: Age comparison

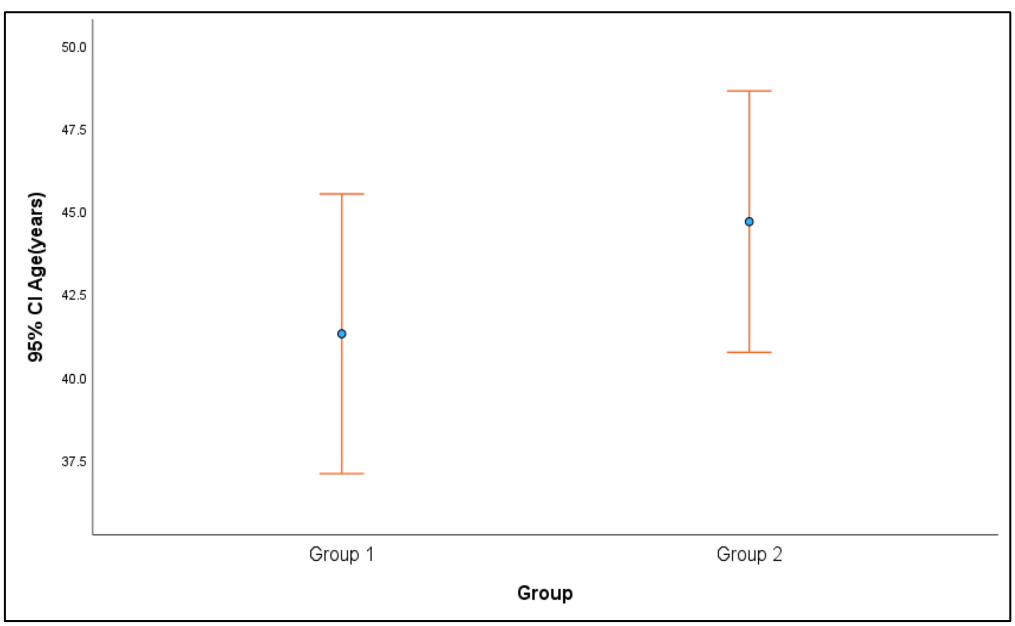


Table 2 : Gender distribution

Gender	Group		Total	Chi-square value	p value
	Group 1	Group 2			
Female	27 (60.0)	18 (40.0)	45	3.877	0.049
Male	15 (38.5)	24 (61.5)	39		
Total	42	42	84		

Regarding sex distribution, the Group 2 consisted of 18 (40.0%)females and 24 (61.5%) males, while the Group 1 had 27 (60.0%) females and 15 (38.5%) males. A significant variation in the distribution of sex among the groups was found using the Chi-square test (p-value = 0.049).

Graph 2 : Gender distribution

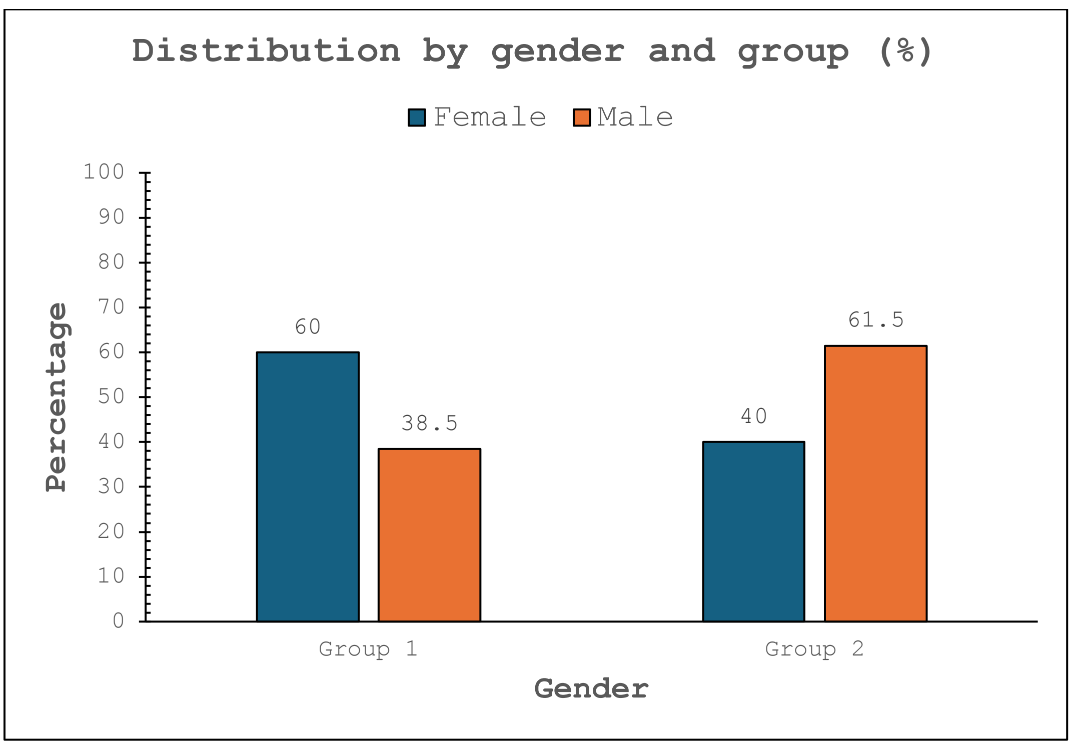


Table 3 : Intragroup comparison of heart rate (bpm) in Group 1

Time	Mean (bpm)	SD	Comparison	Mean Difference	p value
T0	90.10	16.08	…	…	…
T1	82.12	16.08	T0 - T1	7.98	0.001
T2	79.60	15.83	T0 - T2	10.5	0.001
T3	77.64	15.39	T0 - T3	12.45	0.001
T4	75.90	14.13	T0 - T4	14.19	0.001
T5	74.93	14.86	T0 - T5	15.17	0.001
T7	74.17	13.93	T0 - T7	15.93	0.001
T10	71.90	12.08	T0 - T10	18.19	0.001

The mean value at T0 is 90.10, which decreases consistently across all subsequent time points. By T10, the mean has decreased to 71.90. The mean differences increase progressively from T1 (7.98) to T10 (18.19), suggesting a continuous decline over time.

According to the paired t-test, statistically significant variations were noted between T0 and all subsequent time points. The p-values for all comparisons are 0.001, which is well below the 5% significance level.

Table 4 : Intragroup comparison of Systolic Blood Pressure (mm Hg) in Group 1

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	135.60	17.77	…	…	…
T1	130.88	14.76	T0 - T1	4.72	0.002
T2	124.74	13.99	T0 - T2	10.86	0.001
T3	123.90	12.45	T0 - T3	11.69	0.001
T4	121.79	11.57	T0 - T4	13.81	0.001
T5	121.31	10.72	T0 - T5	14.29	0.001
T7	118.50	10.01	T0 - T7	17.1	0.001
T10	117.19	9.67	T0 - T10	18.41	0.001

At T0, the mean value is 135.60.The mean decreases progressively across all time points, reaching 117.19 at T10, indicating a continuous decline over time. The mean differences t increase progressively, starting from 4.72 at T1 and reaching 18.41 at T10. The p-values for all comparisons are ≤ 0.05, which is statistically significant.

Table 5 : Intragroup comparison of Diastolic Blood Pressure (mm Hg) in Group 1

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	88.95	12.22	…	…	…
T1	82.86	9.12	T0 - T1	6.09	0.001
T2	80.64	9.96	T0 - T2	8.31	0.001
T3	79.74	7.92	T0 - T3	9.21	0.001
T4	78.98	9.17	T0 - T4	9.98	0.001
T5	77.43	9.23	T0 - T5	11.52	0.001
T7	76.17	8.40	T0 - T7	12.79	0.001
T10	73.62	11.88	T0 - T10	15.33	0.001

At T0, the mean value is 88.95. The mean decreases progressively across all time points, reaching 73.62 at T10, indicating a continuous decline over time. The mean differences between T0 and each subsequent time point increase progressively, starting from 6.09 at T1 and reaching 15.33 at T10. The p-values for all comparisons are ≤ 0.05, which is statistically significant.

Table 6 : Intragroup comparison of Mean Arterial Pressure (mm Hg) in Group 1

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	105.00	13.27	…	…	…
T1	98.86	10.63	T0 - T1	6.14	0.001
T2	93.95	11.01	T0 - T2	11.05	0.001
T3	93.50	9.60	T0 - T3	11.50	0.001
T4	92.29	9.11	T0 - T4	12.71	0.001
T5	91.45	8.92	T0 - T5	13.55	0.001
T7	89.81	8.09	T0 - T7	15.19	0.001
T10	88.10	7.78	T0 - T10	16.90	0.001

At T0, the mean value is 105.0. The mean decreases progressively across all time points, reaching 88.1 at T10, indicating a continuous decline over time. The mean differences between T0 and each subsequent time point increase progressively, starting from 6.14 at T1 and reaching 16.90 at T10. The p-values for all comparisons are ≤ 0.05, which is statistically significant.

Table 7 : Intragroup comparison of SpO_2 (%) in Group 1

Time	Mean (%)	SD	Comparison	Mean Difference	p value
T0	99.98	0.15	…	…	…
T1	100.00	0.00	T0 - T1	-0.020	0.323
T2	100.00	0.00	T0 - T2	-0.020	0.323
T3	100.00	0.00	T0 - T3	-0.020	0.323
T4	100.00	0.00	T0 - T4	-0.020	0.323
T5	100.00	0.00	T0 - T5	-0.020	0.323
T7	100.00	0.00	T0 - T7	-0.020	0.323
T10	100.00	0.00	T0 - T10	-0.020	0.323

At T0, the mean value is 99.98 with a small standard deviation (0.15). From T1 to T10, the mean remains constant at 100.00 with no variation (SD = 0.00). The small mean difference of -0.020 suggests a very minimal change between T0 and all subsequent time points.
The p-value for all comparisons is 0.323, which means there is no statistical significance within the group.

Table 8 : Intragroup comparison of heart rate (bpm) in Group 2

Time	Mean (bpm)	SD	Comparison	Mean Difference	p value
T0	98.43	18.22	…	…	…
T1	96.74	17.37	T0 - T1	1.69	0.081
T2	95.98	16.51	T0 - T2	2.45	0.074
T3	95.57	15.92	T0 - T3	2.86	0.042
T4	94.31	14.44	T0 - T4	4.12	0.023
T5	94.00	15.69	T0 - T5	4.43	0.034
T7	93.36	15.12	T0 - T7	5.07	0.012
T10	94.14	15.65	T0 - T10	4.29	0.066

At T0, the mean value is 98.43.The mean values decrease over time, reaching a low of 93.36 at T7, before slightly increasing again at T10 (94.14). The mean difference increases over time, from 1.69 at T1 to a maximum of 5.07 at T7, indicating a progressive decline.
Statistically significant reductions are observed at T3, T4, T5, and T7, but not at T1, T2, or T10. This suggests that while there is an overall decreasing trend, the changes are not consistently significant at all evaluation points.

Table 9 : Intragroup comparison of Systolic Blood Pressure (mm Hg) in Group 2

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	136.90	12.94	…	…	…
T1	136.98	12.37	T0 - T1	-0.08	0.946
T2	137.50	12.56	T0 - T2	-0.60	0.646
T3	136.21	11.87	T0 - T3	0.69	0.586
T4	136.98	13.22	T0 - T4	-0.07	0.959
T5	136.36	13.27	T0 - T5	0.55	0.689
T7	136.69	13.24	T0 - T7	0.21	0.874
T10	137.21	14.61	T0 - T10	-0.31	0.861

At T0, the mean value is 136.90.Across all time points (T1 to T10), the mean values fluctuate slightly around 136–137, with no clear increasing or decreasing trend. The changes in mean values are very small (ranging from -0.08 to 0.69), indicating minimal variation over time. The results indicate that there is no significant change in mean values from T0 to T10 (p value >0.05).

Table 10 : Intragroup comparison of Diastolic Blood Pressure (mm Hg) in Group 2

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	91.12	11.53	…	…	…
T1	90.31	11.93	T0 - T1	0.81	0.330
T2	90.05	11.02	T0 - T2	1.07	0.296
T3	88.83	10.46	T0 - T3	2.29	0.048
T4	88.05	9.98	T0 - T4	3.07	0.021
T5	88.36	10.24	T0 - T5	2.76	0.030
T7	89.14	10.82	T0 - T7	1.98	0.168
T10	89.52	11.04	T0 - T10	1.60	0.305

At T0, the mean value is 91.12.The mean gradually decreases over time, reaching a low of 88.05 at T4, before slightly increasing again at later time points. The results suggest a significant decrease in mean values from T0 to T3, T4, and T5, but the trend does not remain significant at later time points (T7 and T10). This indicates that while there is an initial reduction, the values tend to stabilize or slightly recover over time.

