"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL"

By

REG NO. BA0120018

Dissertation

Submitted to the

KLE Academy of Higher Education & Research

(Deemed To Be University) Belagavi, Karnataka

In Partial Fulfillment

of the requirements for the degree of

M. D.

in

ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA

JUNE/JULY 2023

KLE Academy of Higher Education & Research
(Deemed To Be University) Belagavi, Karnataka

ENDORSEMENT BY THE HOD/PRINCIPAL/ HEAD OF THE INSTITUTION

This is to certify that the dissertation **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL"** is a bonafide research work done by **REG NO. BA0120018.**

Dr. RAJESH MANE M.D, DNB
Professor & Head
Department of Anaesthesiology,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date: 02/01/2023
Place: Belagavi

Dr. (Mrs) N.S. Mahantshetti MD(P[illegible])
Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

PRINCIPAL
J.N. Medical College,
BELAGAVI- 590 010

Date: 02/01/2023
Place: Belagavi

KAHER
J.N. MEDICAL COLLEGE
BELAGAVI

UNDER TAKING

I, **REG NO: BA0120018** hereby declare that the information and the data mentioned in my thesis entitled **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL"** belongs to me and is original.

I am aware of definition of plagiarism as detailed below:

- An act or 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 use 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 thesis prepared by me is 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: 02/01/2023

Place: Belagavi

Sushmitha. H. S.

REG NO. BA0120018

PLAGIARISM ACCEPTANCE LETTER

KLE
JAWAHARLAL NEHRU MEDICAL COLLEGE
(Recognized by Medical Council of India, New Delhi)
Accredited 'A+' Grade by NAAC (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA
0831 - 2471350 0831 - 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 12-12-2022.

ACCEPTANCE LETTER

The softcopy of thesis entitled: **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION – A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE: A ONE-YEAR HOSPITAL BASED DOUBLE 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 **05%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide.

KAHER BELAGAVI J.N. MEDICAL COLLEGE

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

To,
Reg. No. BA0120018,
Postgraduate Student,
2020-21 Batch,
Department of Anaesthesiology,
J. N. Medical College, Belagavi.

ETHICAL CLERANCE FORM

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to-be-University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : domc@jnmc.edu
Phone: (+ 91-0831) Office : 2472550
Principal: 2431701
Fax No. +91 (0831) - 2470759

Ref: MDC/DOME/ 9 7 **Date: 25/01/2021**

To

REG NO. BA0120018

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 **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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

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

54

LIST OF ABBREVIATIONS

HR	**-**	**Heart Rate**
SBP	**-**	**Systolic Blood Pressure**
DBP	**-**	**Diastolic Blood Pressure**
MAP	**-**	**Mean Arterial Pressure**
SpO2	**-**	**Percentage of oxygen saturation**
NS	**-**	**Normal Saline**
ECG	**-**	**Elecrocardiogram**
CXR	**-**	**Chest X- Ray**
NIBP	**-**	**Non Invasive Blood Pressure**
PACU	**-**	**Post Anaesthesia Care Unit**
ASA	**-**	**American Society of Anaesthesiologist**
S.D	**-**	**Standard Deviation**
mg	**-**	**milligram**
mcg	**-**	**microgram**
PR	**–**	**Pulse Rate**
BP	**-**	**Blood pressure**
RR	**–**	**Respiratory Rate**
Temp	**–**	**Temperature**
α	**-**	**Alpha**
β	**-**	**Beta**

ABSTRACT

INTRODUCTION:

Direct laryngoscopy and endotracheal intubation following induction of general anesthesia is associated with hemodynamic variations due to reflex sympathetic discharge. Transient hypertension and tachycardia are probably of no consequence in healthy individuals, but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular diseases. A variety of drugs have been used to control this hemodynamic response, such as lignocaine, magnesium sulphate, vasodilators, beta blockers, calcium channel blockers, alfa 2 agonists and opioids.

OBJECTIVES:

Comparison of intranasal dexmedetomidine with intravenous preservative free lignocaine to attenuate stress response to laryngoscopy and endotracheal intubation with respect to hemodynamic variables like Mean arterial pressure, Systolic blood pressure, Diastolic blood pressure & Heart rate and to see the side effects if any.

METHODOLOGY:

Present study was performed on patients aged 18-60 years, of either gender, belonging to ASA grade I and II, undergoing elective surgery in supine position under general anesthesia with tracheal intubationl at KLE'S Dr.Prabhakar Kore hospital. Nehru Nagar, Belagavi between January 2021 to March 2022. A total of 82 patients were divided into two equal groups randomly using a computer generated table. Group A received preservative free IV lignocaine 1.5mg/kg 3mins prior to intubation and Group B received 1mcg/kg of dexmedetomidine intranasal 30mins before intubation. Hemodynamic parameters (MAP, SBP, DBP and HR) were recorded following administration of intranasal drug every 10mins till the patient was shifted inside operation theatre and again at the time of intubation, every minute for the first 5 minutes, at 7th minute and at 10th minute after intubation.

RESULTS:

It was observed that attenuation of hemodynamic response to laryngoscopy and intubation as evidenced by changes in SBP.DBP, MAP and HR was seen in both the groups but statistically significant attenuation was noted in Dexmedetomidine group when compared to Lignocaine group.

CONCLUSION:

Intranasal dexmedetomidine 1mcg/kg is effective in attenuating stress response to laryngoscopy and intubation plus it is easy to administer and devoid of any side effects.

KEYWORDS:

General anaesthesia, Laryngoscopy, Pressor response to intubation, Intranasal dexmedetomidine.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

INTRODUCTION

Direct laryngoscopy and endotracheal intubation following induction of general anaesthesia is associated with hemodynamic variations due to reflex sympathetic discharge because of epi-pharyngeal and laryngopharyngeal stimulation. This increased sympatho - adrenal activity may result in transient, variable and unpredictable hypertension, tachycardia and arrhythmias. [1],[2] .

This transient rise in Blood pressure and heart rate could be harmful in patients with pre-existing cardiovascular[4] and cerebrovascular diseases. [5] Hence it is vital to attenuate this response.

With increasing force as well as duration of laryngoscopy the magnitude of stressor response increases. [6] Following laryngoscopy the arterial pressure raises within five seconds, peaks in 1-2 min and returns to baseline within 5 min. It was Reid and Brace in 1940 who reported the circulatory responses to endotracheal intubation for the first time. [7]

A variety of drugs have been used to attenuate this hemodynamic response such as intravenous preservative free lignocaine, IV magnesium sulphate, vasodilators like nitroglycerine, IV beta blockers like esmolol, labetalol and metoprolol, calcium channel blockers like IV nifedipine, alfa 2 agonists like clonidine IV and dexmedetomidine IV and opioids like IV fentanyl. However, no modality is devoid of limitations.

Lignocaine, introduced in the year 1948 is an amino-ethyl-amide, is the most cheapest, easily available and most widely used local anesthetic even today. In 1961, Bromage showed that its intravenous (IV) administration in the dose of 1.5mg/kg given 3 minutes before intubation blunted the stressor response to intubation.[8]

Dexmedetomidine is an adrenergic agonist at alpha 2 receptor. It has sedative, anxiolytic and analgesic effects, decreases the doses of intravenous anaesthetics, opioids and inhalational agents for induction and maintenance of anaesthesia. Also, it has been shown to decrease perioperative catecholamine concentrations and maintain perioperative hemodynamic and adrenergic stability.

There are various routes by which dexmedetomidine can be administered. The drawbacks of intravenous use is sedation, profound bradycardia and hypotension. The drug when administered through intranasal route penetrates the blood-brain barrier & reaches the CNS directly and is practical because it doesn't cause any pain, has no flavour or smell, and doesn't require intravenous infusion. Dexmedetomidine can access the systemic circulation quickly and avoid the liver's first pass metabolism due to the nasal mucosa's improved vascularity.[9]

Since intranasal dexmedetomidine is a new route recommended for administration, we are comparing its efficacy with more commonly used intravenous preservative free lignocaine for reducing the hemodynamic reaction to intubation and laryngoscopy.

OBJECTIVES

Primary objective:

Comparison of intranasal dexmedetomidine with intravenous preservative free lignocaine for attenuation of stress response to laryngoscopy and endotracheal intubation with respect to hemodynamic variables like Mean arterial pressure, Systolic blood pressure, Diastolic blood pressure & Heart rate.

Secondary objective:

To determine the side effects if any.

BASIC SCIENCES

Endotracheal intubation is a medical procedure in which a tube is placed into the trachea through the mouth or nose. This procedure involves laryngoscopy to aid for the placement of the tube inside the larynx and trachea.

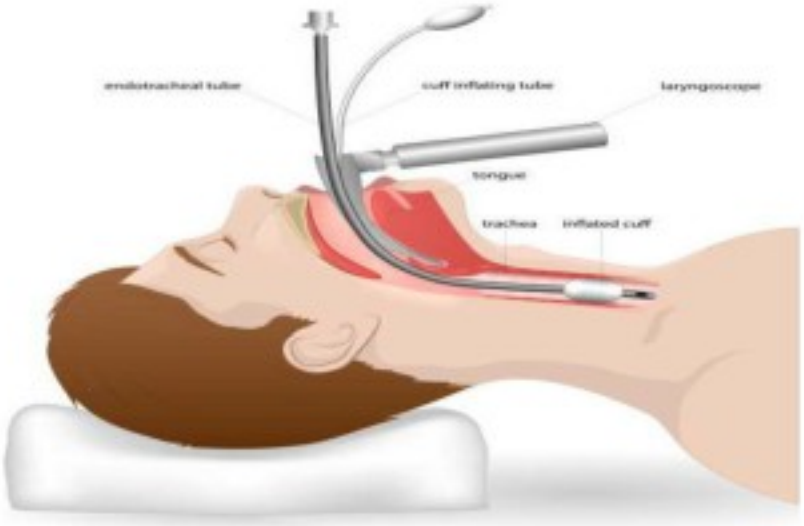


Fig-1 Endotracheal Intubation

The larynx is located within the anterior aspect of the neck, anterior to the inferior portion of the pharynx and superior to the trachea. Its primary function is to protect the lower airway by closing abruptly upon mechanical stimulation, thereby halting respiration and preventing the entry of foreign matter into the airway. Other functions of the larynx include the production of sound (phonation), coughing, the Valsalva maneuver, control of ventilation and acting as a sensory organ.

The larynx is composed of 3 large, unpaired cartilages (cricoid, thyroid, epiglottis); 3 pairs of smaller cartilages (arytenoids, corniculate, cuneiform); and a number of intrinsic muscles (see the image and video below). The hyoid bone, while technically not part of the larynx, provides muscular attachments from above that aid in laryngeal motion.

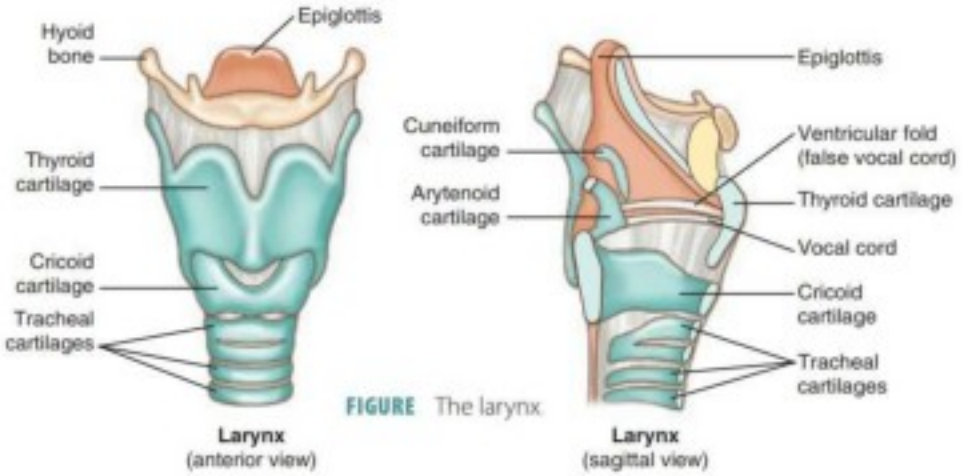


FIGURE The larynx

Fig. 2 Anatomy of Larynx

Pharynx is supplied by branches of glossopharyngeal and vagus nerve. Larynx is supplied by branches of vagus nerve – both sensory and motor components. The right recurrent laryngeal nerve ascends on the contralateral side in the groove of the trachea and oesophagus. Both recurrent laryngeal nerves supply parasympathetic (secretory glands), sensation and motor innervation to the trachea.

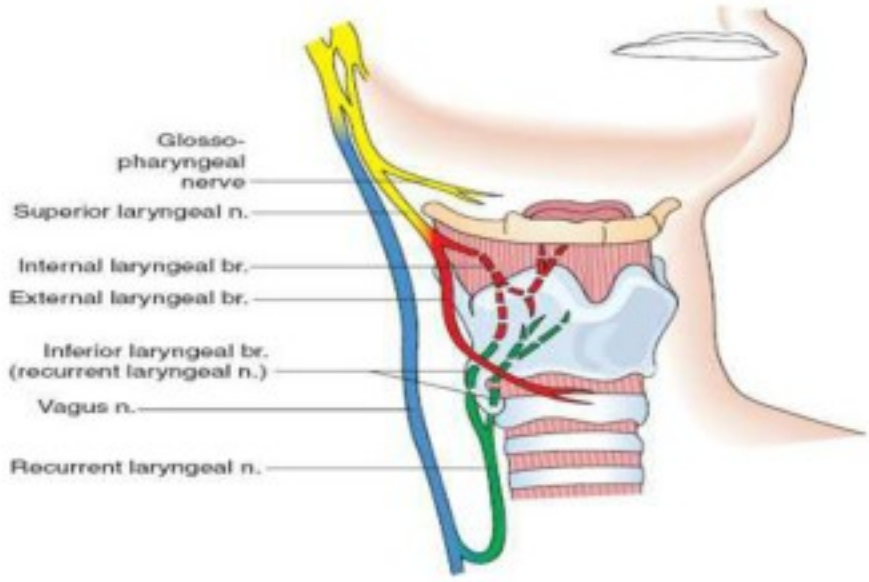


Fig. 3 Branches of Vagus Nerve

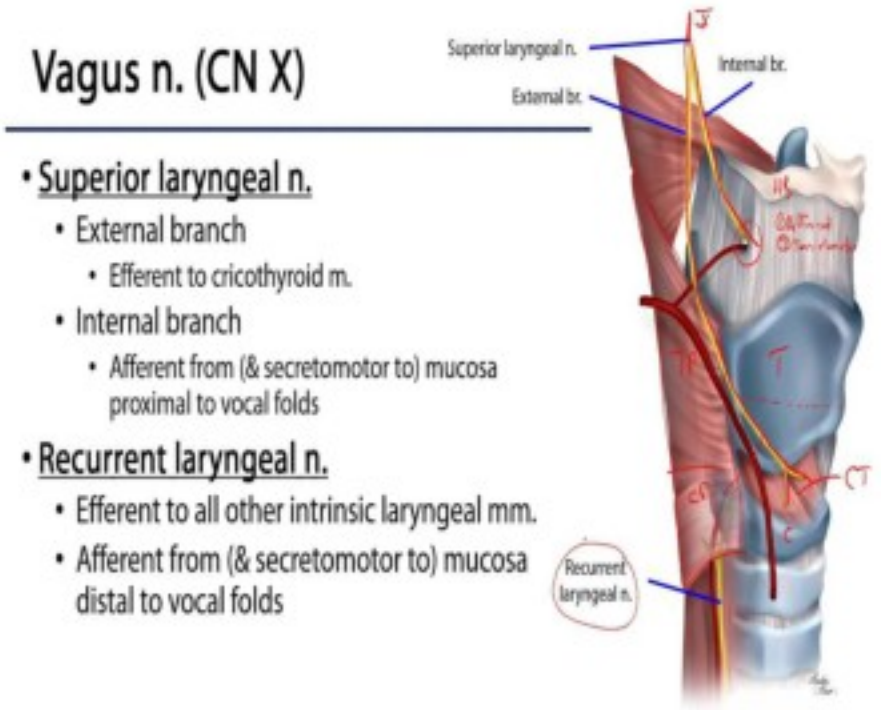


Fig. 4 Branches of Vagus Nerve in larynx

Induction of general anaesthesia, direct laryngoscopy and tracheal intubation induces marked cardiovascular changes as well as autonomic reflex activity. Although the responses of blood pressure and heart rate are short lived, they might have detrimental effects in high risk patients, especially those with cardiovascular disease[18]. Mechanism of cardiovascular response to intubation is considered to be a reflex sympathetic response to the mechanical stimulation of larynx and trachea. These cardiovascular responses are associated with increased plasma levels of catecholamines[19]. The main reason for the intubation induced hypertension seems to be release of noradrenaline and, to a lesser extent, of adrenaline. In addition, increased levels of adrenocorticotrophic hormone (ACTH) and dopamine have also been reported[20].

A variety of factors have been shown to have an effect on this stress response:

1) The choice and dosages of premedication and induction agents

2) The skill of the operator and

3) The technique used[21]

Dexmedetomidine is a highly selective α2 adrenergic agonist. It acts through three types of α2 receptors-α2 A, α2 B and α2 C situated in brain and spinal cord. The resultant action is sedation, anxiolysis, analgesia and sympatholysis, the latter leading to hypotension and bradycardia. Activation of α2 A receptors in brainstem vasomotor centre results in suppression of norepinephrine release causing hypotension and bradycardia. Stimulation of α2 A and α2 C in locus ceruleus causes sedation. In the spinal cord, activation of both α2 A and α2 C receptors directly reduce pain transmission by reducing release of substance P.

IV Dexmedetomidine has been used in infusion form with or without bolus dose. Infusion rates varying from 0.1 to 10 mcg/kg/hr[22,23,24] have been studied. However, with higher dose infusion of dexmedetomidine, high incidence of adverse cardiac effects have been observed[25]. A biphasic response on blood pressure occurs with a bolus dose. Initially there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients. Stimulation of α2 B receptors in vascular smooth muscles is said to be responsible for this. Low dose infusion of 0.25–0.5 mcg/kg/h results in a monophasic response of 10–15% fall in mean arterial blood pressure and pulse rate[26]. Furthermore, in low dose, dexmedetomidine exhibits linear kinetics, meaning that a constant amount of drug is eliminated per hour rather than a constant fraction of drug.

Dexmedetomidine, a centrally acting α2agonists, is widely used in the intensive care unit for its unique sedative, hypnotic, anxiolytic, sympatholytic,

antisecretory and analgesic properties. It has unique pharmacological property of conscious sedation and is devoid of any respiratory depression. It is responsible for producing dose dependant co-operative sedation that allows early interaction and early postoperative neurological assessment[27]. Dexmedetomidine also has a reversal drug for its sedative effect called as atipamizole, which acts by increasing the central turnover of noradrenaline[28,29]. Due to all of these specific characteristics, nowadays dexmedetomidine has become popular as an ideal premedication agent[30,31]

Fig.5. Dexmedetomidine Ampoule and Tuberculin Syringe

The main disadvantages of IV Dexmedetomidine, is that sedative action is more pronounced than analgesic effect with profound bradycardia and hypotension[32]. Moreover, rapid IV dexmedetomidine infusion may cause biphasic alteration of MAP which is undesirable in anaesthesia[33]. To minimise these adverse effects, alternative routes of dexmedetomidine are under trial.

Dexmedetomidine can be administered through various routes like intravenous, intramuscular, intranasal or intraoral [34]. The intranasal route is more convenient as it is painless, odourless and tasteless without need of any intravenous infusion. Intranasal drug can penetrate the blood–brain barrier and reach the central nervous system directly[35]. Due to the higher vascularity of the nasal mucosa, dexmedetomidine may access the systemic circulation rapidly, bypassing the first-pass metabolism of liver[36].

Lignocaine, commonly referred to as "Lidocaine", is an amide linked local anaesthetic agent and a Class 1b anti-arrhythmic. It is a stable, crystalline, colourless solid whose hydrochloride salt is water soluble[37]. Solutions for injection are available with or without adrenaline. All lignocaine solutions should be protected from light and maintained at a room temperature of approximately 25 degree Celsius or 77 degree Fahrenheit[38].

The mechanism of action of lignocaine for local or regional anesthesia is by reversible blockade of nerve fibre impulse propagation[39] by blocking the sodium channel from inner aspect of the cell membrane. An important indication for lignocaine use is for prophylaxis or treatment of life-threatening ventricular arrhythmias. The mechanism of action of lignocaine for its anti-arrhythmic action is by direct effect on mammalian Purkinje fibres. By decreasing the slope of phase 4 and changing the excitability threshold, lignocaine reduces automaticity[40] . This results in

a decrease of both the action potential length and the refractory period duration of the Purkinje fibres. The PR interval, QRS and QT durations are not commonly effected by lignocaine. Lignocaine also has anti-nociceptive and anti-inflammatory effects. Anti-nociceptive action is mediated by blockade of neuronal sodium channels and potassium currents[41] and the blockade of presynaptic muscarinic and dopamine receptors[42] while anti-inflammtory effect is mediated by blocking the release of interleukin-1 (IL-1), an inflammatory mediator acting on polymorphonuclear granulocytes, which in turn activates phagocytosis, respiratory burst, degranulation and chemotaxis.

FIG. 6 Preservative Free Lignocaine Vial

Lignocaine is dealkylated in the liver by the cytochrome P450 system forming numerous metabolites. Monoethylglycine xylidide and glycine xylidide are the key active metabolites, both of which have reduced potency but have comparable pharmacologic activity to lignocaine[41]. Hepatic blood flow appears to be a limiting factor in lignocaine's metabolism. The rate of metabolism is slower reduced in patients with congestive cardiac failure, chronic liver disease and hepatic insufficiency, and after acute myocardial infarction. Lignocaine and its metabolites are predominantly renally excreted. Less than 10% of lignocaine is excreted without being metabolised.

REVIEW OF LITERATURE

Direct laryngoscopy and intubation is the crucial moment in anesthetic practise which is associated with sympathoadrenal discharge leading to hypertension or tachycardia or both. The main objective of the study is to avoid these sequelae by comparing intranasal dexmedetomidine with the time tested and popularly used intravenous lignocaine.

In a study done by Tam S, Chung F, Campbell M[10] in 1987 for attenuation of hemodynamic response and optimal timing of injection of intravenous lignocaine before intubation published in the journal Anesthesia and Analgesia, found that IV lignocaine with a dose of 1.5mg/Kg 3mins before laryngoscopy and intubation was best in attenuating the hemodynamic response. Basically they studied the response to laryngoscopy by administering lignocaine in 4 groups with 14 patients in each group at 1, 2, 3 and 5 mins prior to laryngoscopy and concluded that IV lignocaine at 1.5mg/kg attenuates hemodynamic response only when given 3mins before intubation and offers no protection against post intubation hemodynamic changes when given at 1, 2 and 5mins before intubation.

Similar study was done by Wilson IG, Meiklejohn BH and Smith G[11] in 1991 to study the effect of lignocaine on hemodynamic response following laryngoscopy and intubation in 40 patients by giving 1.5mg/kg of IV lignocaine 2, 3 and 4mins prior to laryngoscopy and comparing with another group receiving placebo. They concluded that IV lignocaine 1.5mg/kg given at least 3mins prior to laryngoscopy and intubation completely attenuates pressor response but has no significant effect on heart rate.

Niyogi S et al[12] published an article in Indian journal of anesthesia in 2019 comparing the efficacy of intravenous versus intranasal dexmedetomidine in attenuating the hemodynamic response to laryngoscopy and intubation. They included total of 70 adult patients ASA1 and 2 in two groups. Group IV received IV dexmedetomidine at a dose of 0.5mcg/kg infusion over 40 mins prior to laryngoscopy and Group IN received intranasal dexmedetomidine 1mcg/kg in undiluted form 40mins before the laryngoscopy. They compared hemodynamic variables in both the groups and concluded that both intravenous and intranasal dexmedetomidine were equally effective in attenuating stress response to laryngoscopy and intubation.

In a similar study done by Singh G et al[13] in 2017 to compare the attenuation of hemodynamic response to laryngoscopy and intubation between dexmedetomidine and lignocaine, intravenous route was used for both the drugs. Basically they included 120 ASA 1 and 2 patients divided into three groups. Group A received 1.5mg/kg IV lignocaine 2mins prior to laryngoscopy and Group B received IV dexmedetomidine 1mcg/kg as infusion over 10mins before induction, while Group C was taken as control. They concluded that Dexmedetomidine 1 mcg/kg IV was more effective in blunting stress response to laryngoscopy and endotracheal intubation as compared to lignocaine 1.5 mg/kg IV.

Researchers Jayaraman L, Sinha A, and Punhani D[14] compared intranasal dexmedetomidine and oral alprazolam in patients who were morbidly obese and having bariatric surgery, as a premedication in a study that was completed and published in Journal of Anaesthesiology & Clinical Pharmacology in 2013. They divided the 40 individuals who were morbidly obese into two groups. Group Dex received 1mcg/kg of intranasal dexmedetomidine, while Group AZ were given 0.5mg of oral alprazolam. Both medications were given 45 minutes prior to laryngoscopy

and intubation. Sedation score and hemodynamic indicators were tracked in both groups. They found that, for sedation in morbidly obese patients, intranasal dexmedetomidine at a dose of 1 mcg/kg of ideal body weight performed better than oral alprazolam but was insufficient for reducing stress response to intubation. They also observed that intranasal dexmedetomidine was better tolerated without any nasal irritation or pain or change in smell or taste.

Prasad SR, Matam UM, Ojili GP[15] performed a study to compare intravenous lignocaine versus intravenous Dexmedetomidine to reduce the hemodynamic response to laryngoscopy and intubation in 2015. They included a total of 100 patients equally divided in two groups of ASA 1 and 2 status. Group L received 1.5mg/kg of lignocaine 3mins prior to laryngoscopy and Group D received intravenous dexmedetomidine 1mcg/kg bolus over 10mins infusion. Hemodynamic parameters was recorded in both the groups pre and post intubation and was compared. They found that IV dexmedetomidine was more efficacious than IV lignocaine in attenuating the pressor response to laryngoscopy and intubation. Also they found that dexmedetomidine reduced the induction dose of thiopentone sodium.

Kumari K, Gombar S, Kapoor D and Sandhu HS[16] did a study to evaluate the role of preoperative dexmedetomidine in attenuation of hemodynamic response to laryngoscopy and intubation in 2015 in 80 patients who were equally divided into two groups, group 1 received dexmedetomidine 0.5mcg/kg IV ten mins prior to intubation and the group 2 received normal saline. They discovered that a single 0.5 mcg/kg intravenous preinduction dosage of dexmedetomidine significantly attenuated the increase in heart rate, systolic blood pressure, diastolic blood pressure, and mean blood pressure during 5 minutes post-intubation. It also had few adverse effects and considerably lowered the dosage of propofol needed for induction.

Sebastian B, Talikoti AT and Krishnamurthy D[17] in 2017 performed a study to evaluate the optimal dose of IV dexmedetomidine to attenuate the hemodynamic response to laryngoscopy and intubation by using two different doses. They included a total of 90 patients and divided into three groups of 30 each. Group A were given normal saline, Group B IV dexmedetomidine 0.5mcg/kg over ten mins infusion and Group C were administred IV dexmedetomidine 0.75mcg/kg over ten mins infusion before induction. Hemodynamic parameters were recorded from all three groups and compared. They found that dexmedetomidine 0.75mcg/kg was optimal dosing for reduction of stress response to endotracheal intubation.