Table 11 : Intragroup comparison of Mean Arterial Pressure (mm Hg) in Group 2

Time	Mean (mm Hg)	SD	Comparison	Mean Difference	p value
T0	106.10	10.54	…	…	…
T1	105.60	10.55	T0 - T1	0.50	0.540
T2	105.69	9.66	T0 - T2	0.41	0.691
T3	103.93	9.55	T0 - T3	2.17	0.070
T4	104.50	9.12	T0 - T4	1.60	0.152
T5	103.88	9.51	T0 - T5	2.21	0.030
T7	104.55	9.22	T0 - T7	1.55	0.160
T10	104.67	10.17	T0 - T10	1.43	0.286

The T0 mean is 106.10. The mean values fluctuate slightly over time, reaching the lowest point at T5 (103.88) before increasing slightly again. The only statistically significant difference is at T5 ($p = 0.030$), indicating a meaningful reduction in the mean value at this time point. The results indicate that there is no strong evidence of a consistent trend or meaningful change in the mean values over time. While a statistically significant decrease is observed at T5, the changes at other time points are not significant.

Table 12 : Intragroup comparison of SpO_2 (%) in Group 2

Time	Mean (%)	SD
T0	100	0
T1	100	0
T2	100	0
T3	100	0
T4	100	0
T5	100	0
T7	100	0
T10	100	0

Comparison is not possible due to no change in the value.

Comparison between Group 1 and 2

Table 13 : Heart Rate (bpm)

Time	Group 2		Group 1		p value
	Mean (SD) (bpm)	Median (Min, Max)	Mean (SD) (bpm)	Median (Min, Max)	
HR (T0)	98.43 (18.22)	99.5 (61, 132)	90.1 (16.08)	89 (66, 132)	0.054
HR(T1)	96.74 (17.37)	98 (65, 134)	82.12 (16.08)	81.5 (52, 120)	0.001
HR(T2)	95.98 (16.51)	95 (64, 136)	79.6 (15.83)	79 (50, 118)	0.001
HR (T3)	95.57 (15.92)	95 (67, 136)	77.64 (15.39)	78.5 (52, 117)	0.001
HR (T4)	94.31 (14.44)	91.5 (74, 134)	75.9 (14.13)	76.5 (50, 114)	0.001
HR (T5)	94 (15.69)	96.5 (70, 137)	74.93 (14.86)	76.5 (49, 116)	0.001
HR (T7)	93.36 (15.12)	95.5 (70, 134)	74.17 (13.93)	73.5 (50, 112)	0.001
HR (T10)	94.14 (15.65)	95.5 (62, 138)	71.9 (12.08)	71.5 (50, 97)	0.001

At T0, the mean HR is more in Group 2 (98.43 bpm) than in the Group 1 (90.1 bpm). In both groups, heart rate gradually decreases from T0 to T10.

The decrease in heart rate is noticeably higher in Group 1 versus Group 2. By T10, the mean HR of Group 1 drops to 71.9 bpm, whereas in the Group 2, it remains at 94.14 bpm.

The p-values at all post-T0 time points (T1 to T10) are 0.001, indicating that the differences in HR of the groups are highly statistically significant at each recording. At all intervals, the HR in Group 1 was considerably lower.

Graph 3 :

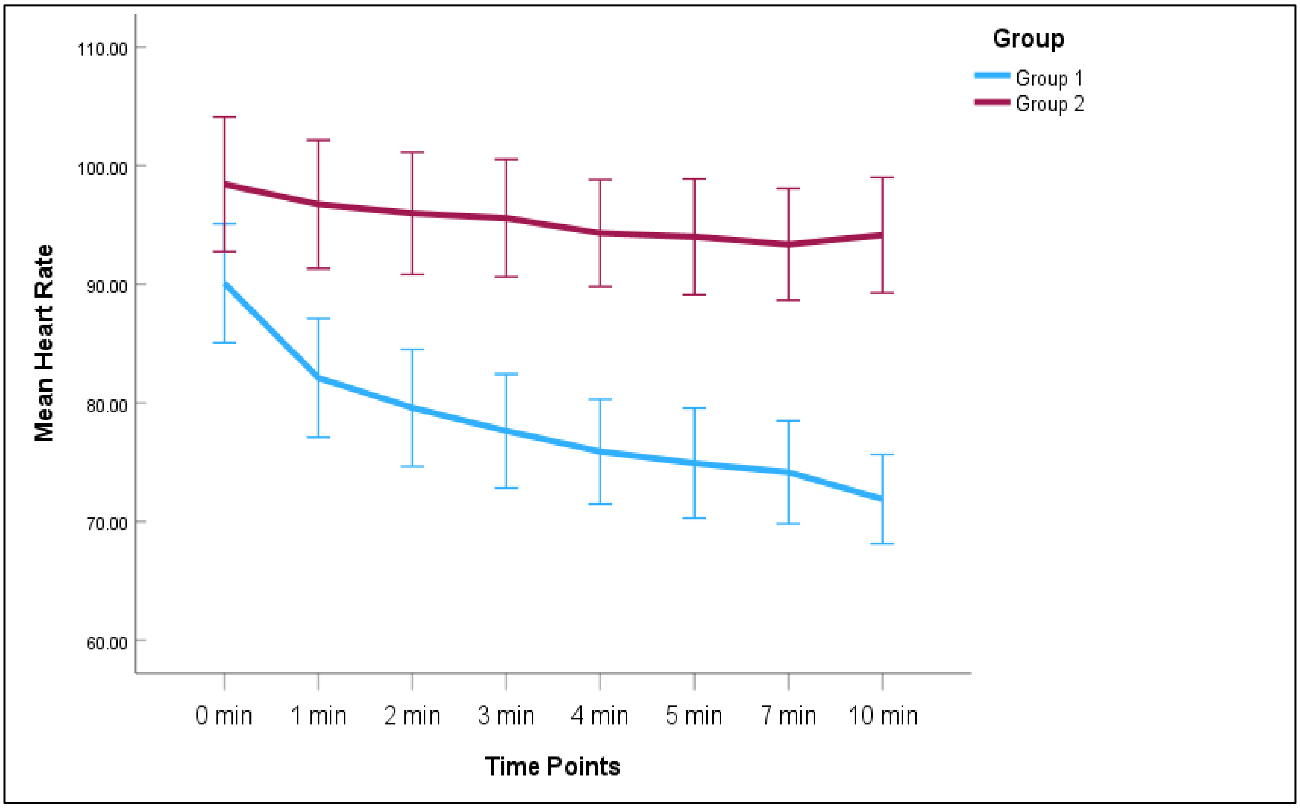

Group
Group 1
Group 2
110.00
100.00
90.00
80.00
70.00
60.00
Mean Heart Rate
0 min
1 min
2 min
3 min
4 min
5 min
7 min
10 min
Time Points

Table 14 : SBP (mm Hg)

Time	Group 2		Group 1		p value
	Mean (SD) (mm Hg)	Median (Min, Max)	Mean (SD) (mm Hg)	Median (Min, Max)	
SBP (T0)	136.9 (12.94)	136 (101, 164)	135.6 (17.77)	135 (105, 180)	0.7
SBP (T1)	136.98 (12.37)	137 (105, 171)	130.88 (14.76)	129 (99, 175)	0.043
SBP (T2)	137.5 (12.56)	136 (113, 172)	124.74 (13.99)	124 (104, 168)	0.001
SBP (T3)	136.21 (11.87)	137 (110, 160)	123.9 (12.45)	124 (103, 166)	0.001
SBP (T4)	136.98 (13.22)	140 (108, 172)	121.79 (11.57)	121 (103, 162)	0.001
SBP (T5)	136.36 (13.27)	138 (108, 172)	121.31 (10.72)	120.5 (100, 141)	0.001
SBP (T7)	136.69 (13.24)	137.5 (108, 170)	118.5 (10.01)	119.5 (99, 138)	0.001
SBP (T10)	137.21 (14.61)	139.5 (108, 168)	117.19 (9.67)	119 (100, 136)	0.001

At T0, the mean SBP in the Group 2 (136.9 mmHg) and Group 1 (135.6 mmHg) are very similar. In the Group 2, SBP remains relatively stable, fluctuating slightly around 136–137 mmHg across all time points.In the Group 1, SBP gradually decreases from 135.6 mmHg (T0) to 117.19 mmHg (T10).This indicates a progressive reduction in SBP in the Group 1, while the Group 2 remains unchanged.

At T0, the p-value (0.7) being greater than 0.05 suggests no statistical significance in SBP between the groups. However, at T1 (p = 0.043), Group 1 shows a slight but statistically significant reduction in SBP. From T2 onwards, the differences in SBP between the groups become highly significant, with a consistent p-value of 0.001.

Graph 4 :

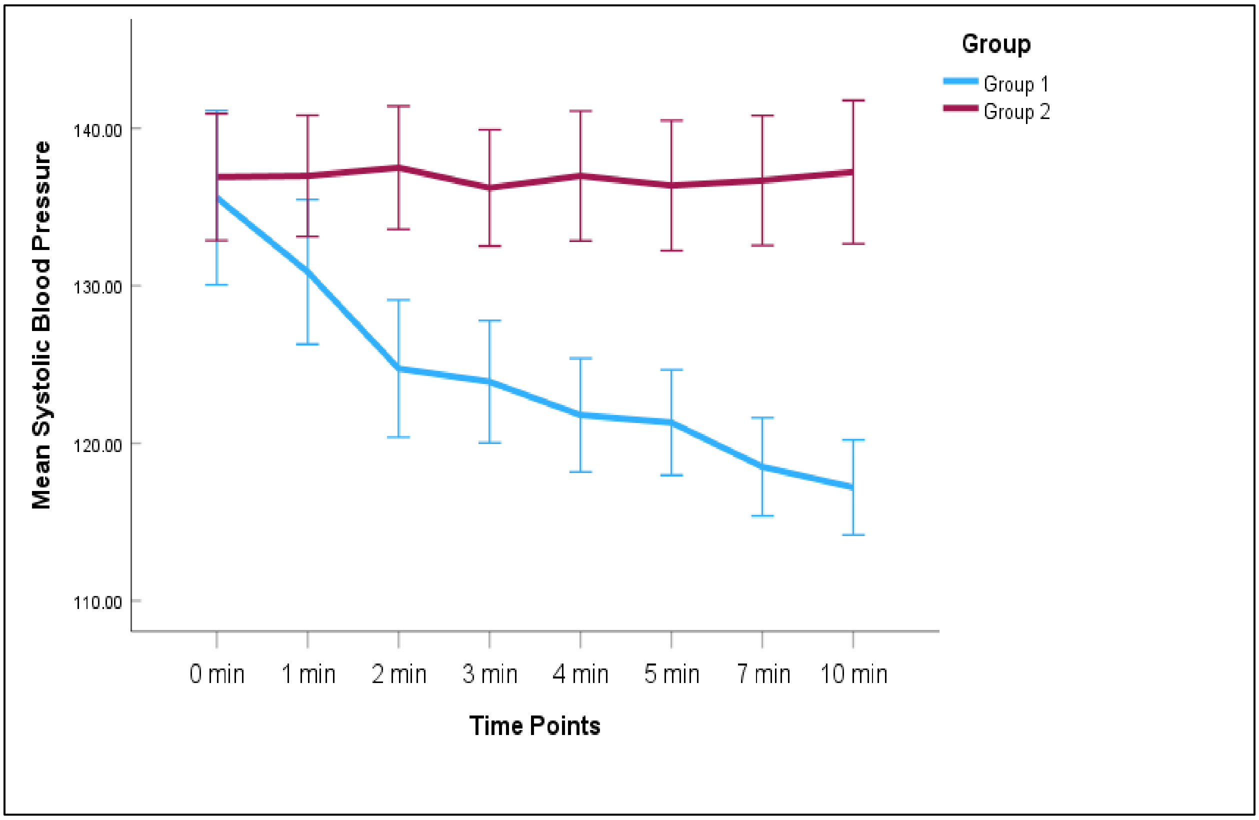

Group
Group 1
Group 2
Mean Systolic Blood Pressure
140.00
130.00
120.00
110.00
0 min
1 min
2 min
3 min
4 min
5 min
7 min
10 min
Time Points

Table 15 : DBP (mm Hg)

Time	Group 2		Group 1		p value
	Mean (SD) (mm Hg)	Median (Min, Max)	Mean (SD) (mm Hg)	Median (Min, Max)	
DBP (T0)	91.12 (11.53)	90 (67, 117)	88.95 (12.22)	88 (65, 127)	0.406
DBP (T1)	90.31 (11.93)	91 (60, 116)	82.86 (9.12)	82 (64, 110)	0.002
DBP (T2)	90.05 (11.02)	90 (65, 116)	80.64 (9.96)	80.5 (60, 104)	0.001
DBP (T3)	88.83 (10.46)	88 (59, 110)	79.74 (7.92)	80 (62, 99)	0.001
DBP (T4)	88.05 (9.98)	88.5 (66, 108)	78.98 (9.17)	79.5 (60, 98)	0.001
DBP (T5)	88.36 (10.24)	88.5 (70, 108)	77.43 (9.23)	77.5 (57, 95)	0.001
DBP (T7)	89.14 (10.82)	89.5 (64, 111)	76.17 (8.4)	77.5 (58, 92)	0.001
DBP (T10)	89.52 (11.04)	90 (70, 112)	73.62 (11.88)	75.5 (20, 92)	0.001

At T0, the mean DBP in the Group 2 (91.12 mmHg) and Group 1 (88.95 mmHg) are similar. In the Group 2, DBP remains relatively stable, fluctuating slightly around 88–90 mmHg across all time points. In the Group 1, DBP steadily decreases from 88.95 mmHg (T0) to 73.62 mmHg (T10).This suggests a progressive reduction in DBP in the Group 1, while the Group 2 remains largely unchanged.