MATERIAL AND METHODS

Present study titled "Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation: A comparison between intranasal dexmedetomidine and intravenous preservative free lignocaine – A one year hospital based double blinded randomised clinical trial" conducted from January 2021 to March 2022, in the department of anaesthesia at KLE'S Dr. Prabhakar Kore Hospital in Belagavi.

Source of data:

Patients in the study were aged from 18 to 60 years, belonging to ASA I and II, undergoing elective surgery under general anesthesia with endo tracheal intubation in supine position in KLE's Dr Prabhakar kore's Charitable Hospital at Nehru Nagar, Belagavi between January 2021 to March 2022 were included.

Type of study:

Double blinded randomized clinical trial.

Study duration:

January 2021 to March 2022.

Criteria for selecting patients were:

Inclusion Criteria:

- Patients who provided consent.
- ASA I and II.
- Age - 18 to 60 years.
- Elective surgeries under general anaesthesia with endotracheal intubation.

Exclusion criteria

- Patient refusal or who are unable to give consent.
- ASA physical status III or more.
- Patients undergoing emergency surgery.
- Patients allergic to the drug under study.
- Patients with contraindication to general anaesthesia.
- Patients with significant cardiac and respiratory disease.
- Patients with difficult airway.
- Patients with nasal pathology.

Sample size calculation:

Based on standard deviation and mean the sample size would be

$$n = \frac{(Z_\alpha + Z_\beta)^2 (S_1^2 + S_2^2)}{(X1 - X2)^2}$$

The test's power is related to z_β, which is related to the level of significance, z_α.

For 80% power of test, z = 1.96

For 5% level of significance z = 0.84.

Referring to: X1 is the group 1 mean for MAP (88.10), and X2 is the group 2 mean (83.26).

S1 is the group 1 standard deviation (9.48), while S2 is the group 2 standard deviation (5.61).

From these values the sample size calculated was 82. There were two groups and each group had 41 cases.

Sampling procedure:

Randomisation was achieved by computer generated randomisation chart.

Methods:

A total of 82 patients undergoing elective surgery under general anaesthesia with endotracheal intubation were included in the study after receiving ethical committee permission and after providing written informed consent.

Once the inclusion and exclusion criteria were satisfied, patients were randomly assigned to one of the two groups using a computer-generated randomization table.

Group 1: Patients received 1.5 mg/kg of intravenous preservative free lignocaine.

Group 2: Patients received 1mcg/kg of intranasal dexmedetomidine.

Detailed pre anesthetic evaluation and routine investigations like complete blood picture, serum creatinine and random blood sugar levels were done. Chest X-ray and ECG were asked for patients over 40 years of age. All patients were kept nil per oral for atleast 6 hours and received tablet alprazolam (0.5mg) as premedication at night before surgery.

All the patients were shifted to the pre-operative room on the day of surgery, where baseline data were taken using routine monitors such as noninvasive blood pressure, electrocardiogram and pulse oximetry. IV ringers lactate as a maintenance fluid was administered using an 18G peripheral venous cannula.

Three minutes prior to intubation, group 1 patients were administered 1.5 mg/kg of preservative-free intravenous lignocaine and Group 2 received the same volume of saline intravenously.

Patients in group 2 received undiluted intranasal dexmedetomidine 1mcg/kg prepared from parenteral preparation (100mcg/ml) about 30 minutes prior to induction

using a 1ml tuberculin syringe, where the medication was dripped evenly into both nostrils keeping the patient in supine position. Group 1 received the same dosage of saline intranasally.

Hemodynamic parameters and Ramsay sedation score were recorded every ten minutes after the administration of the drug till the patient was shifted inside operation theatre.

Routine monitors were connected and baseline parameters were obtained once the patient was shifted inside the OT. Pre-medicated the patients with Inj. glycopyrrolate (0.005 mg/kg), Inj.midazolam (0.05 mg/kg) and Inj.fentanyl (2mcg/kg). The patients were induced with Inj. Propofol 2mg/kg IV and succinylcholine 2mg/kg after a 3-minute preoxygenation with 100% oxygen. Gentle laryngoscopy was done using Macintosh laryngoscope blade in one attempt and in less than 20 seconds and endotracheal intubation was performed using appropriate sized endotracheal tube.

Patients were excluded from the study if intubation was not possible in first attempt or took a long time to intubate. Hemodynamic variables (MAP, SBP, DBP and HR) were recorded at the time of intubation, every minute for the first 5 minutes, at 7th minute and at 10th minute after intubation. Anaesthesia was maintained with 50% O2-N2O, isoflurane 1-1.2 MAC and vecuronium 0.1mg/kg followed by intermittent topups of one-fourth the loading dose.

Once the surgery was completed Inj. glycopyrrolate 0.01mg/kg and Inj. neostigmine 0.05mg/kg were administered to reverse the neuromuscular blockade. Patients were extubated once the clinical criteria was met, in a 30 degree head end elevation and shifted to postoperative ward in recovery position.

Statistical analysis:

The study was focused on comparison of two groups.

For the continuous quantitative variables mean and standard deviation were calculated.

The student paired t test was used to compare two quantitative variables within the same group.

Suitable statistical procedures, such as the unpaired student's t test, were used to compare the continuous variables between groups.

Non-parametric tests were used to compare discrete variables, which were represented by medians.

Categorical data were expressed as rates, ratios, and percentages.

To examine whether there is a relationship between the outcome, clinical, and demographic factors, either the chi-square test or Fisher's exact test was applied.

To depict the comparison appropriate graphs were used.

P value of less than 5% (0.05) was considered significant for all the tests.

RESULTS

This research titled "**ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE & INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL**" was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Medical College, KAHER, Belagavi from January 2021 to March 2022. 82 patients were enrolled in the study after having met inclusion and exclusion criteria. Written informed consent in their own vernacular language was taken from the patients. Patients were randomized into two groups consisting of 41 patients in each group using computer generated randomization table.

The data was tabulated on Microsoft Excel sheet which was represented as Mean and Standard for all sets of data. To obtain the significance of study parameters on a continuous scale for Inter group analysis on metric parameter, Students unpaired "t" test was used.

To determine the categorical significance of study parameters between two or more groups - Chi-square/ Fisher Exact test" was used, Non parametric setting used for Qualitative data analysis.

Software: The statistical software namely "SPSS 22.0, and R environment ver.3.2.2" was used for data analysis.

Microsoft Excel and Word were used to generate Graphs and tables.

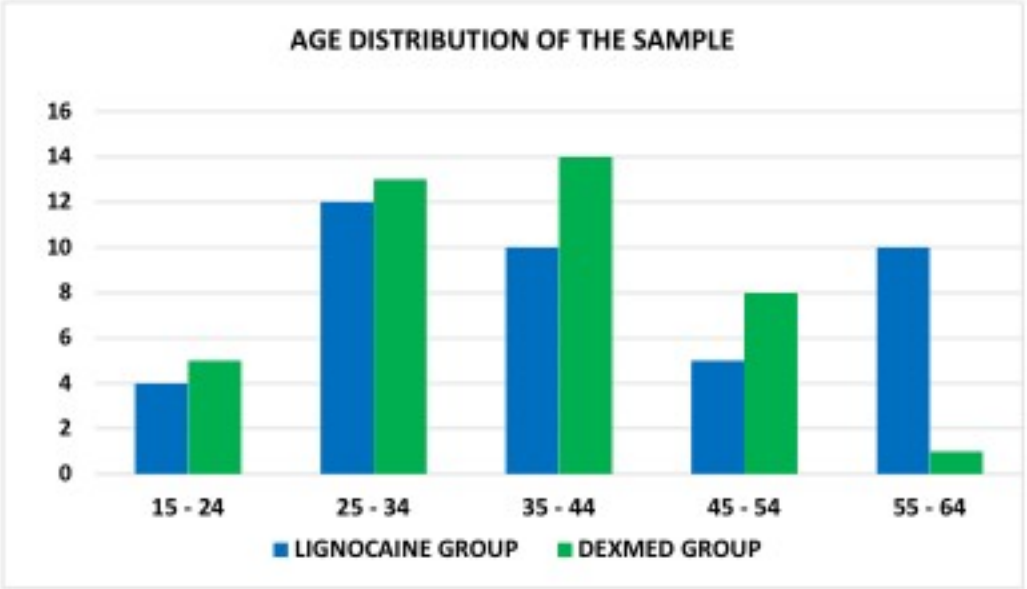
1. AGE DISTRIBUTION

	GROUP 1 LIGNOCAINE		GROUP 2 DEXMED	
AGE	**NUMBER**	**%**	**NUMBER**	**%**
18 - 24	4	9.76	5	12.20
25 - 34	12	29.27	13	31.71
35 - 44	10	24.39	14	34.15
45 - 54	5	12.20	8	19.51
55 - 60	10	24.39	1	2.44
TOTAL	41	100.00	41	100.00

Table 1. Mean Age Distribution of Group 1 and Group 2

The age distribution in each group is classified into 5 sub groups. From the above table we can see that in the age group of 18-24yrs, there were 4 patients in lignocaine group and 5 patients in dexmedetomidine group. There were 12 patients in 25-34yrs age group in lignocaine group and 13 patients in dexmedetomidine group. In 35-44yrs age group, 10 patients in lignocaine group and 14 in dexmedetomidine group were noted. In 45-54yrs age group, 5 patients in lignocaine group and 8 patients in dexmedetomidine group were seen. In the age group of 55-60yrs, there were 10 patients in lignocaine group and 1 patient in dexmedetomidine group.

GRAPH 1. AGE DISTRIBUTION OF THE SAMPLE



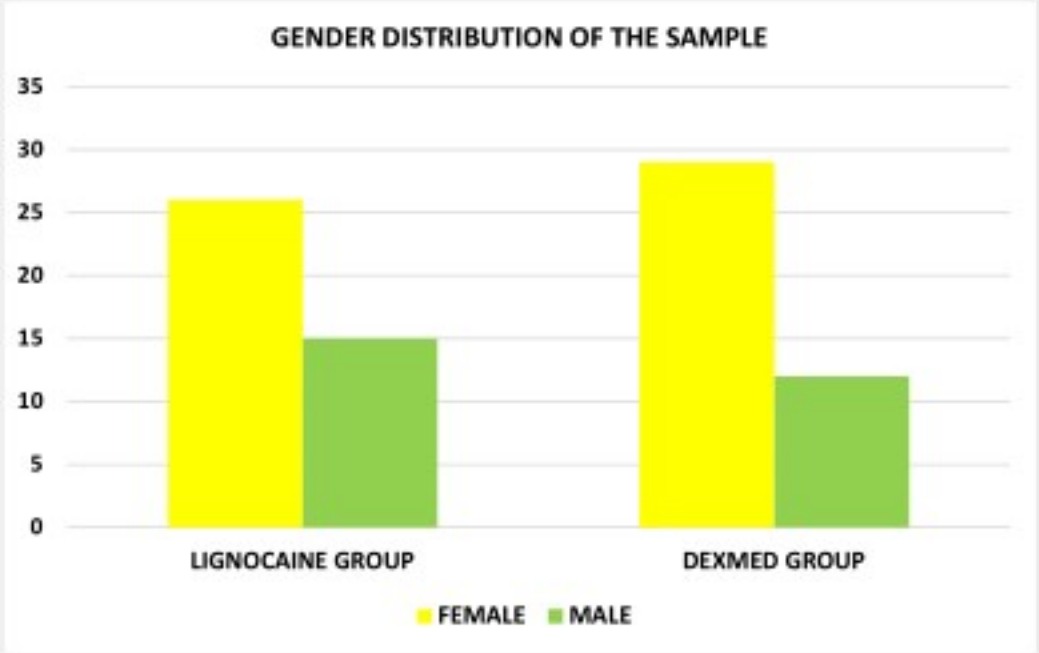
2. GENDER DISTRIBUTION

There were 26 female patients and 15 male patients in lignocaine group while dexmedetomidine group had 29 female patients and 12 male patients.

	GROUP 1 LIGNOCAINE		GROUP 2 DEXMED	
GENDER	**NUMBER**	**%**	**NUMBER**	**%**
FEMALE	26	63.41	29	70.73
MALE	15	36.59	12	29.27
TOTAL	41	100.00	41	100.00

Table 2. Mean Gender Distribution of Group 1 and Group 2

GRAPH 2. GENDER DISTRIBUTION OF THE SAMPLE



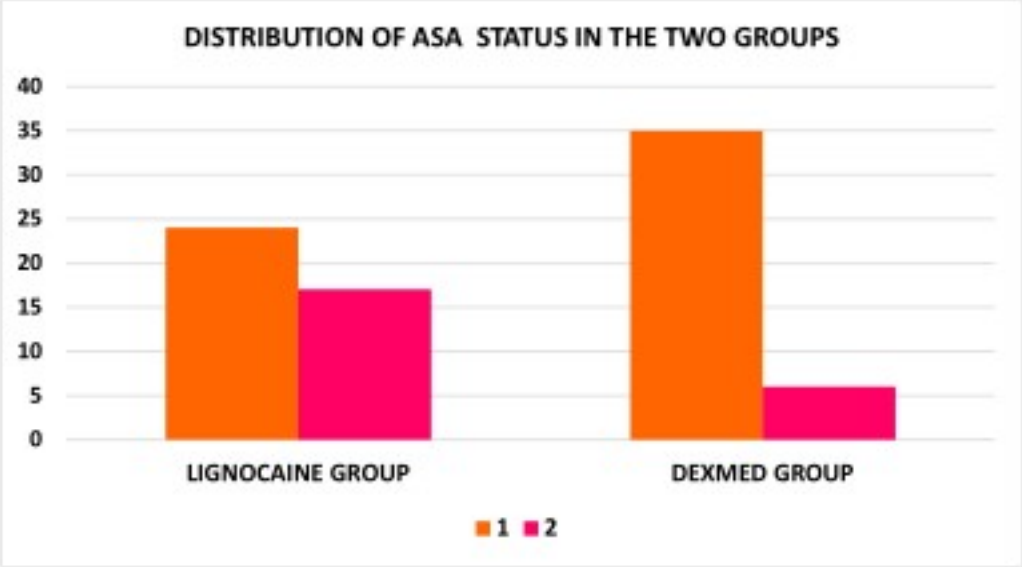
3. ASA STATUS

	GROUP 1		GROUP 2	
ASA	**NUMBER**	**%**	**NUMBER**	**%**
1	24	58.54	35	85.37
2	17	41.46	6	14.63
TOTAL	41	100.00	41	100.00

Table 3. Mean ASA Status of Group 1 and Group 2

ASA 1 and 2 patients were included in the study. There were 24 ASA 1 patients in group 1 and 35 in group 2 while there were 17 ASA 2 patients in group 1(lignocaine) and 6 in group 2(dexmedetomidine).

GRAPH 3. DISTRIBUTION OF ASA STATUS IN THE TWO GROUPS



Both the groups were comparable with respect to mean age, sex and ASA status.

4. SYSTOLIC BLOOD PRESSURE

GROUP 1 (LIGNOCAINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	133.88	16.89	--	--
10 MIN	130.52	16.00	0.21	NS
20 MIN	128.90	15.88	0.12	NS
30 MIN	129.10	15.90	0.44	NS
INDUCTION	120.02	18.44	-	-
L-I	118.54	15.51	< 0.0001	S
1 MIN	115.90	18.76	< 0.0001	S
2 MIN	114.37	26.91	0.0001	S
3 MIN	116.34	19.27	< 0.0001	S
4 MIN	116.34	19.57	< 0.0001	S
5 MIN	112.29	16.58	< 0.0001	S
7 MIN	111.56	16.82	< 0.0001	S
10 MIN	113.27	16.16	< 0.0001	S

Table 4. Mean Systolic Blood Pressure of Group 1

From the above chart we can see that in lignocaine group the mean SBP at basal was 133.88mm Hg. At induction the mean SBP was 120.02mmhg. At the time of laryngoscopy and intubation as well as subsequent time intervals there was a fall in SBP which was statistically significant when compared with SBP at induction.

GROUP 2 (DEXMEDETOMIDNE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	133.22	14.48	--	--
10	127.34	13.66	0.0312	S
20	121.83	13.00	0.0002	S
30	120.63	12.34	< 0.0001	S
INDUCTION	120.32	12.77	-	-
L-I	120.02	14.90	0.0001	S
1 MIN	114.17	12.68	< 0.0001	S
2 MIN	109.71	13.22	< 0.0001	S
3 MIN	105.61	19.74	< 0.0001	S
4 MIN	107.73	11.96	< 0.0001	S
5 MIN	108.54	12.65	< 0.0001	S
7 MIN	105.85	13.99	< 0.0001	S
10 MIN	105.46	12.85	< 0.0001	S

Table 5. Mean Systolic Blood Pressure of Group 2

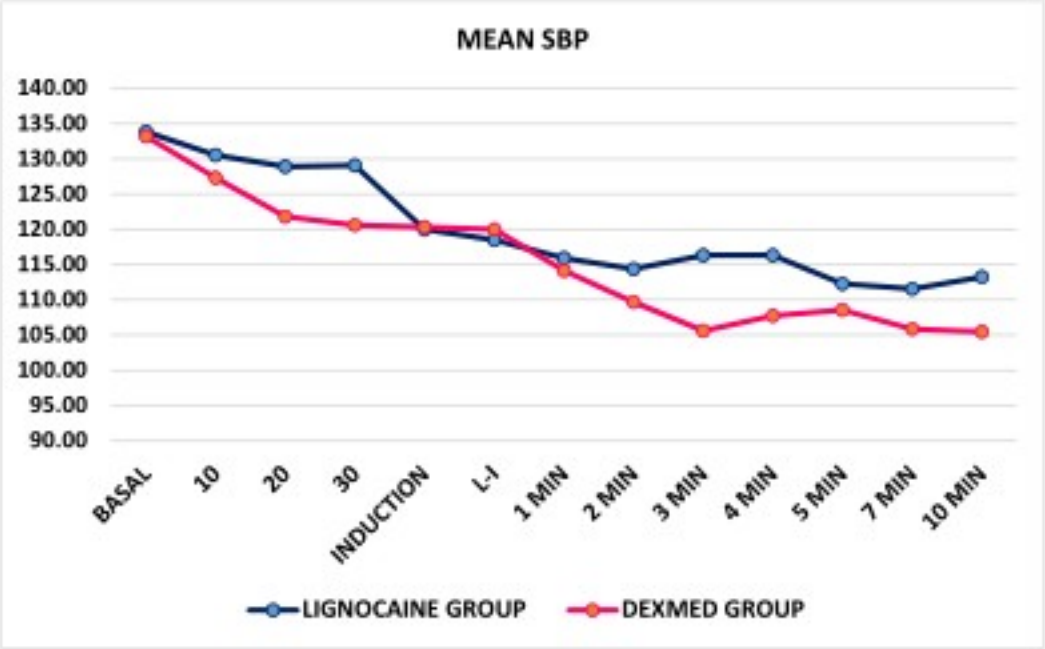
In the dexmedetomidine group, the mean SBP basally was 133.22 mmHg which had a statistically significant fall to 120.63mmHg at 30mins but clinically not significant (fall is less than 20% from basal value) and didn't need any intervention. At the time of laryngoscopy and intubation as well as subsequent time intervals there was a fall in SBP which was statistically significant when compared with SBP at induction.

	SBP					
	GROUP 1		GROUP 2			
	MEAN	S.D.	MEAN	S.D.	p VALUE	INFERENCE
BASAL	133.88	16.89	133.22	14.48	0.8502	NS
10	130.52	16.00	127.34	13.66	0.80	NS
20	128.90	15.88	121.83	13.00	0.78	NS
30	129.10	15.90	120.63	12.34	0.80	NS
INDUCTION	120.02	18.44	120.32	12.77	-	-
L-I	118.54	15.51	120.02	14.90	0.6589	NS
1 MIN	115.90	18.76	114.17	12.68	0.6256	NS
2 MIN	114.37	26.91	109.71	13.22	0.0322	S
3 MIN	116.34	19.27	105.61	19.74	0.0148	S
4 MIN	116.34	19.57	107.73	11.96	0.0186	S
5 MIN	112.29	16.58	108.54	12.65	0.2523	NS
7 MIN	111.56	16.82	105.85	13.99	0.0987	NS
10 MIN	113.27	16.16	105.46	12.85	0.0178	S

Table 6. Mean Systolic Blood Pressure of Group 1 and Group 2

By comparing the two groups it can be seen that both the drugs cause a reduction in the SBP following its administration but the fall in SBP was statistically significant in dexmedetomidine group at 2, 3, 4 and 10mins after induction with P values of 0.032, 0.014, 0.018 and 0.017 respectively.

GRAPH 4. MEAN SBP



5. DIASTOLIC BLOOD PRESSURE

GROUP 1 (LIGNOCAINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	80.20	10.27	--	--
10 MIN	82.24	11.12	0.21	NS
20 MIN	78.80	10.98	0.26	NS
30 MIN	79.24	11.24	0.51	NS
INDUCTION	75.15	12.52	-	-
L-I	75.05	12.72	0.0236	S
1 MIN	74.59	13.94	0.0206	S
2 MIN	76.63	13.02	0.0865	NS
3 MIN	76.51	13.95	0.0886	NS
4 MIN	76.54	14.11	0.0916	NS
5 MIN	74.05	13.15	0.0104	S
7 MIN	73.66	13.46	0.0078	S
10 MIN	73.63	11.74	0.0043	S

Table 7. Mean Diastolic Blood Pressure of Group 1

With the lignocaine group we saw that mean DBP basally was 80.20mmHg and at induction it was 75.15mmHg. Following induction, a statistically significant fall was observed at all the time intervals but insignificant at 2,3 and 4mins.

GROUP 2(DEXMEDETOMIDINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	85.46	11.17	--	--
10	81.34	10.47	0.0443	S
20	78.22	10.47	0.0017	S
30	77.98	12.02	0.0023	S
INDUCTION	78.71	10.27	-	-
L-I	78.54	11.82	0.0039	S
1 MIN	76.15	9.35	0.0001	S
2 MIN	71.15	10.89	< 0.0001	S
3 MIN	70.56	10.18	< 0.0001	S
4 MIN	71.15	9.74	< 0.0001	S
5 MIN	71.93	9.39	< 0.0001	S
7 MIN	70.46	10.11	< 0.0001	S
10 MIN	69.54	9.41	< 0.0001	S

Table 8. Mean Diastolic Blood Pressure of Group 2

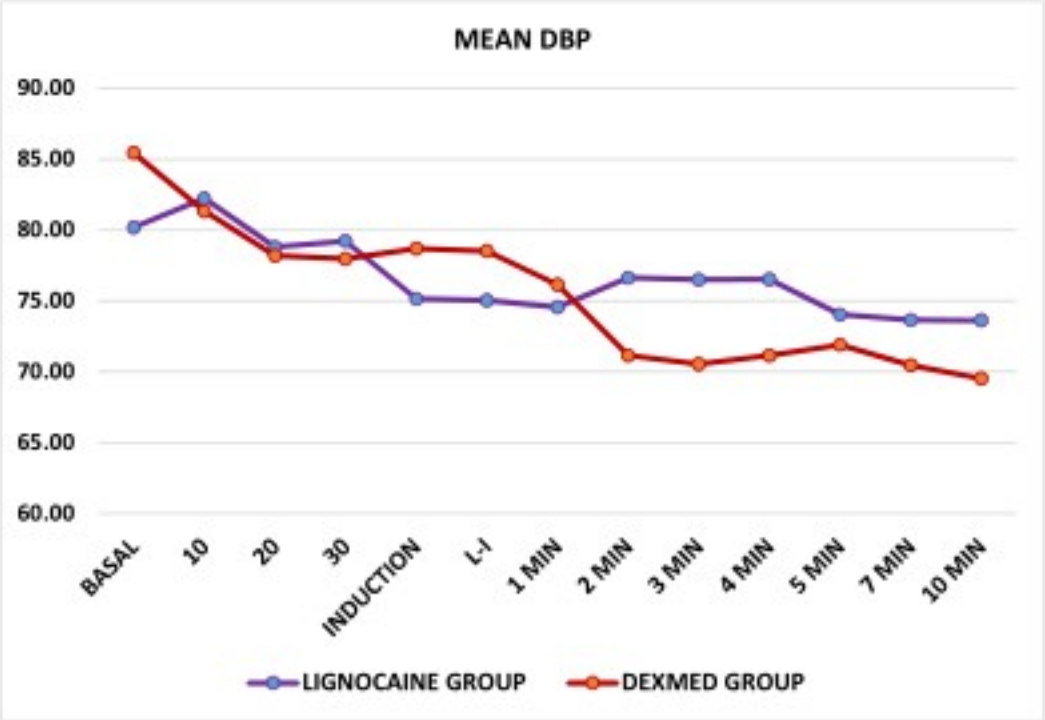
In the dexmedetomidine group, the mean DBP basally was 85.46mmHg which had a statistically significant fall to 77.98mmHg at 30mins but clinically not significant (fall is less than 20% from basal value) and didn't need any intervention. At the time of laryngoscopy and intubation as well as subsequent time intervals there was a fall in DBP which was statistically significant when compared with DBP at induction.

	DBP					
	GROUP 1		GROUP 2			
	MEAN	S.D.	MEAN	S.D.	p VALUE	INFERENCE
BASAL	80.20	10.27	85.46	11.17	0.0291	NS
10	82.24	11.12	81.34	10.47	0.13	NS
20	78.80	10.98	78.22	10.47	0.15	NS
30	79.24	11.24	77.98	12.02	0.16	NS
INDUCTION	75.15	12.52	78.71	10.27	-	-
L-I	75.05	12.72	78.54	11.82	0.2021	NS
1 MIN	74.59	13.94	76.15	9.35	0.5532	NS
2 MIN	76.63	13.02	71.15	10.89	0.0417	S
3 MIN	76.51	13.95	70.56	10.18	0.0302	S
4 MIN	76.54	14.11	71.15	9.74	0.0474	S
5 MIN	74.05	13.15	71.93	9.39	0.4028	NS
7 MIN	73.66	13.46	70.46	10.11	0.2278	NS
10 MIN	73.63	11.74	69.54	9.41	0.0849	NS

Table 9. Mean Diastolic Blood Pressure of Group 1 and Group 2

On comparing the DBP data between the two groups, it was seen that both the drugs reduced the DBP from induction but statistically significant reduction was seen in dexmedetomidine groups at 2, 3 and 4mins with P values of 0.041, 0.030 and 0.047 respectively.

GRAPH 5. MEAN DBP



6. MEAN ARTERIAL PRESSURE

GROUP 1(LIGNOCAINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	97.41	10.69	--	--
10 MIN	98.00	11.22	0.11	NS
20 MIN	96.50	12.45	0.19	NS
30 MIN	99.66	11.56	0.42	NS
INDUCTION	87.76	15.41	-	-
L-I	87.34	13.42	0.0002	S
1 MIN	84.17	13.59	< 0.0001	S
2 MIN	87.07	17.16	0.0008	S
3 MIN	86.29	16.03	0.0002	S
4 MIN	86.02	15.73	0.0001	S
5 MIN	82.76	14.64	< 0.0001	S
7 MIN	83.17	14.79	< 0.0001	S
10 MIN	81.66	13.65	< 0.0001	S

Table 10. Mean of Mean Arterial Pressure of Group 1

The mean MAP basally was 97.41 and during induction it was 87.76. We observed a statistically significant reduction in the MAP from the mean induction value at all time intervals.