At T0, the p-value (0.406) being more than 0.05 indicates no meaningful difference in DBP between the groups. However, pronounced statistical difference in DBP is seen in Group 1 at T1 (p = 0.002) compared to Group 2. From T2 onwards, the p-value remains constant at 0.001, confirming a highly statistical difference in DBP between the two groups, and indicating that the reduction in Group 1 is statistically meaningful.

Graph 5:

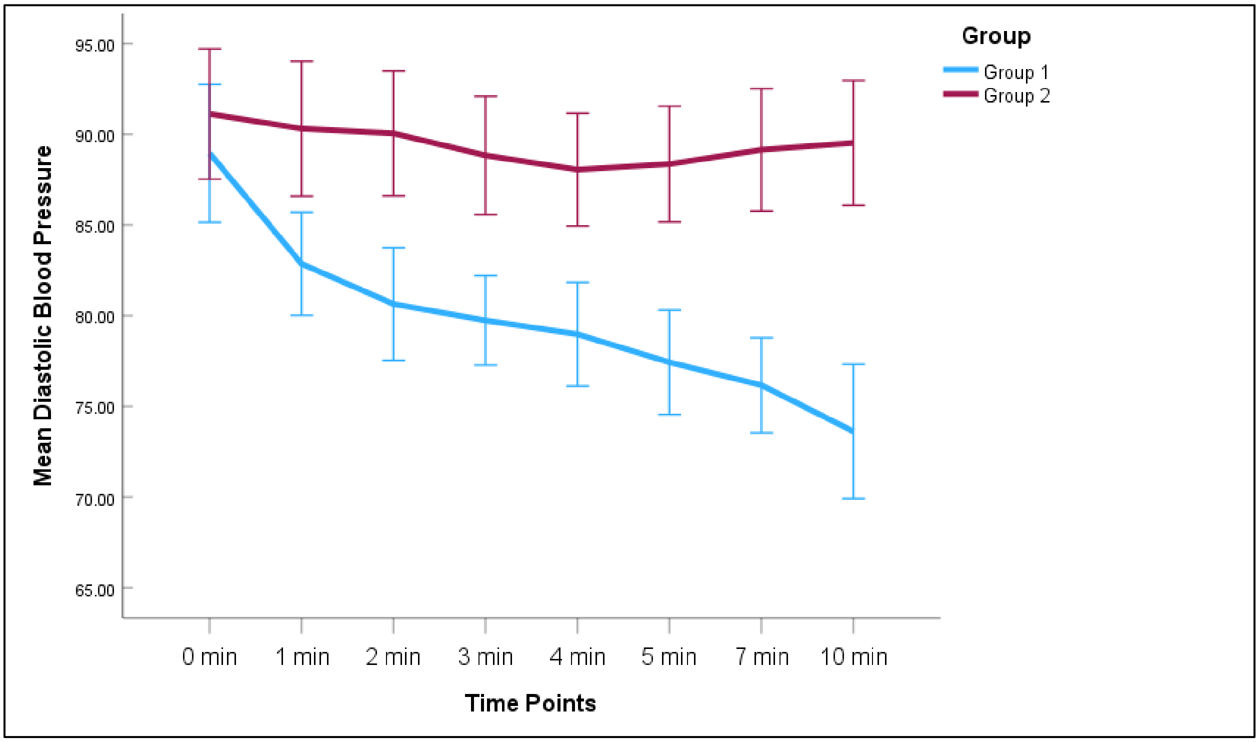

Mean Diastolic Blood Pressure
95.00
90.00
85.00
80.00
75.00
70.00
65.00
0 min
1 min
2 min
3 min
4 min
5 min
7 min
10 min
Time Points
Group
Group 1
Group 2

Table 16 : MAP (mm Hg)

Time	Group 2		Group 1		p value
	Mean (SD) (mm Hg)	Median (Min, Max)	Mean (SD) (mm Hg)	Median (Min, Max)	
MAP (T0)	106.1 (10.54)	105 (81, 131)	105 (13.27)	102.5 (79, 141)	0.676
MAP (T1)	105.6 (10.55)	107 (82, 134)	98.86 (10.63)	98.5 (71, 126)	0.005
MAP (T2)	105.69 (9.66)	106 (85, 131)	93.95 (11.01)	93.5 (75, 121)	0.001
MAP (T3)	103.93 (9.55)	105 (81, 122)	93.5 (9.6)	94 (76, 117)	0.001
MAP (T4)	104.5 (9.12)	106.5 (82, 123)	92.29 (9.11)	93 (74, 111)	0.001
MAP (T5)	103.88 (9.51)	104 (85, 123)	91.45 (8.92)	92 (70, 108)	0.001
MAP (T7)	104.55 (9.22)	106 (87, 124)	89.81 (8.09)	90.5 (72, 105)	0.001
MAP (T10)	104.67 (10.17)	107 (85, 123)	88.1 (7.78)	89 (71, 105)	0.001

At T0, the mean MAP in Group 2 (106.1 mmHg) and Group 1 (105 mmHg) are similar. In the Group 2, MAP remains relatively stable, fluctuating slightly around 104–106 mmHg across all time points. In Group 1, MAP steadily decreases from 105 mmHg (T0) to 88.1 mmHg (T10).

No evident difference in MAP was observed at T0 between the two groups (p-value = 0.676). However, at T1 (p = 0.005), Group 1 showed a significant mitigation in MAP when compared to Group 2. From T2 onwards, the p-value confirms that the MAP reduction in Group 1 is unlikely to be a result of random variation.

Graph 6 :

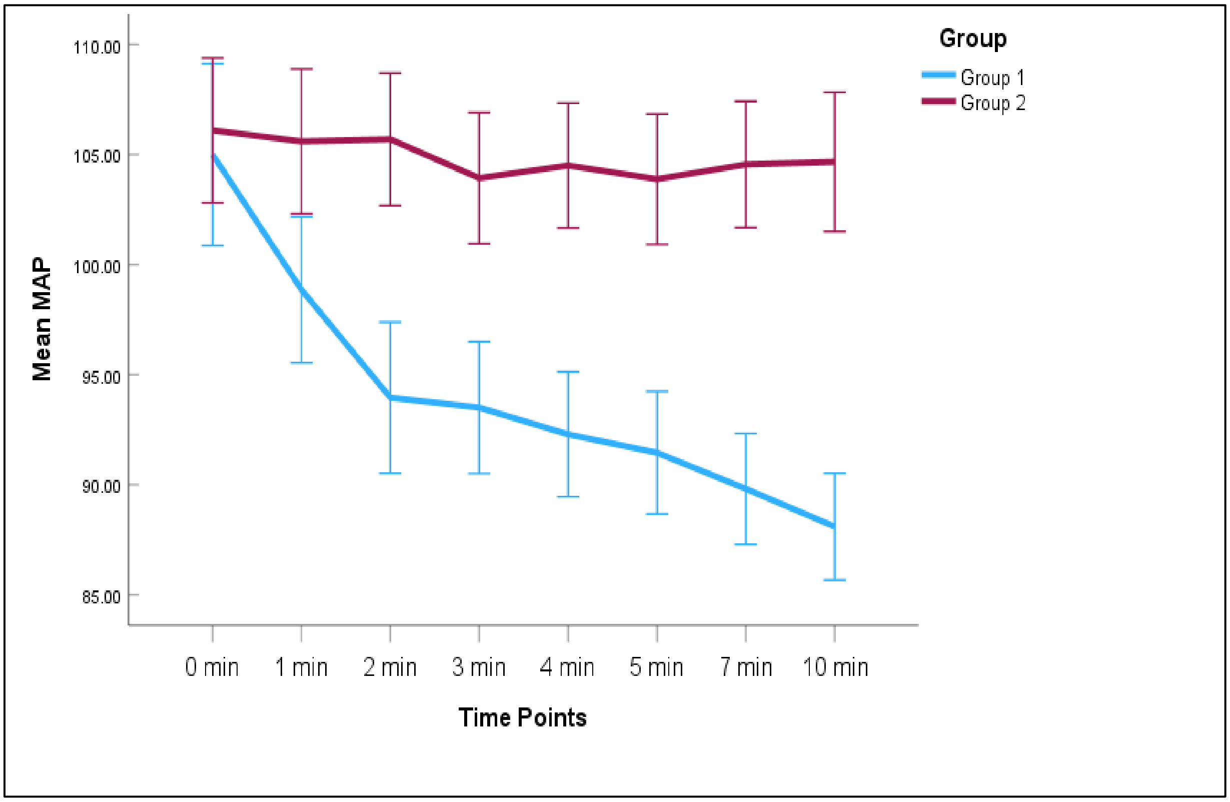

Group
Group 1
Group 2
Mean MAP
110.00
105.00
100.00
95.00
90.00
85.00
0 min
1 min
2 min
3 min
4 min
5 min
7 min
10 min
Time Points

Table 17 : SpO_2 (%)

Time	Group 2		Group 1		p value
	Mean (SD) (%)	**Median (Min, Max)**	**Mean (SD) (%)**	**Median (Min, Max)**	
SPO2 (T0)	100 (0)	100 (100, 100)	99.98 (0.15)	100 (99, 100)	0.32
SPO2 (T1)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T2)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T3)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T4)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T5)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T7)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…
SPO2 (T10)	100 (0)	100 (100, 100)	100 (0)	100 (100, 100)	…

The Group 2 has a mean SpO_2 of 100% (SD = 0).The Group 1 has a mean SpO_2 of 99.98±0.15%. Across all time points (T1–T10), both the groups maintain a mean SpO_2 of 100%.

The p-value at T0 is 0.32, which is not statistically significant.

Graph 7 :