GROUP 2(DEXMEDETOMIDINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	85.46	10.63	--	--
10	87.15	12.58	0.2575	NS
20	85.17	12.17	0.4540	NS
30	81.85	10.79	0.0655	NS
INDUCTION	83.54	17.06	-	-
L-I	85.71	16.30	0.4681	NS
1 MIN	82.80	13.07	0.1577	NS
2 MIN	79.12	13.11	0.0092	S
3 MIN	78.88	12.29	0.0056	S
4 MIN	78.39	11.33	0.0023	S
5 MIN	77.95	12.40	0.0021	S
7 MIN	76.68	12.68	0.0005	S
10 MIN	76.32	12.16	0.0003	S

Table 11. Mean of Mean Arterial Pressure of Group 2

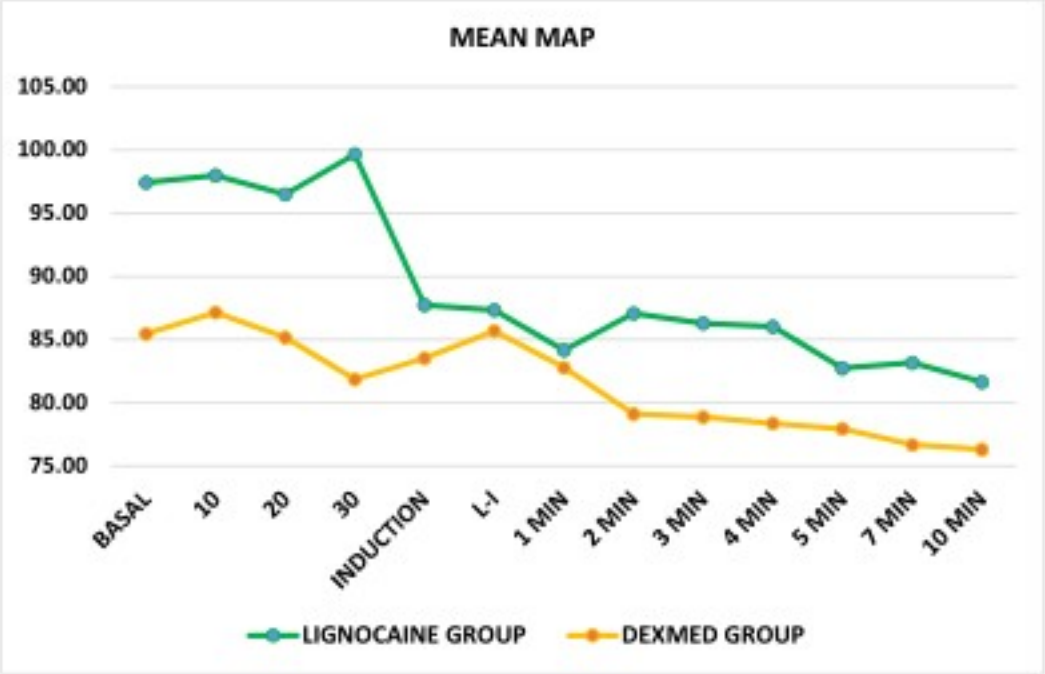
In the dexmedetomidine group, basal MAP was 85.46mmHg and 83.54mmHg during induction. MAP value showed a slight fall following its administration but a statistically significant reduction from the induction value was observed at 2,3,4,5,7 and 10mins after the induction.

	MAP					
	LIGNOCAINE GROUP		DEXMED GROUP			
	MEAN	S.D.	MEAN	S.D.	p VALUE	INFERENCE
BASAL	97.41	10.69	85.46	10.63	0.0765	NS
10	98.00	11.22	87.15	12.58	0.57	NS
20	96.50	12.45	85.17	12.17	0.54	NS
30	99.66	11.56	81.85	10.79	0.65	NS
INDUCTION	87.76	15.41	83.54	17.06	-	-
L-I	87.34	13.42	85.71	16.30	0.6215	NS
1 MIN	84.17	13.59	82.80	13.07	0.6441	NS
2 MIN	87.07	17.16	79.12	13.11	0.0208	S
3 MIN	86.29	16.03	78.88	12.29	0.0212	S
4 MIN	86.02	15.73	78.39	11.33	0.0137	S
5 MIN	82.76	14.64	77.95	12.40	0.1126	NS
7 MIN	83.17	14.79	76.68	12.68	0.0360	S
10 MIN	81.66	13.65	76.32	12.16	0.0651	NS

Table 12. Mean of Mean Arterial Pressure of Group 1 and Group 2

On comparing the two groups with respect to MAP we noted that both the groups reduced the MAP from induction but statistically significant fall in MAP was noted in dexmedetomidine group at 2,3,4 and 7mins with p values of 0.02, 0.021, 0.013 and 0.036 respectively.

GRAPH 6. MEAN MAP



7. HEART RATE

GROUP 1(LIGNOCAINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	86.80	15.57	--	--
10 MIN	87.60	16.66	0.62	NS
20 MIN	88.80	17.02	0.51	NS
30 MIN	90.20	15.90	0.25	NS
INDUCTION	84.49	16.66	-	-
L-I	87.63	16.03	0.4064	NS
1 MIN	84.71	16.25	0.2762	NS
2 MIN	83.05	15.02	0.1348	NS
3 MIN	83.76	13.75	0.1751	NS
4 MIN	83.68	14.05	0.1717	NS
5 MIN	82.32	13.59	0.0842	NS
7 MIN	81.10	12.95	0.0375	S
10 MIN	80.32	12.71	0.0210	S

Table 13. Mean Heart Rate of Group 1

In the lignocaine group there was mild reduction in the HR from the induction levels which was statistically insignificant except at 7 and 10mins after the induction was observed with p values of 0.037 and 0.021 respectively.

GROUP 2 (DEXMEDETOMIDINE)

	MEAN	S.D.	p VALUE	INFERENCE
BASAL	82.44	11.66	--	--
10	78.29	10.81	0.0495	S
20	74.95	11.66	0.0024	S
30	74.27	12.19	0.0013	S
INDUCTION	75.90	12.73	-	-
L-I	81.46	15.75	0.0754	S
1 MIN	77.39	13.35	0.0360	S
2 MIN	77.27	14.09	0.0370	S
3 MIN	75.80	14.50	0.0126	S
4 MIN	73.46	12.37	0.0006	S
5 MIN	71.76	10.49	< 0.0001	S
7 MIN	70.76	10.19	< 0.0001	S
10 MIN	72.49	10.70	0.0001	S

Table 14. Mean Heart Rate of Group 2

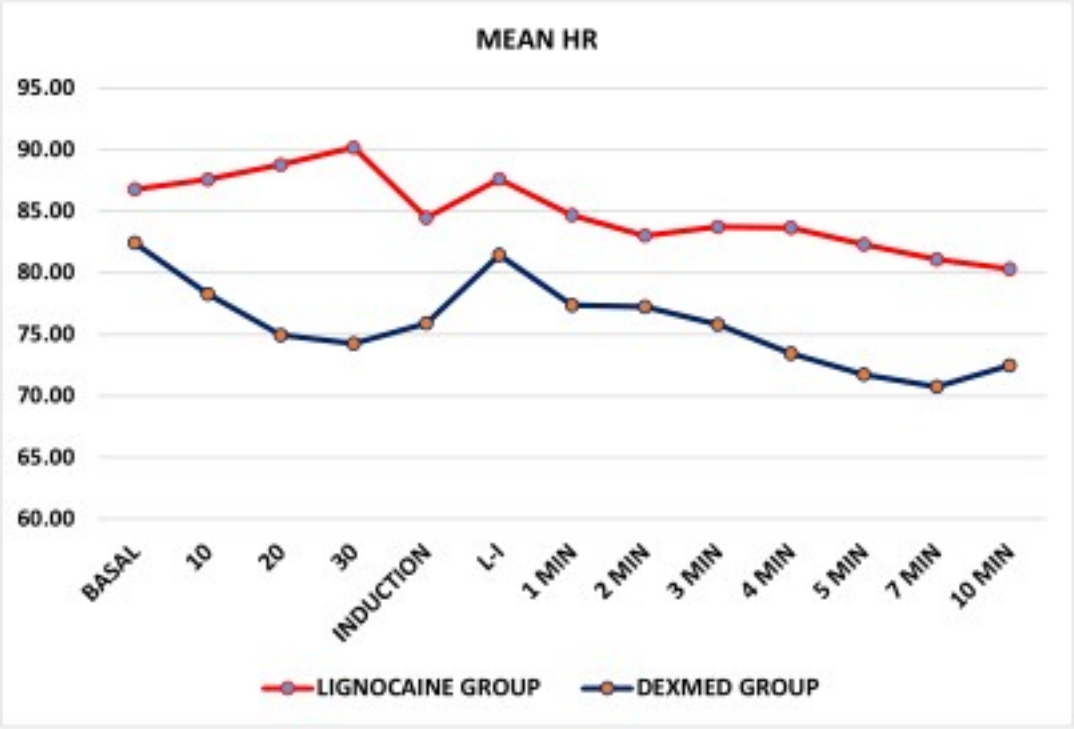
There was a significant fall in the HR statistically at all time intervals from the time of dexmedetomidine administration.

	HR					
	LIGNOCAINE GROUP		DEXMED GROUP			
	MEAN	S.D.	MEAN	S.D.	p VALUE	INFERENCE
BASAL	86.80	15.57	82.44	11.66	0.1547	NS
10	87.60	16.66	78.29	10.81	0.00	S
20	88.80	17.02	74.95	11.66	0.00	S
30	90.20	15.90	74.27	12.19	0.00	S
INDUCTION	84.49	16.66	75.90	12.73	-	-
L-I	87.63	16.03	81.46	15.75	0.0825	NS
1 MIN	84.71	16.25	77.39	13.35	0.0287	S
2 MIN	83.05	15.02	77.27	14.09	0.0761	NS
3 MIN	83.76	13.75	75.80	14.50	0.0128	S
4 MIN	83.68	14.05	73.46	12.37	0.0008	S
5 MIN	82.32	13.59	71.76	10.49	0.0002	S
7 MIN	81.10	12.95	70.76	10.19	0.0001	S
10 MIN	80.32	12.71	72.49	10.70	0.0034	S

Table 15. Mean Heart Rate of Group 1 and Group 2

With respect to Heart Rate between the two groups it was determined to have statistically significant fall in dexmedetomidine group in most of the time intervals except at the time of laryngoscopy/induction and 2mins post induction.

GRAPH 7. MEAN HR



8. OXYGEN SATURATION

With respect to SpO2 levels, both groups were comparable. There was no fall in the SpO2 level and was maintained at 98-100% in the two groups.

TABLE. 16. RAMSAY SEDATION SCORE

	DEXMEDETOMIDINE GROUP	LIGNOCAINE GROUP
BASAL	**1 - 41**	**1 - 41**
10 MINS	**1 – 35; 2 - 6**	**1 - 41**
20 MINS	**1 – 32; 2 -9**	**1 - 41**
30 MINS	**1-30; 2- 11**	**1 - 41**

The Ramsay sedation score was assessed in the two groups and it was noted that the scores were 1 at all intervals in lignocaine group. In Dexmedetomidine group, it was 1 in 35 patients at 10 mins but 2 in 6 patients. The score was 1 in 32 patients at 20 mins and it was 2 in 9 patients. At 30 mins the score was 1 in 30 patients and 2 in 11 patients. The patients were alert and comfortable.

DISCUSSION

Present study titled **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL"** was attempted to study the effects of intranasal dexmedetomidine and intravenous preservative free lignocaine to attenuate the stress response to laryngoscopy and intubation. In this study 82 patients belonging to ASA 1 and 2 were randomized into two groups with 41 patients in each group. Group 1 received 1mcg/kg intanasal dexmedetomidine in undiluted form prepared from parenteral preparation (100mcg/ml). Intranasal drug was dripped into both nostrils in equal volume using 1ml tuberculin syringe in supine position 30 minutes before the induction. The equivalent volume of saline was administered intranasally in Group 2. Hemodynamic parameters were recorded every 10mins after the drug was administered till the patient was shifted inside operation theater. Group 2 received intravenous preservative free lignocaine 1.5mg/kg 3mins before intubation. The equivalent volume of intravenous saline was administered in Group-1 3mins before intubation. SBP, DBP, MAP, HR, SPO2 were recorded at the time of intubation, every minute for the first 5 mins, at 7^{th} minute and at 10^{th} minute after intubation.

The main purpose of this study was to administer dexmedetomidine by an easy and alternative route to IV and evaluate its efficacy in attenuating the stress response to laryngoscopy and intubation by comparing with the gold standard drug IV preservative free Lignocaine.

Dexmedetomidine is a highly selective α2 adrenergic agonist. It acts through three types of α2 receptors-α2 A, α2 B and α2 C situated in brain and spinal cord. The resultant action is sedation, anxiolysis, analgesia and sympatholysis, the latter leading to hypotension and bradycardia. Activation of α2 A receptors in brainstem vasomotor centre results in suppression of norepinephrine release causing hypotension and bradycardia.

In our study it was noted that the age and gender were comparable between two groups. The hemodynamic parameters like SBP, DBP, MAP and HR had a statistically significant fall in the pre operative recovery room before shifting the patient inside the OT in dexmedetomidine group at 10, 20 an 30 mins after its administration. With respect to SBP, p values were 0.0312, 0.0002 and < 0.0001 respectively. With respect to DBP, the P values were 0.0443, 0.0017 and 0.0023 and there was statistically significant fall with respect to HR with P values of 0.0495, 0.0024 and 0.0013 respectively. This fall was not observed in the lignocaine group. Although there was statistically significant reduction in BP in dexmedetomidine group, clinically it was not significant and did not require any intervention.

The Ramsay sedation score was assessed every 10 minutes before shifting the patient to OT and the score was noticed to be 1 in lignocaine group and 1 or 2 in dexmedetomidine group. All patients were alert and comfortable.

With respect to SBP, by comparing the two groups it can be seen that both the drugs cause a reduction in the SBP following its administration but the fall in SBP was statistically significant in dexmedetomidine group at 2, 3, 4 and 10mins with p values 0.0322, 0.0148, 0.0186 and 0.0178 respectively after induction.

On comparing the DBP data between the two groups, it was seen that both the drugs reduced the DBP from induction but statistically significant reduction in DBP

was seen in dexmedetomidine group at 2, 3 and 4 mins with P values of 0.0417, 0.0302 and 0.0474 respectively.

On comparing the two groups with respect to MAP we noted that both the groups reduced the MAP from induction but statistically significant fall was noted in dexmedetomidine group at 2,3,4 and 7mins with P values of 0.0208, 0.0212, 0.0137 and 0.0360 respectively.

With respect to HR between two groups we found that there was a statistically significant reduction in the heart rate in dexmedetomidine group at all time intervals except at the time of laryngoscopy/induction and 2 mins post induction.

Also with respect to SpO2 readings, it was maintained between 98- 100% in all the patients throughout the study.

There are several ways to administer dexmedetomidine like intraoral, intranasal, intravenous, and intramuscular. Sedation, severe bradycardia, and hypotension are the primary drawbacks of intravenous usage. The intranasal method is more practical because it requires no intravenous infusion and is painless, odourless, and tasteless. Intranasal medications can directly access the CNS and cross the blood-brain barrier. Dexmedetomidine can access the systemic circulation quickly by avoiding the liver's first pass metabolism because of the high vascularity of the nasal mucosa[43,44]

Regarding pharmacokinetic and pharmacodynamics of intranasal DEX, in a study by Li *et al*. it has been documented that intranasal dexmedetomidine is associated with a slower and more gradual onset than IV administration[45]. Rapid IV administration may result in much higher peak plasma concentrations and earlier onset than IN route but in our study a more gradual onset was actually desirable in avoiding the alpha 1 agonist effects seen with rapid IV administration (hypotension

and bradycardia). On the other hand, another study with intranasal dexmedetomidine as a sedative premedication induced a favourable perioperative anxiolysis without prolongation in anesthetic recovery[46]. Intranasal dexmedetomidine is a safe and effective agent for procedural sedation in paediatric dental patients with good patient compliance and early recovery. There were no documented episodes of oxygen desaturation or apnoea. Similar effect was noted in our study where there were no desaturation episodes after intranasal administration.

Based on these we can understand that IN dexmedetomidine is linked with mild sedation with no respiratory depression, anxiolysis and minimal hypotension and bradycardia. Hence we used intranasal route in our study.

Regarding the dosage of intranasal dexmedetomidine, 81 adult patients who were posted for surgery under general anaesthesia, were included in a prospective randomised controlled study by Chengxiang Lu et al. These individuals were divided into two equal groups and given either a placebo or intranasal dexmedetomidine (1 mcg/kg) 40 to 45 minutes before to the start of the anaesthetic. It has been shown that the dexmedetomidine group experienced fewer episodes of raised BP and HR during tracheal intubation and extubation. These results prompted us to select 1 mcg/kg as the dose for our trial.

In another study regarding the onset time and duration of action of intranasal dexmedetomidine, Yuen, *et al* proved that with intranasal dexmedetomidine onset of sedation was 25 (25-30) minutes, which lasted for 85 (35-100) minutes. Based on these features, it can be speculated that intranasal dexmedetomidine 25 to 40 minutes before surgery can provide desirable effect[47]. Yuen *et al*. also found that when the preoperative administration was extended to 40-45 minutes, 91% of the children had

achieved satisfactory result. In comparison with the above article, in our study intranasal dexmedetomidine was administred 30mins before the time of induction.

So coming to our study, randomisation was done using a computer generated list. Since it was a double blinded, both the patient and the observer were blinded. They did not know which group they were assigned to. While the drug was prepared by another fellow doctor and the syringe was blindly labelled as intranasal or intravenous without the name of the drug on the syringe. This helped in avoiding any bias during the study.

Regarding the observations in our study, following intranasal administration vitals were recorded every 10mins. The concept behind this being the pharmacodynamics and pharmacokinetics of intranasal route which is associated with slow and gradual onset resulting in peak concentration achieved slowly. Also since the hemodynamic variations were not as much compared to intravenous route as evidenced in other studies. Parameters were noted every 10mins until the patient was shifted inside operating theatre.[48]

The efficacy of Intranasal dexmedetomidine has also been proven in adult patients during both local and general anaesthesia.[49,50] Jayaraman L *et al* in a comparative study evaluated the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery. They noted that intranasal dexmedetomidine was effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation in adult obese patients[50]. Likewise in our study as well Intranasal dexmedetomidine was found to be effective in attenuating pressor response to L – I when compared to IV lignocaine.

Similarly in a study done by Niyogi et al for comparison of intranasal and intravenous dexmedetomidine for attenuation of stress responses found that both the routes were equally efficacious in attenuating stress response to L-I.[51]

In a study done by Hrishi P A *et al*., it has been well proven that Intranasal DEX (1 µg/kg) provided good surgical field condition along with the added advantages of lesser haemodynamic fluctuation during transnasal transphenoidal base of skull surgery[52]. There were no statistically significant variations in heart rate and blood pressure with reduced anesthetic requirement in Intranasal DEX group. It was also seen that Intranasal DEX provided considerable effect to attenuate the increase in MAP during intubation response.

Another research by Wang SS et al. established that intranasal DEX (1 mcg/kg) had a significant impact in reducing the rise in MAP brought on by the intubation response. Changes in HR and BIS also show that this type of premedication effectively lessens the effects of intubation[52] .We found the same thing in our study.

There were certain limitations to our study. Our study included ASA 1 and 2 patients only but the merits of using intranasal dexmedetomidine would have been helpful for ASA 3 patients as well.

Regarding future scope of the study I believe that intranasal dexmedetomidine fits as an ideal drug because of many advantages as discussed earlier in our previous observations. These benefits could be used in other fields like in laparoscopic surgeries to attenuate pressor response to intraabdominal gas insufflation that is creation of pneumoperitoneum. Also we can consider intranasal dexmedetomidine before performing regional blocks in adult and paediatric patients because of the added benefit of analgesia, anxiolysis without respiratory depression.

Thus we found that intranasal dexmedetomidine was more effective in attenuating stress response to laryngoscopy and intubation without any significant side effects.

CONCLUSION

Both intranasal dexmedetomidine and intravenous preservative free lignocaine caused attenuation of hemodynamic stress response to laryngoscopy and intubation. However, Intranasal dexmedetomidine was more effective than Intravenous lignocaine in attenuating the stress response without any significant side effects. Also intranasal route was easy to administer and comfortable to the patient.

SUMMARY

The present study entitled **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION: A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE & INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL."** was conducted at "KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Nehru Nagar, Belagavi- 590010".

After obtaining clearance from hospital's ethical committee, 82 patients of ASA I and II between age group 18-60 years were randomized to two groups having 41 patients in each Group.

Group 1: Patients received 1.5 mg/kg of intravenous preservative free lignocaine.

Group 2: Patients received 1mcg/kg of intranasal dexmedetomidine.

Hemodynamic parameters were recorded every 10mins after the drug was administered till the patient was shifted inside operation theater. SBP, DBP, MAP, HR, SPO2 were recorded at the time of intubation, every minute for the first 5 mins, at 7^{th} minute and at 10^{th} minute after intubation.

We observed that both the drugs helped to attenuate the stress response to laryngoscopy and endotracheal intubation with respect to SBP, DBP, MAP and HR but SBP, DBP, MAP was significantly reduced in dexmedetomidine group at 2, 3 and 4 mins after intubation.

Intranasal dexmedetomidine was more effective than intravenous preservative free lignocaine in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation and was easy to administer without any side effects.

BIBLIOGRAPHY

1. Robert K. Stoelting MD. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation. Influence of viscous or intravenous lidocaine. Anaesth Analg 1978;57:197-9.
2. Prys-Roberts, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension-II. Hemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971;43:531-47.
3. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complication related to the pressor response to endotracheal intubation. Anaesthesiology 1977;47:524-5.
4. Dalton B, Guiney T. Myocardial ischemia from tachycardia and hypertension in coronary heart disease - Patient's undergoing anaesthesia. Ann. Mtg. Boston: American Society of Anesthesiologists; 1972. p. 201-2.
5. Donegan MF, Bedford RF. Intravenously administered lignocaine prevents intracranial hypertension during endotracheal suctioning. Anaesthesiology 1980;52:516-8.
6. Rose DK, Cohen MM. The airway: Problems and predictions in 18500 patients. Can J Anaesth 1991;41:372-83.
7. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon heart. Surg Gynaec Obst 1940;70:157-62.
8. Bromage PR, Robson JG. Concentrations of lignocaine in the blood after intravenous, intramuscular epidural and endotracheal administration. Anaesthesia. 1961;16:461–78.
9. Kumar L, Kumar A, Panikkaveetil R, Vasu KB, Rajan S, Nair GS. Efficacy of intranasal dexmedetomidine versus oral midazolam for paediatric premedication. Indian J Anaesth. 2017;61:125–30.

10. Tam S, Chung F, Campbell M. Intravenous lidocaine: optimal time of injection before tracheal intubation. Anesthesia and Analgesia.1987; 66:1036-8.
11. I G Wilson, B H Meiklejohn & G Smith. Intravenous lignocaine and sympathoadrenal responses to laryngoscopy and intubation. Anaesthesia 1991;46:177- 180.
12. Niyogi S, Biswas A, Chakraborty I, Chakraborty S Acharjee A. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine: A comparison between intravenous and intranasal route.Indian J Anaesth. 2019 Nov; 63(11): 915–923.
13. Singh G, Kaur H, Aggarwal S, Sharda G, Singh A, Jha A, Aggarwal H. Intravenous dexmedetomidine vs. lignocaine in attenuating the hemodynamic responses during laryngoscopy and endotracheal intubation: a randomized double blind study. Anesth Pain & Intensive Care 2017;21(2):181-186.
14. Jayaraman L, Sinha A, Punhani D. A comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery.J Anaesthesiol Clin Pharmacol. 2013 Apr-Jun; 29(2): 179–182.
15. Prasad SR, Matam UM, Ojili GP.Comparison of intravenous lignocaine and intravenous dexmedetomidine for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation. J NTR Univ Health Sci 2015;4:86-90.
16. Kumari K, Gombhar S, Kapoor D, Sandhu HS. Clinical study to evaluate the role of preoperative dexmedetomidine in attenuation of hemodynamic response to direct laryngoscopy and tracheal intubation. Acta Anaesthesiologica Taiwanica 2015; 53: 123-130.

17. Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian J Anaesth 2017;61: 48-54.
18. SIEDLECKI J. Disturbances in the function of cardiovascular system in patients following endotracheal intubation and attempts to their prevention by pharmacological blockade of the sympathetic system. Anaesthesia, Resuscitation and Intensive Therapy 1975, 3: 107-23.
19. RUSSELL WJ, MORRIS RG, FREWIN DB, DREW SE. Changes in plasma catecholamine concentration during endotracheal intubation. British Journal qf Anaesthesia 1981; 53 837-9.
20. DERBYSHIRE DR, CHMIELEWSKI A, FELL D, VATER M, ACHOLA KJ, SMITH G. Plasma catecholamine responses to tracheal intubation. British Journal of Anaesthesia 1983; 55: 85540.
21. WEATHERILL D, SPENCE AA. Anaesthesia and disorders of the adrenal cortex. British Journal of Anaesthesia 1984; 56: 741-9.
22. BucxMJL, VAN GEEL RTM, SCHECK PAE, STIJNEN T. Cardio- vascular effects of forces applied during laryngoscopy. The importance of tracheal intubation. Anaesthesia 1992; 47:
23. CUMMINGS MF, RUSSELL WJ, FREWIN DB. Effects of pancuronium and alcuronium on the changes intraarterial pressure and plasma catecholamine concentrations during tracheal intubation. British Journal of Anaesthesia 1983; 55 619-23.

24. Ramsay MA, Saha D, Hebeler RF. Tracheal resection in the morbidly obese patient: The role of dexmedetomidine. J Clin Anesth. 2006;18:452–4.

25. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: The effect on recovery outcome variables. AnesthAnalg. 2008;106:1741–8.

26. Haselman MA. Dexmedetomidine: A useful adjunct to consider in some high-risk situations. AANA J. 2008;76:335–9.

27. Sun Y, Liu C, Zhang Y, Luo B, She S, Xu L, *et al*. Low-dose intramuscular dexmedetomidine as premedication: A randomized controlled trial. Med Sci Monit 2014;20:2714-9.

28. Kavya Prabhu M, Mehandale SG. Comparison of oral dexmedetomidine versus oral midazolam as premedication.

29. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol 2006;18:1043-58.

30. Karhuvaara S, Kallio A, Salonen M, Tuominen J, Scheinin M. Rapid reversal of alpha 2-adrenoceptor agonist affects by atipamizole in human volunteers. Br J Clin Pharmacol 1991;31:160-5.