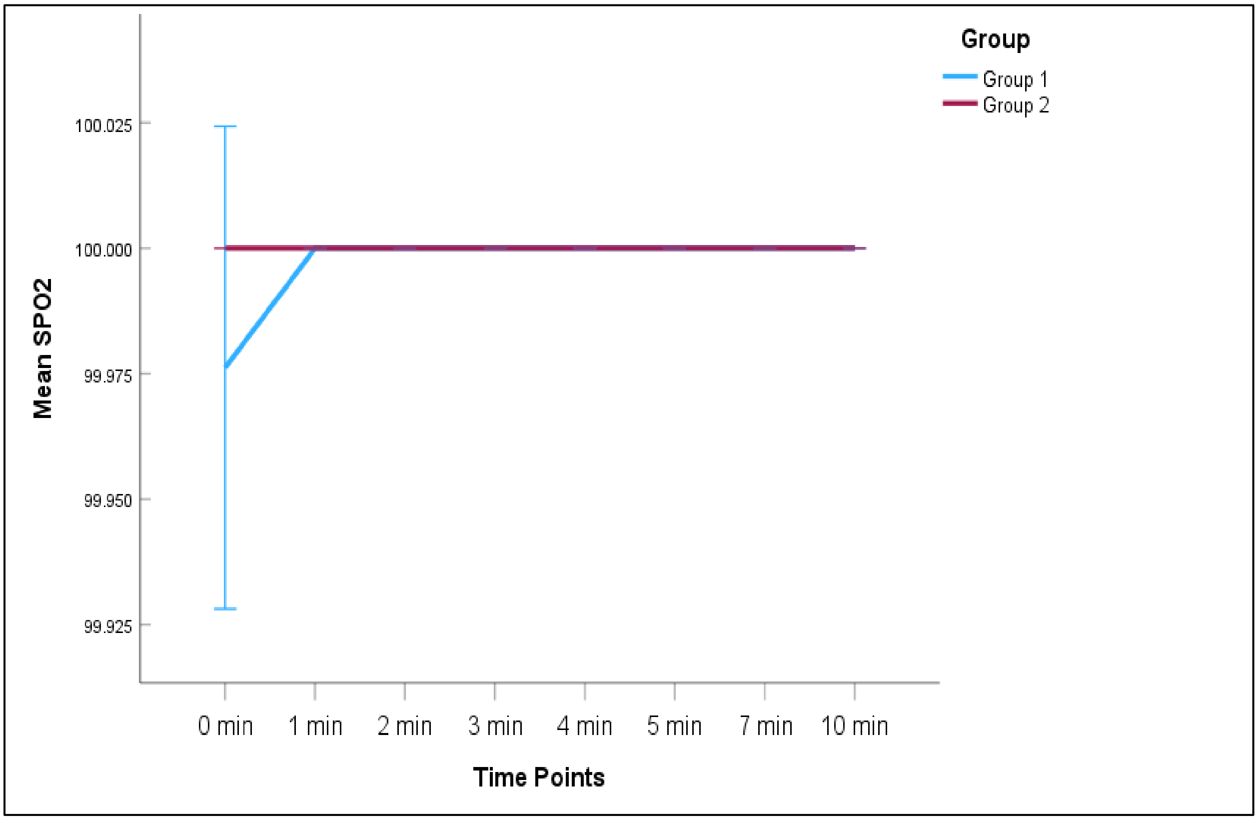
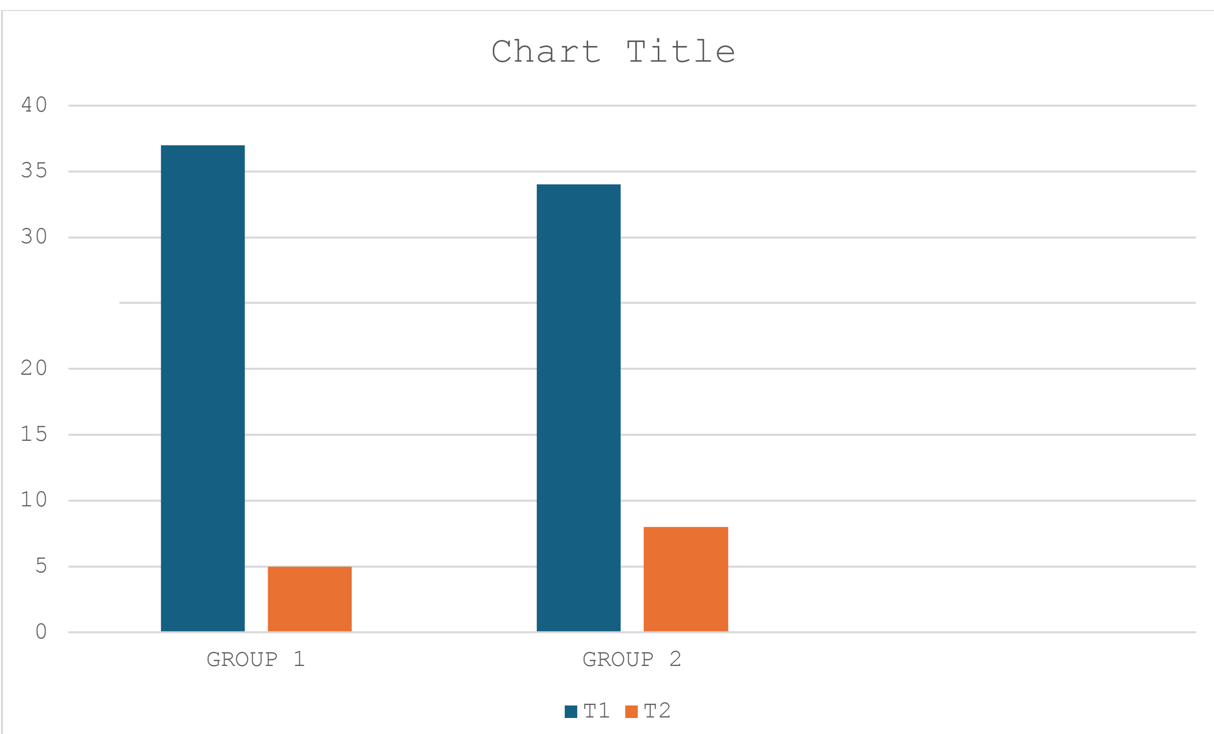

Group
Group 1
Group 2
100.025
100.000
99.975
99.950
99.925
Mean SPO2
0 min
1 min
2 min
3 min
4 min
5 min
7 min
10 min
Time Points

Table 18 : Time of extubation

Time of extubation	Group 1	Group 2
Baseline	0	0
TR	0	0
T0	0	0
T1	37	34
T2	5	8
T3	0	0
T4	0	0
T5	0	0
T7	0	0
T10	0	0

Majority of patients were extubated at T1 in both the groups.

Graph 8 :



Neither group experienced any adverse effects like bradycardia, PONV, or allergic reactions associated with the administration of either drug.

DISCUSSION

The hemodynamic reaction to extubation is a widely recognized physiological occurence characterized by transient tachycardia and hypertension due to sympathetic stimulation.

The precise mechanism underlying the extubation response remains unclear, but it is thought to involve the sympathetic and parasympathetic nervous system. Sympathetic response is mediated through a polysynaptic pathway involving the glossopharyngeal and vagus nerves as the afferent limb, traveling via brainstem and spinal cord. Stimulation in the epipharyngeal and laryngopharyngeal regions induces sympathoadrenergic activation, causing an increase in catecholamines like norepinephrine and epinephrine. Consequently, this leads to a rise in HR and BP. In contrast, the parasympathetic reflex follows a monosynaptic pathway and is predominantly observed in children.

Attenuation of this response is crucial to prevent adverse cardiovascular events, particularly in susceptible patients. Our study assessed the effectiveness of IV Esmolol versus preservative-free Lidocaine in minimizing the hemodynamic response associated with extubation in patients under general anesthesia.

Comparison of Demographic profile

In this study, the age and sex distribution of participants in Group 1 and Group 2 were compared to identify whether there were any notable differences between the two groups. The findings of these comparisons shed light into the demographic characteristics of the groups and their possible contribution to the study's outcomes.

Age Comparison

The age distribution analysis depicted the average age in Group 2 as 44.67 ± 12.65 years, while in Group 1 it was slightly lower at 41.29 ± 13.53 years. The Independent t-test, however, indicated no marked statistical difference (p-value = 0.24). This suggests that the age variation is insufficient to influence the study results, eliminating age as a confounding factor.

Sex Distribution Comparison

A distinct variation in sex distribution was noted between the two groups. In the Group 2, 40.0% subjects were female, while 60.0% were male. In contrast, Group 1 consisted of 61.5% females and 38.5% males. The Chi-square test used for comparison produced a p-value of 0.049, indicating a significant statistical variation. The unequal allocation of males and females in the two groups may introduce potential biases if gender plays a role in the study outcomes. However, it is not expected to have a meaningful impact on the interpretation of our study results as it aims at the mitigation of hemodynamic response following extubation.

Comparison of Hemodynamic Parameters

Heart Rate Control

In Group 1, the mean heart rate at T0 was 90.10 bpm. Over the course of the study, the mean heart rate progressively decreased at each time point, reaching 71.90 bpm by T10. Statistical analysis using the paired t-test revealed significant variations between T0 and all subsequent time points, with p-values of 0.001.

The progressive increase in the mean differences from T1 (7.98 bpm) to T10 (18.19 bpm) further supports the idea that the effect of the intervention continued to exert influence as time progressed, providing an ongoing attenuation of the heart rate response.

In contrast, Group 2, showed a different pattern. The mean heart rate at T0 was 98.43 bpm, which gradually decreased over time, reaching 94.14 bpm at T10. However, this reduction was less pronounced compared to Group 1, with the mean HR dropping by only 4.29 bpm from T0. The paired t-test results show that significant reductions in heart rate were observed at T3, T4, T5, and T7, but not at T1, T2, or T10. This suggests that while there was a general trend toward a decrease in heart rate, the changes were not consistent or statistically significant at all time points, particularly in the earlier and later phases of the measurement period. The lack of sustained significance at all time points could indicate that the control condition alone does not produce a consistent or long-lasting effect on heart rate.

When comparing Group 1 and Group 2, significant differences in heart rate were observed at all time points (T1 to T10). At T0, Group 2 had a higher mean heart rate (98.43 bpm) compared to Group 1 (90.10 bpm). However, by T10, the mean heart rate in Group 1 decreased to 71.90 bpm, while Group 2 remained at 94.14 bpm. The p-values at all time points (T1-T10) were 0.001, indicating a significant statistical variation.

This suggests that Group 1, which received the intervention, experienced a more substantial and sustained reduction in heart rate compared to Group 2, where the decline was less pronounced. The significantly lower heart rate in Group 1 at all time points demonstrates the effectiveness of the treatment in managing the hemodynamic response to extubation, particularly in comparison to Group 2, where the heart rate reduction was minimal and inconsistent.

[31] "Kshama, S. A.; Shenoy, Laxmi; Sinha, Shweta conducted a study on Comparison of two doses of intravenous esmolol in attenuation of hemodynamic response to extubation in laparoscopic surgeries" and concluded that IV esmolol was efficacious in mitigating heart rate during extubation. This corresponds with the outcome of our study.

Systolic Blood Pressure Control

In Group 1, T0 mean SBP was 135.60 mmHg. Over the course of the study, the SBP showed a consistent and progressive decline at each subsequent time point, reaching 117.19 mmHg by T10. The mean differences between T0 and each time point gradually increased, from 4.72 mmHg at T1 to 18.41 mmHg at T10, suggesting that the intervention was effective in gradually reducing SBP over time. The paired t-test results indicate that all comparisons between T0 and subsequent time points were statistically significant (p-values ≤ 0.05).

In contrast, Group 2, showed a different pattern. The mean SBP at T0 was 136.90 mmHg, very similar to Group 1's T0. However, over time, the SBP in Group 2 remained relatively stable, fluctuating slightly between 136 and 137 mmHg from T1 to T10. The mean changes in SBP were minimal, ranging from -0.08 mmHg to 0.69

mmHg, suggesting that there was little to no significant fluctuation or reduction in SBP during the observation period. Statistical analysis of Group 2 revealed no significant changes in SBP across the time points, with a p-value greater than 0.05 for all comparison.

When comparing the SBP between Group 1 and Group 2, a clear and statistical significance is observed. At T0, the mean SBP in both groups was very similar, with the Group 2 at 136.90 mmHg and the Group 1 at 135.60 mmHg. However, as the study progressed, the SBP in the Group 1 showed a continuous and statistically significant decrease, while the Group 2 remained relatively stable.

At T1, a small but statistically significant reduction in SBP was observed in the Group 1 ($p = 0.043$), indicating the onset of the drug's effect. From T2 onwards, the statistical analysis showed a highly pronounced deviation in SBP between the two groups., with p-values of 0.001 at each subsequent time point. By T10, the Group 1's SBP had decreased by 18.41 mmHg, while the Group 2's SBP remained virtually unchanged. These findings suggest that the intervention in the Group 1 was highly effective in lowering SBP, whereas the Group 2 showed no such significant change over time.

A study titled [14] "Khadke SJ, Agrawal CG. Comparison of IV magnesium sulphate and IV esmolol in attenuating hemodynamic extubation response after general anesthesia" concluded that esmolol was better than magnesium sulphate in alleviating systolic blood pressure. This mirrors the observations made in our study.

Diastolic Blood Pressure Control

In the Group 1, the mean DBP at T0 was 88.95 mmHg. Over the course of the study, the mean DBP decreased progressively at each subsequent time point, reaching 73.62 mmHg by T10. This indicates a sustained and continuous decline in DBP. The mean differences between T0 and each time point increased progressively, starting from 6.09 mmHg at T1 and reaching 15.33 mmHg at T10. The paired t-test consistently showed statistically significant changes at each time point, with p-values not exceeding 0.05.

In contrast, the Group 2, showed a different pattern. The mean DBP at T0 was 91.12 mmHg, similar to the Group 1's T0 value. However, the DBP in the Group 2 exhibited only a modest reduction, reaching 88.05 mmHg at T4. After this point, the values slightly increased at later time points. Statistically significant reductions in DBP were observed from T0 to T3, T4, and T5, but no significant change was observed at T7 or T10. The p-value for comparisons between T0 and later time points in the Group 2 was greater than 0.05 for T7 and T10, indicating that the changes were not statistically significant and that the DBP values remained relatively stable after an initial decrease.

The intergroup comparison revealed that, at (T0), the mean DBP was similar between the Group 2 (91.12 mmHg) and the Group 1 (88.95 mmHg), with no statistically significant difference (p = 0.406). However, from T1 onwards, Group 1 exhibited a significant reduction in DBP compared to the Group 2. A sharp decline in DBP was noticed in Group 1 at T1 (p-value = 0.002). From T2 onwards, a statistically notable difference was present between the groups, with consistent p-values of 0.001. In contrast, Group 2's DBP remained relatively stable, with no significant changes after the initial reductions at T3, T4, and T5.

[32] "Korukonda, Viditha & Kaladhar, S. (2020). Attenuation of haemodynamic response to laryngoscopy and endotracheal intubation a comparative study between IV labetalol and IV lidocaine" concluded that IV labetalol was more superior in mitigating the rise in DBP during these procedures compared to IV lidocaine. Our study with esmolol supports these findings.

Mean Arterial Pressure Control

In the Group 1, the T0 MAP was 105 mmHg, which steadily decreased over the course of the study, reaching 88.1 mmHg at T10. This indicates a significant and progressive decline in MAP. The mean differences between T0 and each subsequent time point increased progressively, from 6.14 mmHg at T1 to 16.90 mmHg at T10.