31. Maksimow A, Snaoir A, Sarkela M, Kentala E, Koskenvuo J, Posti J, *et al*. Assessing the depth of dexmedtomidine-induced sedation with electroencephalogram (EEG)-based spectral entropy. Acta Anaesthesiol Scand 2007;51:222-30.

32. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699-705.

33. Talon MD, Woodson LC, Sherwood ER, Aarsland A, McRae L, Benham T. Intranasal dexmedetomidine premedication is comparable with midazolam in burn children undergoing reconstructive surgery. J Burn Care Res 2009;30:599-605.

34. Mason KP, Zgleszewski SE, Dearden JL, Dumont RS, Pirich MA, Stark CD, *et al.* Dexmedetomedine for pediatric sedation for computed tomography imaging studies. Anesth Analg 2006;103:57-62.

35. Nooh N, Sheta SA, Abdullah WA, Abdelhalim AA. Intranasal atomized dexmedetomidine for sedation during third molar extraction. Int J Oral Maxillofac Surg 2013;42:857-62.

36. Jayaraman L, Sinha A, Punhani D. A comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery. J Anaesth Clin Pharmacol 2013;29:179-82

37. Limited PP. Lignocaine injection: Product information. Pfizer Pty Limited, 2006

38. Xylocaine and xylocaine with adrenaline: Product information. AstraZeneca Pty Ltd A, 2010.

39. Catterall W, Mackie K. Goodman and Gilman's the pharmacological basis of therapeutics. 9th ed. New York: McGraw-Hill, 1996.

40. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. *Acta Anaesthesiol Scand* 2006; **50**: 265-282.

41. Bryant B, Knights K. Pharmacology for Health Professionals. 3rd ed. Chatswood: Elsevier Australia, 2011.

42. Eriksson E, Granberg PO. Studies on the renal excretion of Citanest and Xylocaine. *Acta Anaesthesiol Scand Suppl* 1965; 16: 79-85.

43. Bromage PR, Robson JG. Concentrations of lignocaine in the blood after intravenous, intramuscular epidural and endotracheal administration. Anaesthesia. 1961;16:461–78.

44. Kumar L, Kumar A, Panikkaveetil R, Vasu KB, Rajan S, Nair GS. Efficacy of intranasal dexmedetomidine versus oral midazolam for paediatric premedication. Indian J Anaesth. 2017;61:125–30.

45. Li A, Yuen VM, Goulay-Dufay S, Sheng Y, Standing JF. Pharmacokinetic and pharmacodynamic study of intranasal and intravenous dexmedetomidine. Br J Anaesth 2018;12:960-8.

46. Lu C, Zhang LM, Zhang Y, Ying Y, Li L, Xu L, et al. Intranasal dexmedetomidine as a sedative premedication for patients undergoing suspension laryngoscopy: A randomized double-blind study. PLoS One 11:e0154192.

47. Yuen VM, Hui TW, Irwin MG, Yao TJ, Wong GL, Yuen MK. Optimal timing for the administration of intranasal dexmedetomidine for premedication in children. Anaesthesia 2010;65:922-9.

48. Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy andendotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian J Anaesth 2017;61:48-54.

49. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.

50. Tanskanen PE, Kyttä JV, Randell TT, Aantaa RE. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: A double-blind, randomized and placebo-controlled study. Br J Anaesth 2006; 97:658-65.

51. Jayaraman L, Sinha A, Punhani D. A comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery. J Anaesth Clin Pharmacol 2013; 29:179-82

52. Mustafa A, Isik B, Ozsoylar O, Akcabay M. The effects of alfa2 adrenargic agonist dexmedetomidine on haemodybamic response to direct laryngoscopy. Open Otorhinolaryngol J 2007; 107:157.

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enrole you in study titled **"ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION : A COMPARISON BETWEEN INTRANASAL DEXMEDETOMIDINE AND INTRAVENOUS PRESERVATIVE FREE LIGNOCAINE – A ONE YEAR HOSPITAL BASED DOUBLE BLINDED RANDOMISED CLINICAL TRIAL",** conducted by **REG NO. BA0120018** Post Graduate in M.D. Anaesthesiology under the guidance of Dr._____ Professor, Department of Anaesthesiology, J.N. Medical College, Belagavi under KLE University, Belagavi.

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

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

Purpose of the study:

The purpose of this research is to know whether Intranasal dexmedetomidine is useful in attenuating hemodynamic response to laryngoscopy and intubation by comparing with the time tested drug IV preservative free lignocaine.

Procedure Involved:

If you agree to enroll in my study, I will ask you present, past and family history. Then you will be clinically examined in detail. You will be allotted into one of the two groups randomly using computer generated software. Group A patients will receive 1mcg/kg of dexmedetomidine intranasal 30mins before intubation, while Group B patients will receive preservative free IV lignocaine 1.5mg/kg 3mins before intubation

Risks:

There is almost no risk involved with using intranasal dexmedetomidine.

Benefits: Attenuation of pressor response to endotracheal intubation.

Voluntary Participation/Withdrawal:

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

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

Privacy and Confidentiality: The only people to know that you is as research subject is you and members of the research team. No information provided by you during the research will be disclosed to other without your written permission except:

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

Authorization to Publish Results:

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

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

Compensation: In the event of injury related to the study, treatment will be made available through KLE Hospital, Belagavi. There is no compensation or payment for such medical treatment by law. If you get injured you may contact Dr. Sushmitha H S at Department of Anaesthesiology, KLES Hospital or by Ph. No: 9980020860.

Questions: In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact **REG NO. BA0120018** Department of Anaesthesiology, KLES Hospital, Belagavi. Ph. number: _____ or Dr. _____ Professor, Dept. Of Anaesthesiology, KLES Hospital and MRC, Belagavi. Ph. No: _____.

If you have any queries about your rights as a study subject, you may call Dr.Roopa Bellad, Professor, Department of Paediatrics and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number- 9448113403, or extension 1887 at J.N. Medical College, Belagavi.

PROFORMA

Title: "Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation: A comparison between intranasal dexmedetomidine and intravenous preservative free lignocaine – A one year hospital based double blinded randomised clinical trial"

Patient's Name	:	I.P No	:
Age	:	Weight	:
Height	:	Gender	:
Date of operation	:	Occupation	:
Address	:	Anaesthesiologist:	

Chief complaints:

HOPI:

Past History

- HTN / DM/ IHD / Arrhythmia / LVH / Valvular heart disease
- H/o uncontrolled hypertension/diabetes mellitus
- H/o previous surgery/(s) where airway difficulty was encountered.

Family History:

General physical examination:

Weight (Kg)	:	Temperature (^{0}F)	:	Pallor	:
Cyanosis	:	Pedal oedema	:	Clubbing	:
PR	:	BP	:	RR	:

Systemic examination:

RS : CNS :

CVS : GIT :

Airway Assessment –

Spine-

Investigations

Hb% : Urine routine :

Blood urea : Serum creatinine:

FBS : CXR :

ECG

Diagnosis

Proposed surgery

Preoperative physical status ASA Grade I

II

III

IV

V

Inclusion Criteria:

- Patients who provided consent
- ASA I and II.
- Age - 18 to 60 years.
- Patients scheduled for elective surgeries under general anaesthesia.

Exclusion criteria

- Patient refusal or who are unable to give consent.
- ASA physical status III or more.
- Patients undergoing emergency surgery.
- Patients allergic to the drug under study.
- Patients with contraindication to general anaesthesia.
- Patients with significant cardiac and respiratory disease.
- Patients with difficult airway.
- Patients with nasal pathology.

Methodology

After obtaining the approval of ethical committee and written informed consent, a total of 82 patients undergoing surgery under general anaesthesia with endotracheal intubation will be included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients will be randomized based on computer generated randomization table into one of the two groups with 41 patients each.

Group 1: Patients received 1.5 mg/kg of intravenous preservative free lignocaine.

Group 2: Patients received 1mcg/kg of intranasal dexmedetomidine.

Detailed pre anesthetic evaluation and routine investigations like complete blood picture, serum creatinine and random blood sugar levels were done. Chest X-ray and ECG were asked for patients over 40 years of age. All patients were kept nil per oral for atleast 6 hours and received tablet alprazolam (0.5mg) as premedication at night before surgery.

All the patients were shifted to the pre-operative room on the day of surgery, where baseline data were taken using routine monitors such as noninvasive blood pressure, electrocardiogram and pulse oximetry. IV ringers lactate as a maintenance fluid was administered using an 18G peripheral venous cannula.

Three minutes prior to intubation, group 1 patients were administered 1.5 mg/kg of preservative-free intravenous lignocaine and Group 2 received the same volume of saline intravenously.

Patients in group 2 received undiluted intranasal dexmedetomidine 1mcg/kg prepared from parenteral preparation (100mcg/ml) about 30 minutes prior to induction using a 1ml tuberculin syringe, where the medication was dripped evenly into both nostrils keeping the patient in supine position. Group 1 received the same dosage of saline intranasally.

Hemodynamic parameters and Ramsay sedation score were recorded every ten minutes after the administration of the drug till the patient was shifted inside operation theatre.

Routine monitors were connected and baseline parameters were obtained once the patient was shifted inside the OT. Pre-medicated the patients with Inj. glycopyrrolate (0.005 mg/kg), Inj.midazolam (0.05 mg/kg) and Inj.fentanyl (2mcg/kg). The patients were induced with Inj. Propofol 2mg/kg IV and succinylcholine 2mg/kg after a 3-minute preoxygenation with 100% oxygen. Gentle

laryngoscopy was done using Macintosh laryngoscope blade in one attempt and in less than 20 seconds and endotracheal intubation was performed using appropriate sized endotracheal tube.

Patients were excluded from the study if intubation was not possible in first attempt or took a long time to intubate. Hemodynamic variables (MAP, SBP, DBP and HR) were recorded at the time of intubation, every minute for the first 5 minutes, at 7th minute and at 10th minute after intubation. Anaesthesia was maintained with 50% O2-N2O, isoflurane 1-1.2 MAC and vecuronium 0.1mg/kg followed by intermittent topups of one-fourth the loading dose.

Once the surgery was completed Inj. glycopyrrolate 0.01mg/kg and Inj. neostigmine 0.05mg/kg were administered to reverse the neuromuscular blockade. Patients were extubated once the clinical criteria was met, in a 30 degree head end elevation and shifted to postoperative ward in recovery position.

ANALYSIS PLAN

Sl. No & DATE	NAME	AGE	ASA	DIAGNOSIS	SURGERY

DRUG GIVEN:

PRE INDUCTION				
VITALS	BASAL	10mins	20mins	30mins
SBP				
DBP				
HR				
SPO2				

POST INDUCTION									
VITALS	INDUCTION	L-I	1min	2min	3min	4min	5min	7min	10min
SBP									
DBP									
MAP									
HR									
SPO2									

ANY OTHER SIDE EFFECTS NOTED:

SIGNATURE OF THE ANAESTHESIOLOGIST - _____

- SIGNATURE OF THE WITNESS - _____
- SIGNATURE OF THE PRINCIPAL INVESTIGATOR -_____

PHOTOGRAPHS

FIG.1 DEXMEDETOMIDINE VIAL AND TUBERCULIN SYRINGE

FIG.2 PRESERVATIVE FREE LIGNOCAINE VIAL

ANNEXURE IV - KEY TO MASTERCHART

ASA	–	American Society of Anaesthesiologists
HR	–	Heart Rate
SBP	-	Systolic Blood Pressure
DBP	–	Diastolic Blood Pressure
MAP	–	Mean Arterial Pressure
SpO2	–	Peripheral Oxygen Saturation