This progressive decrease in MAP showed a noticeable statistical impact at all evaluation points, with p-values ≤ 0.05, confirming that the intervention was effective in reducing MAP over time.

In contrast, the Group 2, showed more variability in MAP values. The MAP at T0 was 106.1 mmHg, and the values fluctuated over time, with the lowest point observed at T5 (103.88 mmHg), followed by a slight increase at later time points. While there was a small reduction in MAP at T5, the changes at other time points were not significant. The p-value for T5 was 0.030, indicating a statistically proven reduction at this specific time point. However, the fluctuations observed at other time points, such as T1, T2, and T10, were not significant, suggesting that the Group 2 did not experience a consistent trend in MAP reduction.

The Group 1 exhibited a significant reduction in MAP starting from T1, with a p-value of 0.005. From T2 onwards, the difference between the groups became highly quantifiable, with consistent p-values of 0.001 at all subsequent time points. These results confirm that the decrease in MAP in the Group 1 was not only statistically apparent but also sustained over the entire study period. In contrast, the Group 2 did not show any similar sustained changes, with MAP fluctuating slightly around the T0 values.

[26] "Khadke SJ, Agrawal CG in the study titled Comparison of IV magnesium sulphate and IV esmolol in attenuating hemodynamic extubation response after general anesthesia" concluded that increases in MAP were attenuated in both groups, E showing a more substantial effect. This is in line with our study.

SpO_2 Control

This study revealed that the Group 1 and Group 2 both exhibit stable and consistent SpO_2 levels across the different time points measured. At T0, the Group 1 shows a mean SpO_2 of 99.98±0.15 %, which indicates minimal variability in the measurements. From T1 to T10, the Group 1 maintained a mean SpO_2 of 100.00%, with no variation (SD = 0.00). This stability is noteworthy and suggests that there were no significant changes or fluctuations in SpO_2 levels over the period under observation.

In the Group 2, the SpO_2 levels remained constant at 100% with no observed variability (SD = 0), and hence comparisons were not possible.

The lack of statistical significance in the inter-group comparison ($p = 0.32$) suggests that there were no notable differences in SpO_2 levels between the study and Group 2s. Both groups exhibited similar trends, with no significant variation observed over the time points measured.

Time of extubation

T1 was the most common time for extubation, with 37 subjects in Group 1 and 24 subjects in Group 2.

Side effect of drug

In both groups, there were no reported side effects like bradycardia, post-operative nausea and vomiting, or allergic reactions associated with the use of either drug.

Clinical Implications

The study demonstrates that Esmolol has a greater ability to reduce hemodynamic responses during extubation compared to preservative-free lidocaine. It offers superior control of heart rate and blood pressure with a favorable safety profile. However, Lidocaine remains a viable alternative, particularly in patients where beta-blockade is contraindicated.

Limitations

- A key limitation was the single-center design, coupled with a limited sample size, which might restrict applicability of the results on a broader population.

Future scope

- Future multicenter trials with greater patient cohorts and extended postoperative monitoring could provide more definitive conclusions.
- Additionally, investigating combination therapies involving both Esmolol and Lidocaine may offer insights into synergistic benefits for hemodynamic control during extubation.

CONCLUSION

- Intravenous Esmolol is more superior than preservative-free Lidocaine in mitigating hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) during the extubation process.

- Esmolol consistently reduced heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure at all time intervals. In contrast, preservative-free lidocaine resulted in more variable trends, with inconsistent declines across the time points. Additionally, No notable changes in systolic blood pressure were observed in this group, and the SpO2 levels remained comparable between both groups.

- Both interventions were free of significant side effects such as bradycardia, post-operative nausea and vomiting and allergic reaction, supporting their potential utility in clinical practice during extubation.

SUMMARY

The study titled **"COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL"**was conducted.

84 individuals belonging to ASA I or II who met our inclusion and exclusion criteria, undergoing elective surgeries under general anesthesia were enrolled into two randomized groups. Group 1- received 0.5 mg/kg of Esmolol and Group 2- received 1.5mg/kg of preservative free lidocaine. The main goal was to assess the impact of administration of intravenous esmolol and preservative free lidocaine on various hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation) during the process of extubation. Hemodynamic parameters, including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), was recorded at several time points: before the administration of the reversal agents (baseline), immediately after the reversal agent (TR), immediately following the study drug administration (T0), one minute after the reversal agent), every minute for the first five minutes after the study drug administration (T1 to T5), at seven minutes (T7), and at ten minutes (T10). Additionally, the time of extubation was documented.

This study supports the use of Intravenous Esmolol as a superior agent in controlling hemodynamic instability during extubation compared to preservative-free Lidocaine. Its ability to attenuate the sympathetic response effectively and contribute towards a more controlled and predictable extubation process makes it a valuable option.

BIBLIOGRAPHY

1. Prajwal Patel HS, Shashank MR, Shivaramu BT. Attenuation of Hemodynamic Response to Tracheal Extubation: A Comparative Study between Esmolol and Labetalol. Anesth Essays Res. 2018 Jan-Mar;12(1):180-185. doi: 10.4103/aer.AER_130_17. PMID: 29628578; PMCID: PMC5872860.
2. Swamy SN, Madhusudhana R. Attenuation of Hemodynamic Responses to Endotracheal Extubation with Different Doses of Diltiazem with Lignocaine: A Placebo-Controlled Study. Anesth Essays Res. 2018 Apr-Jun;12(2):428-433. doi: 10.4103/aer.AER_28_18. PMID: 29962611; PMCID: PMC6020606.
3. Maroof, M.; Ajmani, P.; Khan, R.M. MD. COMPARATIVE STUDY OF LIDOCAINE AND ESMOLOL ON THE HEMODYNAMIC CHANGES AND QUALITY OF EXTUBATION. Anesthesia & Analgesia 88(2S):p 359S, February 1999. | DOI: 10.1097/00000539-199902001-00356.
4. Koju, Ram & Dongol, Yashad. (2016). Comparative effects of lidocaine and esmolol in attenuating the hemodynamic response to laryngoscopy and intubation. Journal of the Korean Surgical Society. 17. 23-30. 10.3126/jssn.v17i2.17144.
5. Gaidhankar, Neha T.; Mohan, K. Chandra; Kumar, R. Arun1; Kumar, Amar Nandha. Alleviating hemodynamic response to tracheal extubation: A comparative study between dexmedetomidine and lignocaine in surgical patients. The Indian Anaesthetists Forum 24(1):p 21-28, Jan–Jun 2023. | DOI: 10.4103/TheIAForum.TheIAForum_74_22.
6. Bindu B, Pasupuleti S, Gowd UP, Gorre V, Murthy RR, Laxmi MB. A double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation. J Anaesthesiol Clin Pharmacol. 2013 Apr;29(2):162-7. doi: 10.4103/0970-9185.111665. PMID: 23878434; PMCID: PMC3713660.
7. Shetabi H, Nazemroaya B, Mahjobipoor H, Majidi S. Comparative study of the effect of two different doses of intravenous labetalol on the cardiovascular response to endotracheal extubation. J Cardiovasc Thorac

Res. 2023;15(2):98-105. doi: 10.34172/jcvtr.2023.31623. Epub 2023 Jun 29. PMID: 37654815; PMCID: PMC10466463.

8. Mistry, Tuhin & Purohit, Shobha & Arora, Gunjan & Gill, Nitesh & Sharma, Jaya. (2016). Attenuation of extubation responses: Comparison of prior treatment with verapamil and dexmedetomidine. Journal of Neuroanaesthesiology and Critical Care. 3. 33. 10.4103/2348-0548.173234.
9. Kireeti A, Jonnavithula N, Sundar AS, Kar AK, Prashanth NVSSK, Priya KS, Veronica J. Effect of pre-extubation low-dose fentanyl on attenuation of haemodynamic response and quality of extubation: A prospective randomised trial. *Trends Anaesth Crit Care.* 2021;39:44-8. doi:10.1016/j.tacc.2021.04.002.
10. Nigussie E, Aregawi A, Abrar M, Hika A, Aberra B, Tefera B, Teshome D. Lidocaine versus propofol administration on the attenuation of hemodynamic responses during extubation in the adult elective surgical patient: A prospective cohort. Heliyon. 2021 Aug 8;7(8):e07737. doi: 10.1016/j.heliyon.2021.e07737. PMID: 34409194; PMCID: PMC8361261.
11. Luthra A, Prabhakar H, Rath GP. Alleviating Stress Response to Tracheal Extubation in Neurosurgical Patients: A Comparative Study of Two Infusion Doses of Dexmedetomidine. J Neurosci Rural Pract. 2017 Aug;8(Suppl 1):S49-S56. doi: 10.4103/jnrp.jnrp_91_17. PMID: 28936072; PMCID: PMC5602261.
12. Thangavelu R, Ventakesh RR, Ravichandran K. Comparison of Effect of Airway Nebulization with Lignocaine 2% versus Ropivacaine 0.25% on Intubation and Extubation Response in Patients Undergoing Surgery under General Anesthesia: A Randomized Double-Blind Clinical Trial. Anesth Essays Res. 2018 Apr-Jun;12(2):338-343. doi: 10.4103/aer.AER_83_18. PMID: 29962594; PMCID: PMC6020607.
13. Gaidhankar, Neha T.; Mohan, K. Chandra; Kumar, R. Arun1; Kumar, Amar Nandha. Alleviating hemodynamic response to tracheal extubation: A comparative study between dexmedetomidine and lignocaine in surgical patients. The Indian Anaesthetists Forum 24(1):p 21-28, Jan–Jun 2023. | DOI: 10.4103/TheIAForum.TheIAForum_74_22.

14. Agrawal C G, Khadke S J , Comparison of IV magnesium sulphate and IV esmolol in attenuating hemodynamic extubation response after general anesthesia. Indian J Clin Anaesth 2020;7(3):457-465.
15. Marashi SM, Hassan Nikkhouei R, Movafegh A, Shoeibi G, Marashi S. Comparison of the Effects of Magnesium Sulfate and Remifentanil on Hemodynamic Responses During Tracheal Extubation After Laparotomy: A Randomized Double-blinded Trial. Anesth Pain Med. 2015 Aug 26;5(4):e25276. doi: 10.5812/aapm.25276. PMID: 26478862; PMCID: PMC4604289.
16. Drugs.com. Esmolol injection. 2024 [cited 2025 Mar 22]. Available from: https://www.drugs.com/pro/esmolol-injection.html.
17. Pevtsov A, Kerndt CC, Ahmed I, et al. Esmolol. [Updated 2024 Jan 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK518965/
18. Wiest D. Esmolol. A review of its therapeutic efficacy and pharmacokinetic characteristics. Clin Pharmacokinet. 1995 Mar;28(3):190-202. doi: 10.2165/00003088-199528030-00002. PMID: 7758250.
19. Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anesthesia. 9th ed. Philadelphia: Elsevier; 2020. p. 1555-1582.
20. SecondMedic. Loxicard 2% Inj 50ml . 2024 [cited 2025 Mar 22]. Available from: https://www.secondmedic.com/app/view-product/loxicard-2-inj-50ml-75456
21. Hendrickx JFA, Eger EI, Sonner JM, Shafer SL. Stoelting’s Pharmacology and Physiology in Anesthetic Practice. 5th ed. Philadelphia: Wolters Kluwer; 2015.
22. Beecham GB, Nessel TA, Goyal A. Lidocaine. [Updated 2024 Aug 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539881/
23. Smith J, Doe A. Lidocaine. In: Brown P, Green R, editors. Stoelting's Pharmacology and Physiology in Anesthetic Practice. 5th ed. Philadelphia: Wolters Kluwer; 2021. p. 123-130.
24. Wong TH, Weber G, Abramowicz AE. Smooth Extubation and Smooth Emergence Techniques: A Narrative Review. Anesthesiol Res Pract. 2021

Jan 15;2021:8883257. doi: 10.1155/2021/8883257. PMID: 33510786; PMCID: PMC7822686.

25. MedicineNet. Equipment and medications for endotracheal intubation. Available from:https://www.medicinenet.com/equipment_medications_endotracheal_intubation/drug-class.htm.
26. Verywell Health. Endotracheal tube information. Available from: https://www.verywellhealth.com/endotracheal-tube-information-2249093.
27. Stoelting RK, Hines RL, Marschall KE. Stoelting's Anesthesia and Co-Existing Disease. 7th ed. Philadelphia: Elsevier; 2018.
28. Anaesthesia MMC. Criteria for extubation. Available from: https://www.anaesthesiammc.com/images/CRITERIA%20FOR%20EXTUBATION%20final%20%20%281%29-converted.pdf.
29. Difficult Airway Society. Guidelines for the safe management of tracheal extubation in adult perioperative practice. London: Difficult Airway Society; [cited 2025 Mar 7].
30. Khadke SJ, Agrawal CG. Comparison of IV magnesium sulphate and IV esmolol in attenuating hemodynamic extubation response after general anesthesia. *Indian J Clin Anaesth*. 2020 Sep;7(3):457-465.
31. Kshama, S. A.; Shenoy, Laxmi; Sinha, Shweta. Comparison of two doses of intravenous esmolol in attenuation of hemodynamic response to extubation in laparoscopic surgeries. The Indian Anaesthetists Forum 23(2):p 125-130, Jul–Dec 2022. DOI: 10.4103/TheIAForum.TheIAForum_49_22.
32. Korukonda, Viditha & Kaladhar, S. (2020). Attenuation of haemodynamic response to laryngoscopy and endotracheal intubation a comparative study between I.V. labetalol and I.V. lignocaine. Indian Journal of Clinical Anaesthesia. 7. 676-680. 10.18231/j.ijca.2020.121.

ANNEXURE I – INFORMED CONSENT FORM

KAHERs JNMC
BELAGAVI
INFORMED CONSENT FORM

"COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL"

Introduction:

General anesthesia involves endotracheal extubation which could result in tachycardia and hypertension. This could eventually lead to disastrous complications such as myocardial ischemia, heart failure, cerebrovascular hemorrhage, and pulmonary edema. In order to prevent these life-threatening events, IV esmolol and preservative free lidocaine will be administered to the allotted patients after taking due informed consent.

Explanation of procedure:

After shifting the patient to the operation theatre, monitors will be attached, and baseline readings will be recorded. At the end of surgery, 1 minute after giving the reversal agent, study drug, i.e., IV esmolol and preservative free lidocaine will be administered.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and Spo_2 will be measured after the reversal agent was administered (TR), after the study drug was administered (T0- one minute after administering the reversal agent), then for every minute for the first 5 min post-administration of study(T1 to T5), 7 minutes after administering study drug (T7) and finally at 10 minutes (T10). Time of extubation will also be noted.

Withdrawal from participation in the study:

Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study:

You will not get any benefits by participating in this study. The data gathered will help population at large.

Possible risks from participating in the study:

There are no risks involved in participating in this study.

Privacy and confidentiality:

The information collected from you will be coded, to prevent any person to identify you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives:

You will not receive any payment for participating in this study.

Cost of investigations done during study will be paid by the **principal investigator / Participant.**

Authorization for publication of aggregated data:

Results obtained after processing of the aggregated data will be published for scientific purpose and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions regarding this study, you are free to contact: **Ethical committee of JNMC, 0831-2473777 Extension 4052.**

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

"**COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL**".

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

Subject Name: ______________________

Signature or the Left Thumb Print of Subject: _______________________

Date:

Investigator's Name: ________________ Signature: ________________

Date:

Place:

ANNEXURE II – PROFORMA

PROFORMA

"**COMPARISON OF EFFECT OF INTRAVENOUS ESMOLOL AND PRESERVATIVE FREE LIDOCAINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION IN ELECTIVE SURGERIES UNDER GENERAL ANESTHESIA – A ONE YEAR HOSPITAL BASED SINGLE BLINDED RANDOMIZED CLINICAL TRIAL**".

Patient's Name : I.P No. :

Age : Date of Examination :

Gender : Anesthesiologist :

Address :

Pre-anesthetic evaluation:

Chief complaints:

Past History:

- H/o co-morbidities and drug intake:
- H/o previous surgery/(s) where difficult airway was encountered:
- Previous anesthetic experience:

General physical examination:

Height (cm): Weight (Kg): BMI:

Pallor : Icterus :

Cyanosis : Clubbing : BP :

PR : RR : SpO2:

Systemic examination:

RS: **CVS:**

CNS: **GIT:**

Airway Assessment:

Teeth: Jaw movements:

Investigations:

Hb (gm/dl): TLC: Platelet count:

Serum Creatinine**:** FBS: Chest x-ray: ECG:

Preoperative physical status: ASA Grade I II

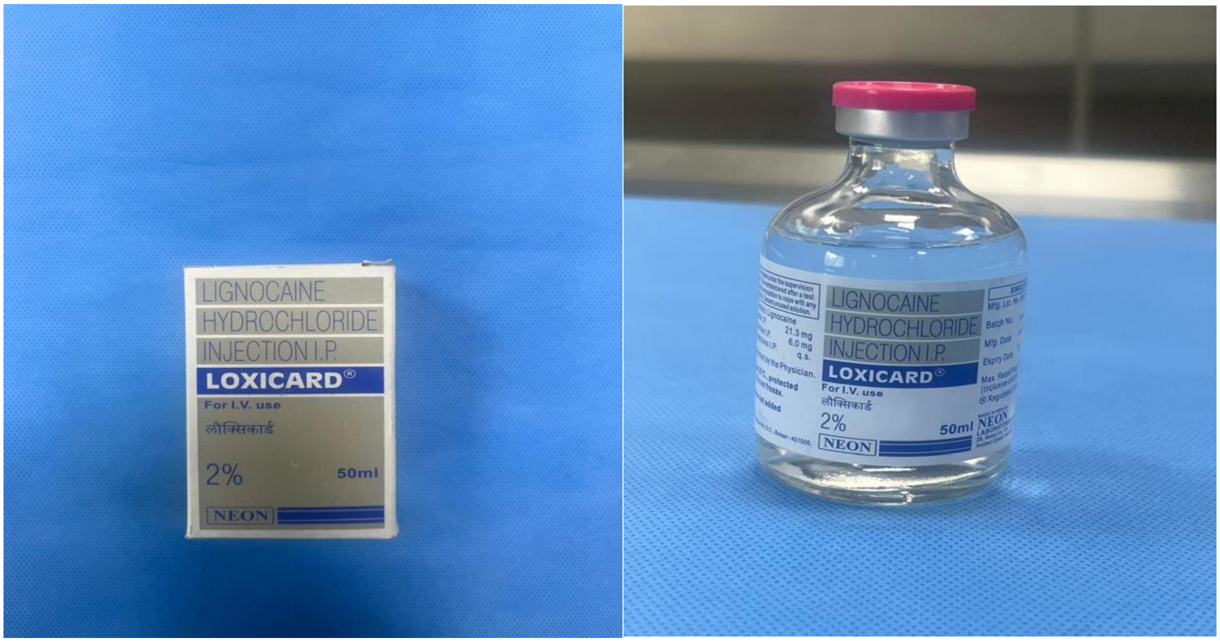
Diagnosis:

Proposed surgery:

	HR	SBP	DBP	MAP	SPO2
BASELINE(BEFORE ADMINISTRATION OF REVERSAL AGENT)					
AFTER ADMINISTRATION OF REVERSAL AGENT (TR)					
AFTER ADMINISTRATION OF STUDY DRUG (T0)					
1					
2					
3					
4					
5					
7					
10					
TIME OF EXTUBATION-					

ANNEXURE III : PHOTOGRAPHS

Photograph 1: Esmolol vial



Photograph 2 : Preservative free lidocaine

ANNEXURE IV: MASTER CHART

Group 1

IP NO	Age (years)	Gender (M/F)	HR (BASELINE)	HR (TR)	HR (T0)	HR(T 1)	HR(T 2)	HR (T3)	HR (T4)	HR (T5)	HR (T7)	HR (T10)
10055173	52	F	82	97	88	80	82	83	83	83	84	83
10053110	62	M	110	108	100	98	92	90	91	90	88	80
10054424	40	M	97	96	92	80	65	67	64	64	67	72
10053548	65	M	110	88	80	86	86	78	76	70	68	66
10054557	59	F	84	78	73	67	66	65	66	67	68	70
10053947	52	F	120	118	115	106	100	80	77	60	64	66
10053844	52	F	87	68	66	64	60	63	58	61	60	54
10000686	19	F	128	124	121	120	118	117	114	116	112	97
10001926	30	M	96	88	84	84	82	82	83	82	80	80
10008860	30	F	99	86	84	82	80	80	81	78	75	78
10009130	42	F	76	102	99	91	87	86	77	77	74	70
10009776	38	M	100	115	101	77	66	62	62	61	62	60
10007798	70	M	78	80	74	52	50	52	50	49	50	50
10014128	66	M	107	98	100	100	86	88	87	83	86	85
10011205	35	F	93	134	116	80	83	82	82	84	81	80
10012437	37	F	94	92	72	63	78	70	64	62	62	60
10020674	45	F	95	87	82	81	83	80	78	78	76	72
10012707	27	F	108	110	132	100	77	80	79	80	77	72
10033524	50	F	57	90	84	83	78	70	65	63	61	60
10055566	43	F	80	74	72	75	75	72	74	76	78	75
10056068	35	F	93	99	102	100	102	100	98	98	92	90
10056117	52	F	75	74	67	75	76	82	81	80	80	78
10072346	21	F	108	106	110	82	91	73	70	68	68	68
10063204	25	M	110	100	101	98	98	96	97	94	90	88
10066388	46	M	97	85	84	79	74	74	73	70	72	71
10066637	51	M	77	77	78	78	72	67	64	77	92	64
10069429	18	F	78	77	105	82	86	85	82	82	80	78
10067739	58	M	73	83	71	60	57	68	63	67	70	78
10069261	46	F	75	78	74	65	56	57	58	58	57	58
10067898	43	M	93	88	70	62	55	54	53	51	51	51
10071833	40	F	66	108	107	89	78	74	76	61	57	57
10070271	36	M	97	78	82	65	63	62	65	60	62	58
10071840	28	F	115	103	91	93	92	93	95	92	91	90
10070893	46	M	120	95	91	113	112	117	93	92	90	88
10071063	46	F	74	75	68	78	80	79	78	77	73	70
10070961	31	F	112	100	88	56	57	52	54	54	52	55
10071105	35	F	97	101	104	102	101	101	98	97	96	94
10072516	19	F	91	102	97	102	95	97	92	98	91	83
10072325	26	F	101	98	96	93	94	84	83	90	84	77
10072672	50	F	87	92	90	56	58	63	61	57	59	62
10072814	44	F	75	76	73	70	75	70	72	71	70	68
10072115	24	M	102	103	100	82	77	66	71	69	65	64

IP NO	Age (years)	Gender (M/F)	SBP (BASELINE)	SBP (TR)	SBP (T0)	SBP (T1)	SBP (T2)	SBP (T3)	SBP (T4)	SBP (T5)	SBP (T7)	SBP (T10)
10055173	52	F	125	132	112	121	114	135	125	121	120	120
10053110	62	M	126	120	105	99	108	110	110	108	106	110
10054424	40	M	136	139	125	124	112	108	108	104	108	101
10053548	65	M	160	158	150	146	144	140	130	136	130	128
10054557	59	F	174	158	150	140	138	138	136	139	130	130
10053947	52	F	163	150	146	129	119	121	121	123	117	120
10053844	52	F	172	168	148	136	134	130	128	124	126	124
10000686	19	F	128	126	126	124	122	122	120	116	118	114
10001926	30	M	116	116	108	110	108	108	104	108	100	102
10008860	30	F	128	120	118	116	116	116	115	106	110	107
10009130	42	F	126	142	180	156	142	130	140	136	130	130
10009776	38	M	108	128	135	130	126	124	124	124	122	120
10007798	70	M	162	166	164	143	144	130	128	126	128	124
10014128	66	M	149	173	140	138	124	115	114	111	108	106
10011205	35	F	153	160	130	116	114	112	109	109	110	110
10012437	37	F	117	164	136	127	145	130	130	126	124	128
10020674	45	F	106	130	126	128	126	124	124	120	120	118
10012707	27	F	134	148	135	135	124	119	120	122	120	118
10033524	50	F	162	170	153	144	127	128	135	130	132	130
10055566	43	F	185	193	178	175	168	166	162	140	138	136
10056068	35	F	138	131	170	150	117	114	110	112	111	110
10056117	52	F	147	148	135	143	133	126	117	120	120	118
10072346	21	F	128	126	123	117	104	106	103	100	99	100
10063204	25	M	150	148	138	136	120	118	122	124	122	126
10066388	46	M	153	132	136	129	131	130	130	128	126	124
10066637	51	M	138	148	135	125	104	124	113	129	110	122
10069429	18	F	111	112	119	106	104	103	103	103	100	102
10067739	58	M	151	165	169	160	155	156	138	141	121	122
10069261	46	F	165	152	138	140	130	128	129	124	126	120
10067898	43	M	113	115	128	127	128	126	131	137	123	121
10071833	40	F	160	152	131	148	129	128	114	117	113	100
10070271	36	M	152	147	125	124	127	128	121	132	138	129
10071840	28	F	125	123	128	130	129	131	129	132	132	130
10070893	46	M	157	145	115	124	123	134	122	120	118	117
10071063	46	F	123	116	107	122	116	117	117	120	119	120
10070961	31	F	149	137	143	123	121	118	118	117	116	112
10071105	35	F	115	117	125	113	107	107	110	114	114	111
10072516	19	F	159	151	135	138	133	130	133	134	129	124
10072325	26	F	138	136	129	131	122	115	120	114	105	105
10072672	50	F	148	141	134	118	113	114	112	110	115	111
10072814	44	F	141	142	136	135	129	128	126	118	117	116
10072115	24	M	130	132	131	121	109	117	114	120	106	106

IP NO	Age (years)	Gender (M/F)	DBP (BASELINE)	DBP (TR)	DBP (T0)	DBP (T1)	DBP (T2)	DBP (T3)	DBP (T4)	DBP (T5)	DBP (T7)	DBP (T10)
10055173	52	F	77	96	77	77	77	82	96	77	74	74
10053110	62	M	88	78	68	80	60	68	70	68	66	64
10054424	40	M	79	84	68	72	70	73	73	70	71	70
10053548	65	M	90	90	88	84	80	80	73	70	70	70
10054557	59	F	109	98	96	90	90	88	88	84	80	82
10053947	52	F	79	79	70	90	73	85	84	89	84	79
10053844	52	F	97	77	78	84	84	80	76	78	82	80
10000686	19	F	80	80	82	82	82	82	78	76	78	74
10001926	30	M	80	76	70	72	72	74	72	70	72	20
10008860	30	F	88	84	86	82	82	80	75	70	66	70
10009130	42	F	80	88	110	84	96	90	94	90	92	86
10009776	38	M	70	83	85	80	80	82	78	80	80	80
10007798	70	M	102	104	100	82	86	88	86	86	84	82
10014128	66	M	108	111	88	89	80	73	70	75	74	72
10011205	35	F	93	102	84	67	79	74	70	73	76	72
10012437	37	F	90	100	90	80	92	82	82	80	80	76
10020674	45	F	82	100	90	88	88	86	86	86	84	80
10012707	27	F	100	99	101	95	84	87	84	80	82	78
10033524	50	F	79	94	92	67	65	68	70	70	66	60
10055566	43	F	105	137	101	83	80	82	86	90	88	90
10056068	35	F	94	73	102	90	99	99	98	94	92	92
10056117	52	F	88	87	88	82	81	76	74	72	70	70
10072346	21	F	92	90	88	73	77	76	67	67	66	72
10063204	25	M	100	102	98	88	63	63	60	66	68	70
10066388	46	M	115	96	97	86	88	86	88	88	80	76
10066637	51	M	100	103	88	86	70	80	81	90	77	81
10069429	18	F	71	68	79	70	63	62	61	57	60	60
10067739	58	M	106	122	127	110	104	88	84	89	83	87
10069261	46	F	112	104	95	89	83	80	80	79	79	80
10067898	43	M	95	80	84	79	85	79	80	80	80	75
10071833	40	F	88	108	101	96	98	89	89	67	58	57
10070271	36	M	112	93	88	82	84	79	79	80	82	77
10071840	28	F	93	99	84	88	86	88	88	87	84	80
10070893	46	M	115	92	89	64	74	72	83	82	82	80
10071063	46	F	92	91	65	83	77	77	72	73	76	73
10070961	31	F	115	107	104	81	69	74	74	74	73	70
10071105	35	F	77	74	83	74	74	71	60	68	66	60
10072516	19	F	112	113	100	103	96	94	92	95	87	87
10072325	26	F	78	72	88	90	83	84	83	69	61	58
10072672	50	F	111	95	95	81	81	80	82	78	81	78
10072814	44	F	90	89	77	77	76	78	76	76	76	74
10072115	24	M	96	96	92	80	76	70	75	59	69	76

IP NO	Age (years)	Gender (M/F)	MAP (BASELINE)	MAP (TR)	MAP (T0)	MAP (T1)	MAP (T2)	MAP (T3)	MAP (T4)	MAP (T5)	MAP (T7)	MAP (T10)
10055173	52	F	96	109	95	83	82	117	106	92	89	89
10053110	62	M	100	92	80	86	76	82	83	81	79	79
10054424	40	M	102	103	91	98	77	76	80	80	83	85
10053548	65	M	113	113	109	105	101	93	80	92	80	89
10054557	59	F	136	100	117	110	106	105	104	102	97	98
10053947	52	F	111	114	95	108	83	91	91	98	93	86
10053844	52	F	128	110	101	113	101	97	93	93	97	97
10000686	19	F	96	95	96	96	95	95	92	89	91	87
10001926	30	M	92	89	82	84	84	85	82	82	81	80
10008860	30	F	101	96	97	93	93	92	88	82	81	82
10009130	42	F	96	106	132	108	111	104	100	100	105	92
10009776	38	M	83	98	102	95	92	95	94	93	93	90
10007798	70	M	122	125	121	102	106	102	100	99	99	96
10014128	66	M	122	132	105	105	94	87	85	83	85	83
10011205	35	F	113	12	99	93	81	76	76	84	85	81
10012437	37	F	99	121	105	96	110	98	98	95	93	93
10020674	45	F	90	111	102	101	101	99	99	97	96	93
10012707	27	F	111	115	112	108	89	99	96	94	95	91
10033524	50	F	102	128	128	96	90	81	95	88	86	81
10055566	43	F	127	154	124	110	109	110	111	107	105	105
10056068	35	F	111	110	127	114	108	104	102	100	98	98
10056117	52	F	111	112	109	102	86	86	81	75	87	86
10072346	21	F	104	102	100	87	84	83	80	77	76	78
10063204	25	M	117	117	111	104	82	81	81	85	86	89
10066388	46	M	128	108	110	100	102	101	102	101	95	92
10066637	51	M	113	118	104	99	81	95	92	103	88	95
10069429	18	F	84	82	92	84	75	76	74	70	72	71
10067739	58	M	121	136	141	126	121	106	105	105	97	96
10069261	46	F	129	120	109	103	99	97	96	95	95	93
10067898	43	M	101	91	98	97	100	100	97	101	95	91
10071833	40	F	112	122	111	113	108	102	97	89	80	71
10070271	36	M	125	111	100	97	91	94	93	97	99	94
10071840	28	F	103	107	96	100	98	99	100	99	98	97
10070893	46	M	129	109	97	85	94	87	96	95	94	92
10071063	46	F	102	99	79	96	89	89	87	88	90	85
10070961	31	F	126	117	117	94	91	90	90	89	88	86
10071105	35	F	89	83	97	85	83	85	77	83	82	77
10072516	19	F	127	125	111	114	108	106	105	108	101	99
10072325	26	F	98	93	102	104	96	94	95	84	76	74
10072672	50	F	123	110	108	95	91	90	91	89	91	87
10072814	44	F	107	106	95	71	94	94	93	90	90	88
10072115	24	M	107	108	103	92	84	84	89	87	81	84

IP NO	Age (years)	Gender (M/F)	SP02 (BASELINE)	SPO 2 (TR)	SPO 2 (T0)	SPO 2 (T1)	SPO 2 (T2)	SPO 2 (T3)	SPO 2 (T4)	SPO 2 (T5)	SPO 2 (T7)	SPO 2 (T10)	TIME OF EXTUBATION
10055173	52	F	99	100	99	100	100	100	100	100	100	100	T2
10053110	62	M	100	100	100	100	100	100	100	100	100	100	T1
10054424	40	M	100	100	100	100	100	100	100	100	100	100	T1
10053548	65	M	100	100	100	100	100	100	100	100	100	100	T2
10054557	59	F	100	100	100	100	100	100	100	100	100	100	T1
10053947	52	F	100	100	100	100	100	100	100	100	100	100	T1
10053844	52	F	100	100	100	100	100	100	100	100	100	100	T1
10000686	19	F	100	100	100	100	100	100	100	100	100	100	T1
10001926	30	M	100	100	100	100	100	100	100	100	100	100	T1
10008860	30	F	100	100	100	100	100	100	100	100	100	100	T1
10009130	42	F	100	100	100	100	100	100	100	100	100	100	T1
10009776	38	M	100	100	100	100	100	100	100	100	100	100	T1
10007798	70	M	100	100	100	100	100	100	100	100	100	100	T2
10014128	66	M	100	100	100	100	100	100	100	100	100	100	T1
10011205	35	F	100	100	100	100	100	100	100	100	100	100	T1
10012437	37	F	100	100	100	100	100	100	100	100	100	100	T2
10020674	45	F	100	100	100	100	100	100	100	100	100	100	T1
10012707	27	F	100	100	100	100	100	100	100	100	100	100	T1
10033524	50	F	100	100	100	100	100	100	100	100	100	100	T1
10055566	43	F	100	100	100	100	100	100	100	100	100	100	T1
10056068	35	F	100	100	100	100	100	100	100	100	100	100	T1
10056117	52	F	100	100	100	100	100	100	100	100	100	100	T1
10072346	21	F	100	100	100	100	100	100	100	100	100	100	T1
10063204	25	M	100	100	100	100	100	100	100	100	100	100	T1
10066388	46	M	100	100	100	100	100	100	100	100	100	100	T1
10066637	51	M	100	100	100	100	100	100	100	100	100	100	T1
10069429	18	F	100	100	100	100	100	100	100	100	100	100	T1
10067739	58	M	100	100	100	100	100	100	100	100	100	100	T1
10069261	46	F	100	100	100	100	100	100	100	100	100	100	T1
10067898	43	M	100	100	100	100	100	100	100	100	100	100	T1
10071833	40	F	100	100	100	100	100	100	100	100	100	100	T1
10070271	36	M	100	100	100	100	100	100	100	100	100	100	T2
10071840	28	F	100	100	100	100	100	100	100	100	100	100	T1
10070893	46	M	100	100	100	100	100	100	100	100	100	100	T1
10071063	46	F	100	100	100	100	100	100	100	100	100	100	T1
10070961	31	F	100	100	100	100	100	100	100	100	100	100	T1
10071105	35	F	100	100	100	100	100	100	100	100	100	100	T1
10072516	19	F	100	100	100	100	100	100	100	100	100	100	T1
10072325	26	F	100	100	100	100	100	100	100	100	100	100	T1
10072672	50	F	100	100	100	100	100	100	100	100	100	100	T1
10072814	44	F	100	100	100	100	100	100	100	100	100	100	T1
10072115	24	M	100	100	100	100	100	100	100	100	100	100	T1

ANNEXURE IV : MASTER CHART

Group 2

IP NO	Age (years)	Gender (M/F)	HR (BASELINE)	HR (TR)	HR (T0)	HR(T1)	HR(T2)	HR (T3)	HR (T4)	HR (T5)	HR (T7)	HR (T10)
10003746	25	M	71	65	61	65	64	67	79	75	71	79
10004017	50	M	83	99	99	80	83	82	79	74	70	62
10002491	55	M	79	76	78	76	76	74	75	79	80	83
10012426	40	M	92	98	101	112	108	87	90	88	84	92
10012201	43	F	82	118	115	96	84	85	78	70	76	75
10102836	65	M	100	110	110	99	100	111	98	110	106	108
10103541	65	M	110	103	102	112	108	100	100	98	106	102
10065532	40	M	86	73	71	71	86	88	88	85	84	89
10037611	37	F	60	58	102	96	93	99	91	112	109	109
10062151	34	F	112	126	124	120	119	114	112	108	96	96
10061821	30	M	116	124	120	119	116	118	109	108	102	96
10060102	40	F	96	102	97	94	92	94	90	86	88	80
10070313	63	F	75	78	72	71	75	73	74	73	73	75
10073063	41	F	79	82	85	86	85	79	80	76	77	79
10073844	44	F	88	118	115	96	84	85	78	70	76	75
10100975	54	M	118	115	96	98	94	96	92	98	99	99
10101593	53	F	95	99	82	81	85	90	97	96	89	86
10078658	66	M	108	106	100	99	95	91	91	91	91	90
10105687	44	M	90	100	110	108	104	104	102	100	108	106
10104733	45	M	108	106	100	99	95	91	91	91	91	90
10105246	60	F	88	98	94	96	90	92	88	94	96	99
10101582	59	F	96	102	97	94	92	94	90	86	88	80
10102834	53	M	116	124	120	119	118	115	116	110	114	112
10103239	46	M	71	65	61	65	64	67	79	75	71	79
10100464	41	M	112	126	124	120	119	112	108	98	98	99
10102929	36	M	65	61	64	67	79	71	74	76	74	76
10102706	21	F	108	102	103	99	96	98	99	100	96	95
10103619	56	F	98	102	100	99	98	101	97	97	95	92
10010046	41	M	87	90	92	89	89	101	96	97	96	100
10101709	51	F	101	102	100	99	98	99	97	98	96	99
10108265	45	M	78	77	76	75	77	78	77	74	78	79
10104825	35	F	118	117	116	112	115	114	113	110	98	100
10105451	58	F	111	112	110	109	106	108	107	104	108	102
10101146	28	M	90	92	88	88	87	87	86	86	84	82
10101060	65	M	120	118	122	124	126	124	122	126	124	130
10101734	18	F	98	96	98	100	102	101	103	100	98	106
10101456	31	F	130	130	132	134	136	136	134	137	134	138
10102506	46	F	78	78	76	78	74	78	77	80	84	86
10103110	40	M	98	96	98	100	102	98	98	97	96	100
10102749	50	M	130	128	128	126	124	122	122	124	126	128
10103596	22	M	98	99	98	98	96	96	94	98	98	98
10101710	40	M	98	96	97	94	97	94	90	93	93	103

IP NO	Age (years)	Gender (M/F)	SBP (BASELINE)	SBP (TR)	SBP (T0)	SBP (T1)	SBP (T2)	SBP (T3)	SBP (T4)	SBP (T5)	SBP (T7)	SBP2
10003746	25	M	130	132	136	144	146	146	150	148	148	152
10004017	50	M	182	168	162	128	132	138	142	148	148	140
10002491	55	M	138	140	144	142	146	144	148	148	146	150
10012426	40	M	164	118	148	150	150	130	146	144	150	146
10012201	43	F	132	120	134	141	134	148	154	140	142	146
10102836	65	M	150	165	164	171	172	160	172	172	168	166
10103541	65	M	144	143	145	145	144	140	140	138	140	142
10065532	40	M	144	142	146	147	142	138	145	139	142	158
10037611	37	F	106	105	153	151	148	144	147	137	139	143
10062151	34	F	130	130	130	128	128	127	120	120	116	114
10061821	30	M	92	130	130	128	128	126	126	120	120	116
10060102	40	F	130	128	128	126	126	120	120	118	114	114
10070313	63	F	151	159	150	158	170	152	151	158	170	168
10073063	41	F	109	127	130	124	113	110	108	123	124	126
10073844	44	F	130	132	136	144	146	150	146	152	142	146
10100975	54	M	144	143	145	146	144	143	142	140	138	142
10101593	53	F	126	150	137	133	129	132	134	135	135	134
10078658	66	M	130	130	130	132	134	130	122	120	122	108
10105687	44	M	160	158	158	156	154	158	152	154	156	154
10104733	45	M	130	130	130	132	134	130	122	120	122	108
10105246	60	F	110	120	126	124	124	128	117	118	126	130
10101582	59	F	130	138	136	136	138	138	140	138	136	138
10102834	53	M	130	132	136	144	146	146	150	152	148	148
10103239	46	M	130	128	128	126	126	128	130	132	134	132
10100464	41	M	150	162	158	154	154	152	156	154	148	150
10102929	36	M	130	132	144	146	146	144	142	140	148	148
10102706	21	F	106	110	112	120	118	112	124	108	108	110
10103619	56	F	140	153	147	137	144	146	140	142	140	142
10010046	41	M	140	142	140	138	136	136	138	137	138	139
10101709	51	F	110	118	116	118	120	116	116	116	117	120
10108265	45	M	130	132	128	130	127	126	130	128	132	128
10104825	35	F	140	138	138	138	136	140	142	138	137	136
10105451	58	F	130	130	132	130	128	128	127	128	130	128
10101146	28	M	140	138	138	137	136	136	138	138	137	137
10101060	65	M	140	142	146	144	144	146	144	146	148	150
10101734	18	F	120	118	118	122	122	124	120	122	124	126
10101456	31	F	138	140	142	144	146	148	148	146	144	146
10102506	46	F	128	128	130	134	134	134	132	132	132	132
10103110	40	M	128	128	130	130	134	132	132	134	132	134
10102749	50	M	138	139	140	142	142	144	144	142	140	143
10103596	22	M	126	126	128	128	130	132	132	130	130	132
10101710	40	M	146	120	101	105	124	119	124	132	130	141

IP NO	Age (years)	Gender (M/F)	DBP (BASELINE)	DBP (TR)	DBP (T0)	DBP (T1)	DBP (T2)	DBP (T3)	DBP (T4)	DBP (T5)	DBP (T7)	DBP (T10)
10003746	25	M	82	88	90	98	96	96	92	92	96	98
10004017	50	M	110	114	108	90	96	96	94	100	94	90
10002491	55	M	84	86	86	84	82	80	82	80	82	88
10012426	40	M	100	84	96	100	100	83	87	90	92	92
10012201	43	F	85	85	89	92	90	96	78	70	74	72
10102836	65	M	90	118	115	115	110	100	98	98	102	100
10103541	65	M	100	85	69	72	70	78	82	82	84	80
10065532	40	M	100	91	93	96	88	88	90	89	96	97
10037611	37	F	74	77	112	108	103	108	101	105	96	102
10062151	34	F	90	86	84	82	84	82	78	74	74	70
10061821	30	M	86	84	82	84	82	80	78	76	76	101
10060102	40	F	80	80	80	80	76	78	78	76	74	74
10070313	63	F	88	73	75	60	65	59	66	73	64	76
10073063	41	F	83	89	96	77	72	69	69	75	78	73
10073844	44	F	100	85	93	96	99	88	89	90	90	90
10100975	54	M	108	110	100	100	99	97	98	102	100	99
10101593	53	F	82	103	80	76	76	78	77	77	80	80
10078658	66	M	96	96	92	94	92	92	84	85	79	78
10105687	44	M	99	99	98	98	98	96	98	94	96	94
10104733	45	M	96	96	92	94	92	92	84	85	79	78
10105246	60	F	80	88	86	84	86	84	80	82	80	80
10101582	59	F	92	94	96	96	98	94	99	92	94	92
10102834	53	M	90	92	88	88	86	88	84	86	88	86
10103239	46	M	88	88	82	86	84	88	80	80	82	84
10100464	41	M	90	92	88	86	88	86	84	88	86	86
10102929	36	M	78	76	80	82	88	84	80	80	82	80
10102706	21	F	80	80	82	87	80	78	76	74	78	80
10103619	56	F	74	77	72	70	70	68	72	74	77	70
10010046	41	M	100	100	101	102	99	99	99	98	100	104
10101709	51	F	70	78	90	87	88	88	88	87	89	88
10108265	45	M	90	88	90	88	86	88	92	84	88	88
10104825	35	F	102	102	100	99	98	99	97	98	96	94
10105451	58	F	110	108	110	106	106	104	104	106	108	106
10101146	28	M	98	98	97	96	96	95	98	96	97	100
10101060	65	M	118	118	117	116	116	110	108	108	110	110
10101734	18	F	80	82	80	80	78	84	82	84	88	86
10101456	31	F	98	98	96	98	100	100	96	98	111	112
10102506	46	F	88	88	88	89	90	92	94	96	98	96
10103110	40	M	92	92	90	94	94	92	94	96	92	94
10102749	50	M	96	96	98	98	94	94	96	98	98	96
10103596	22	M	98	99	99	98	97	96	96	98	99	99
10101710	40	M	101	76	67	67	90	84	96	95	97	97

IP NO	Age (years)	Gender (M/F)	MAP (BASELINE)	MAP (TR)	MAP (T0)	MAP (T1)	MAP (T2)	MAP (T3)	MAP (T4)	MAP (T5)	MAP (T7)	MAP (T10)
10003746	25	M	98	103	105	113	112	112	111	110	113	116
10004017	50	M	133	133	126	103	108	110	110	116	112	106
10002491	55	M	102	104	105	103	103	101	104	102	103	108
10012426	40	M	121	95	113	117	117	100	107	90	111	110
10012201	43	F	101	97	104	108	105	113	103	94	97	97
10102836	65	M	110	134	131	134	131	120	123	123	124	122
10103541	65	M	114	104	94	96	95	99	101	101	103	101
10065532	40	M	115	108	111	113	106	105	108	106	111	117
10037611	37	F	84	86	125	122	118	120	117	117	111	118
10062151	34	F	92	90	88	86	87	97	92	89	88	87
10061821	30	M	101	99	99	99	97	95	93	92	91	89
10060102	40	F	97	96	94	95	93	92	92	90	87	87
10070313	63	F	109	103	100	93	100	90	94	101	99	107
10073063	41	F	91	101	107	91	85	81	82	94	94	91
10073844	44	F	110	101	107	112	115	109	108	111	107	109
10100975	54	M	120	121	115	115	114	112	113	115	113	113
10101593	53	F	93	117	99	96	94	98	96	98	98	98
10078658	66	M	107	107	105	107	106	90	98	97	91	85
10105687	44	M	119	119	118	117	117	117	116	114	116	114
10104733	45	M	107	107	105	107	106	90	98	97	91	85
10105246	60	F	96	99	99	97	99	99	92	94	95	97
10101582	59	F	105	109	109	109	111	109	113	107	108	107
10102834	53	M	103	105	104	107	106	107	106	108	108	107
10103239	46	M	102	101	97	99	98	101	97	97	99	100
10100464	41	M	110	115	111	109	110	108	108	110	107	107
10102929	36	M	95	95	101	103	107	104	101	100	104	103
10102706	21	F	89	90	92	98	93	89	92	85	88	90
10103619	56	F	96	102	97	92	95	94	95	97	98	94
10010046	41	M	113	114	114	114	111	111	112	111	113	116
10101709	51	F	83	91	99	97	99	97	97	96	98	99
10108265	45	M	103	103	103	102	100	101	105	99	103	101
10104825	35	F	115	114	113	112	111	113	112	111	110	108
10105451	58	F	117	115	117	114	113	112	112	113	115	113
10101146	28	M	112	111	111	110	109	109	111	110	110	112
10101060	65	M	125	126	127	125	125	122	120	121	123	123
10101734	18	F	93	94	93	94	93	97	95	97	100	99
10101456	31	F	111	112	111	113	115	115	116	115	112	114
10102506	46	F	101	101	102	104	105	106	107	108	109	108
10103110	40	M	104	104	103	106	107	105	107	109	105	107
10102749	50	M	110	110	112	113	110	111	112	113	112	112
10103596	22	M	107	108	109	108	108	108	108	109	109	110
10101710	40	M	115	90	81	82	105	96	105	96	105	109

IP NO	Age (years)	Gender (M/F)	SP02 (BASELINE)	SPO2 (TR)	SPO2 (T0)	SPO2 (T1)	SPO2 (T2)	SPO2 (T3)	SPO2 (T4)	SPO2 (T5)	SPO2 (T7)	SPO2 (T10)	TIME OF EXTUBATION
10003746	25	M	100	100	100	100	100	100	100	100	100	100	T1
10004017	50	M	100	100	100	100	100	100	100	100	100	100	T1
10002491	55	M	100	100	100	100	100	100	100	100	100	100	T1
10012426	40	M	100	100	100	100	100	100	100	100	100	100	T1
10012201	43	F	100	100	100	100	100	100	100	100	100	100	T1
10102836	65	M	100	100	100	100	100	100	100	100	100	100	T1
10103541	65	M	100	100	100	100	100	100	100	100	100	100	T1
10065532	40	M	100	100	100	100	100	100	100	100	100	100	T2
10037611	37	F	118	100	100	100	100	100	100	100	100	100	T2
10062151	34	F	100	100	100	100	100	100	100	100	100	100	T2
10061821	30	M	100	100	100	100	100	100	100	100	100	100	T1
10060102	40	F	100	100	100	100	100	100	100	100	100	100	T1
10070313	63	F	100	100	100	100	100	100	100	100	100	100	T1
10073063	41	F	100	100	100	100	100	100	100	100	100	100	T1
10073844	44	F	100	100	100	100	100	100	100	100	100	100	T1
10100975	54	M	100	100	100	100	100	100	100	100	100	100	T2
10101593	53	F	100	100	100	100	100	100	100	100	100	100	T1
10078658	66	M	100	100	100	100	100	100	100	100	100	100	T1
10105687	44	M	100	100	100	100	100	100	100	100	100	100	T2
10104733	45	M	100	100	100	100	100	100	100	100	100	100	T1
10105246	60	F	100	100	100	100	100	100	100	100	100	100	T1
10101582	59	F	100	100	100	100	100	100	100	100	100	100	T1
10102834	53	M	100	100	100	100	100	100	100	100	100	100	T1
10103239	46	M	100	100	100	100	100	100	100	100	100	100	T1
10100464	41	M	100	100	100	100	100	100	100	100	100	100	T1
10102929	36	M	100	100	100	100	100	100	100	100	100	100	T1
10102706	21	F	100	100	100	100	100	100	100	100	100	100	T2
10103619	56	F	100	100	100	100	100	100	100	100	100	100	T2
10010046	41	M	100	100	100	100	100	100	100	100	100	100	T1
10101709	51	F	100	100	100	100	100	100	100	100	100	100	T1
10108265	45	M	100	100	100	100	100	100	100	100	100	100	T2
10104825	35	F	100	100	100	100	100	100	100	100	100	100	T1
10105451	58	F	100	100	100	100	100	100	100	100	100	100	T1
10101146	28	M	100	100	100	100	100	100	100	100	100	100	T1
10101060	65	M	100	100	100	100	100	100	100	100	100	100	T1
10101734	18	F	100	100	100	100	100	100	100	100	100	100	T1
10101456	31	F	100	100	100	100	100	100	100	100	100	100	T1
10102506	46	F	100	100	100	100	100	100	100	100	100	100	T1
10103110	40	M	100	100	100	100	100	100	100	100	100	100	T1
10102749	50	M	100	100	100	100	100	100	100	100	100	100	T1
10103596	22	M	100	100	100	100	100	100	100	100	100	100	T1
10101710	40	M	100	100	100	100	100	100	100	100	100	100	T1