						SBP													DBP								
SL.NO	IP NUMBER	SEX	AGE	WEIGHT	ASA	BASAL	10mins	20mins	30mins	INDUCTION	L-I	1MIN	2MIN	3MIN	4MIN	5MIN	7MIN	10MIN	BASAL	10mins	20mins	30mins	INDUCTION	L-I	1MIN	2MIN	3MIN
1	1034957	F	17	50	1	148	140	138	136	106	150	130	150	134	130	120	114	114	72	70	66	68	68	100	80	100	88
2	1035969	M	20	55	1	112	120	122	122	84	108	100	100	98	96	94	94	96	70	68	68	70	62	50	73	74	74
3	1035463	M	51	50	1	116	118	120	124	112	130	132	126	124	122	122	118	116	86	80	88	86	82	86	96	90	88
4	1039421	F	50	50	2	170	160	162	158	166	124	84	160	150	160	150	148	140	100	102	108	88	94	80	68	105	100
5	1039843	F	57	65	2	150	144	140	140	150	110	126	93	95	81	89	106	110	82	80	78	76	82	72	72	55	55
6	1043632	M	40	75	1	140	138	140	138	136	110	100	100	96	90	82	78	82	90	88	88	82	86	74	80	76	74
7	1043596	M	38	65	1	120	122	120	122	118	112	110	104	104	107	107	98	96	70	76	78	74	72	70	70	68	70
8	1042308	F	40	50	2	128	130	132	134	107	120	116	112	106	108	110	104	102	76	78	76	76	61	80	70	72	68
9	1043825	F	28	50	1	116	120	118	120	110	129	130	136	130	129	121	125	130	71	77	74	72	61	78	84	77	82
10	1044825	F	40	50	1	140	140	138	134	142	126	115	111	92	99	91	90	100	90	90	88	78	84	72	74	65	61
11	1044916	F	38	55	1	128	130	126	124	88	100	102	98	92	90	90	88	88	62	66	68	70	60	68	68	70	72
12	1044891	F	25	45	1	146	150	144	140	140	115	114	120	130	140	136	136	129	84	86	80	76	100	69	68	78	87
13	1045007	F	28	45	1	119	120	122	120	123	152	111	132	130	132	130	136	137	65	66	70	72	76	98	58	78	86
14	1046600	F	31	50	1	153	150	146	146	103	101	100	100	110	119	120	120	120	97	90	88	88	81	47	72	72	70
15	1046456	F	27	45	1	110	120	118	120	102	110	94	111	119	125	117	120	120	74	76	76	75	66	76	58	82	81
16	1047543	M	60	60	1	126	118	120	118	120	112	114	118	124	128	130	124	126	75	80	78	74	78	72	70	80	76
17	1048189	M	60	65	2	126	120	122	120	119	95	113	118	120	122	101	95	103	76	77	80	78	69	64	85	80	81
18	1048039	F	55	60	2	174	170	168	160	92	104	98	83	120	119	119	124	137	58	60	68	70	54	60	55	62	67
19	1045281	M	34	65	1	130	140	146	144	128	118	118	140	138	137	110	96	110	90	92	90	88	84	82	85	90	90
20	1045258	M	40	80	1	156	154	140	138	150	131	190	188	154	140	109	109	119	94	90	92	86	92	80	126	116	96
21	1045821	M	51	70	1	128	130	112	122	107	120	116	112	106	108	110	104	102	76	78	80	78	61	80	70	72	68
22	1084512	M	20	55	1	112	119	140	146	116	109	104	120	122	127	121	119	115	72	70	68	70	62	58	57	72	73
23	1083275	M	26	70	1	130	128	130	138	114	112	108	106	102	105	101	106	100	80	82	80	78	72	70	68	68	66
24	1084127	F	39	55	2	145	140	140	144	127	117	121	103	99	92	100	106	103	88	88	86	86	79	83	82	77	70
25	1084124	F	32	48	1	122	120	122	120	103	107	108	106	94	97	97	100	102	90	92	90	88	75	84	76	74	70
26	1083215	F	26	68	1	136	128	128	130	130	107	108	108	112	106	115	116	116	86	88	86	86	90	67	68	65	70
27	1084129	F	29	45	2	132	130	128	128	133	140	134	154	177	158	153	151	156	97	80	78	76	98	101	103	108	133
28	1083036	F	42	50	2	112	110	112	120	116	109	104	120	122	127	121	119	115	72	70	66	65	62	58	57	72	73
29	1083189	F	40	70	1	110	114	112	116	102	110	94	111	119	125	117	120	120	74	76	76	77	66	76	58	82	81
30	1083397	F	30	58	2	130	124	120	118	129	178	168	140	138	138	110	96	110	90	99	90	88	81	110	98	90	90
31	1084985	F	49	57	1	174	170	168	150	92	104	98	83	120	119	119	124	137	78	80	78	68	54	60	55	62	67
32	1086242	F	58	48	2	145	140	140	136	127	115	121	10	99	92	100	106	103	88	88	80	80	79	83	82	77	70
33	1086541	F	24	45	1	140	146	148	150	142	126	115	111	92	99	91	90	100	90	90	78	76	84	72	74	65	61
34	1087542	F	40	68	2	140	150	144	144	110	129	130	136	130	129	121	125	130	71	78	80	82	61	78	84	77	82
35	1078456	M	63	58	2	128	130	130	130	107	120	116	112	106	108	110	104	102	76	76	78	70	61	80	70	72	68
36	1074593	F	60	60	2	120	124	122	120	118	112	110	104	104	107	108	98	96	70	67	70	68	72	70	70	68	70
37	1084612	F	55	50	2	146	144	146	140	140	115	114	120	130	140	136	136	129	84	80	88	80	100	69	68	78	87
38	1087642	M	58	67	2	138	140	130	126	128	126	115	112	111	100	99	92	91	92	77	76	78	80	72	74	72	65
39	1087651	M	52	60	2	118	120	120	128	116	123	132	130	132	136	137	132	130	66	64	66	68	68	78	86	78	86
40	1039843	F	57	65	2	150	148	144	144	150	110	126	93	95	87	90	106	110	82	80	68	66	82	72	72	55	55
41	1065482	M	25	48	1	125	124	120	118	118	114	113	98	94	96	100	101	102	84	84	80	78	82	78	74	68	66

				MAP													HR									
4MIN	5MIN	7MIN	10MIN	BASAL	10mins	20mins	30mins	INDUCTION	L-I	1MIN	2MIN	3MIN	4MIN	5MIN	7MIN	10MIN	BASAL	10mins	20mins	30mins	INDUCTION	L-I	1MIN	2MIN	3MIN	4MIN
84	74	68	68	78	80	78	68	80	116	96	116	103	99	89	83	83	84	88	86	88	100	114	116	121	114	104
72	66	64	66	84	76	78	78	69	90	82	83	82	76	75	74	75	64	65	68	70	74	86	79	86	84	74
90	88	84	84	96	90	88	80	92	98	106	102	111	100	100	96	96	99	90	98	90	96	100	90	90	90	92
104	99	98	94	123	112	100	98	118	96	73	126	119	126	119	115	110	70	78	67	68	70	84	81	90	90	94
46	50	57	68	104	100	98	98	105	85	90	68	68	60	60	73	69	70	68	78	67	75	73	70	67	64	68
68	50	46	50	106	104	100	89	96	92	90	88	85	79	57	54	57	79	78	76	75	68	70	72	74	72	74
71	67	62	60	86	88	80	88	95	91	90	86	80	80	76	80	78	72	70	76	76	70	70	68	70	71	67
66	70	66	64	93	95	94	90	71	82	74	74	70	72	72	76	68	89	88	87	87	67	68	69	70	70	68
85	81	87	85	86	88	88	80	72	90	95	89	94	96	90	96	95	93	96	88	87	81	91	94	96	100	110
63	65	60	68	106	102	100	102	95	84	82	74	69	70	69	63	70	90	88	85	80	95	100	88	68	65	67
68	66	62	60	84	86	78	80	68	74	75	84	82	72	73	69	68	100	98	96	95	90	82	79	78	76	78
83	91	82	88	107	106	100	98	114	79	78	87	83	91	82	88	92	99	99	96	88	100	99	95	96	92	88
78	86	96	90	83	84	78	80	87	111	71	88	96	88	96	98	100	88	87	84	80	100	111	113	104	102	100
92	80	91	81	115	114	100	98	86	59	78	78	90	97	87	95	87	100	98	99	94	100	105	99	89	92	94
90	83	87	84	86	88	80	82	74	83	67	89	90	99	83	87	84	98	90	97	90	95	95	75	74	90	93
82	76	78	75	92	90	88	80	70	81	80	80	102	102	93	88	84	62	60	68	66	65	70	71	68	72	74
81	70	76	71	93	98	90	88	85	75	94	99	92	94	80	84	82	97	90	98	92	88	89	92	88	87	84
66	63	66	68	96	98	98	88	66	74	69	69	84	82	81	95	88	55	56	55	58	58	60	56	68	77	76
92	69	67	73	103	100	88	88	97	90	85	75	74	95	83	77	85	78	70	76	78	64	68	68	64	70	74
81	71	72	72	114	102	100	98	114	96	85	150	82	92	93	76	70	80	78	74	76	92	96	85	82	92	93
66	70	66	64	93	98	90	88	71	82	74	75	84	82	72	73	69	85	88	82	80	78	74	75	78	75	72
71	65	68	63	88	86	86	88	80	75	73	88	89	90	84	85	80	80	78	78	80	105	103	101	98	93	100
68	70	69	70	97	96	90	92	82	86	82	76	71	68	67	62	62	86	87	83	81	78	76	76	74	74	72
65	79	80	77	107		87	88	95	94	95	85	79	72	86	88	85	71	70	80	78	82	100	92	85	84	85
75	76	78	69	100	104	88	90	84	91	86	82	78	82	81	86	80	120	110	102	110	126	125	126	121	116	116
88	79	78	77	102	100	98	92	103	80	81	79	80	84	91	90	90	102	100	98	99	103	81	80	79	80	84
115	119	117	115	108	102	100	98	109	114	113	118	147	129	130	128	128	126	110	114	120	126	119	119	115	115	101
71	65	68	63	86	87	98	88	80	75	72	78	89	90	84	85	80	80	78	80	82	105	103	101	98	93	100
90	83	87	84	86	88	86	88	74	83	67	89	90	99	91	94	95	98	98	90	96	95	95	75	74	90	93
92	69	67	73	103	98	88	90	97	131	133	115	114	107	83	77	85	78	80	82	84	64	85	86	84	85	85
66	63	66	68	110	110	100	88	54	60	55	62	67	66	63	66	68	55	56	60	62	58	60	56	68	77	76
65	79	80	77	110	104	99	98	95	94	95	85	79	72	86	88	85	107	106	105	100	71	82	100	82	85	84
63	65	60	68	106	98	90	88	95	84	82	74	69	70	69	63	70	90	88	80	83	95	100	88	68	65	67
85	81	87	85	94	90	92	90	72	90	95	89	94	96	90	96	95	93	94	90	92	81	91	94	96	100	110
66	70	66	64	93	90	98	90	71	82	74	74	70	72	76	68	69	89	88	80	82	67	68	69	70	70	68
71	72	62	60	86	88	86	88	95	91	90	86	80	80	82	80	78	72	70	72	76	72	70	64	62	67	66
83	91	82	88	105	98	80	87	114	79	78	88	97	98	100	102	92	99	98	90	96	90	99	95	96	92	90
68	65	61	65	107	88	87	86	88	84	82	76	74	70	70	69	69	90	88	86	88	86	88	78	78	76	72
96	90	78	76	84	86	88	80	86	87	88	96	88	96	98	100	88	80	80	82	78	82	88	87	90	86	82
46	50	57	68	104	100	98	98	105	85	90	68	68	60	60	73	69	105	104	102	90	70	75	73	70	67	64
66	70	74	76	90	88	86	88	94	88	86	82	75	74	72	70	70	86	88	80	78	82	80	78	76	74	72

			SPO2												
5MIN	7MIN	10MIN	BASAL	10mins	20mins	30mins	INDUCTION	L-1	1MIN	2MIN	3MIN	4MIN	5MIN	7MIN	10MIN
98	96	94	99	99	99	99	99	100	100	98	99	100	99	100	100
73	70	70	98	99	99	99	99	98	97	99	100	100	98	99	99
96	92	92	100	100	99	100	100	100	99	99	99	99	99	99	99
84	84	84	96	99	97	98	98	99	99	99	98	99	99	99	100
64	68	66	99	99	99	99	99	99	99	99	97	99	99	99	99
76	72	64	99	100	98	98	98	99	99	99	100	100	100	99	99
62	60	66	97	96	99	99	99	99	99	99	99	99	99	99	99
66	66	68	98	98	97	97	100	100	100	100	100	100	100	100	100
100	94	94	99	99	98	98	99	99	99	99	98	99	100	100	100
68	64	66	98	99	99	99	99	99	100	100	100	100	100	100	100
75	80	80	98	98	99	99	98	99	99	99	99	99	99	99	99
100	92	88	100	100	99	98	100	99	99	99	99	99	100	100	99
101	100	100	99	100	99	99	99	99	99	99	100	99	99	99	99
92	90	86	100	100	99	98	99	100	100	100	100	100	100	100	100
94	93	90	98	99	98	99	99	99	99	99	98	98	99	99	99
80	84	80	97	98	98	98	99	99	99	99	98	99	98	98	99
86	92	88	100	100	100	99	99	99	99	99	99	99	100	100	100
68	67	66	100	99	100	99	100	100	100	100	100	100	99	99	99
76	76	75	99	99	99	98	99	99	99	98	100	100	99	100	100
76	70	70	99	100	99	98	99	100	100	100	100	100	100	100	100
70	68	70	98	98	99	99	99	99	99	99	99	99	99	99	99
100	98	99	100	100	99	99	100	100	100	100	100	100	100	100	100
72	71	71	97	98	98	99	99	99	99	99	100	99	100	99	99
86	88	86	100	99	99	99	100	100	100	100	100	100	99	99	98
112	107	105	97	98	98	99	99	99	98	99	99	99	100	100	100
91	90	90	96	97	98	98	98	98	99	99	99	99	99	99	100
102	102	99	99	98	98	99	99	99	99	99	99	100	99	100	99
100	98	99	100	99	100	99	99	99	100	100	99	99	99	99	99
94	90	93	99	100	99	99	99	99	99	99	99	99	99	100	99
78	76	65	98	97	98	98	99	99	99	99	99	99	99	99	99
68	67	66	98	99	99	99	99	99	99	99	99	99	99	100	100
85	86	88	100	100	99	99	100	100	100	100	100	99	98	99	100
68	64	66	99	98	98	98	99	98	100	100	100	100	98	98	100
100	94	94	98	99	99	99	99	99	99	100	99	100	99	99	99
66	66	68	100	99	99	99	100	100	100	100	100	99	99	99	99
70	74	68	99	98	98	98	99	99	98	99	98	99	99	99	99
88	86	85	97	98	97	98	99	99	100	100	100	100	100	100	100
70	72	70	98	99	99	97	98	99	99	99	99	99	99	99	99
8	84	88	100	99	98	97	99	99	99	99	99	99	99	99	99
68	64	68	98	97	98	98	99	99	100	100	100	100	100	100	100
72	70	68	98	98	98	98	98	99	99	99	100	100	100	100	100

						SBP											
Sl.NO	IP NUMBER	GENDER	AGE	WEIGHT	ASA	BASAL	10	20	30	INDUCTION	L-I	1	2	3	4	5	7
1	1094682	F	45	60	1	120	124	112	112	114	170	128	118	114	98	128	108
2	1034674	M	27	80	1	130	120	109	118	120	140	130	120	112	118	128	126
3	1034849	F	38	50	1	112	110	112	120	112	150	140	126	132	146	140	140
4	1035446	F	35	60	1	138	134	120	126	128	130	122	116	114	114	108	106
5	1035665	F	36	50	1	150	148	126	125	118	120	122	116	112	108	108	110
6	1035979	F	21	50	1	110	118	120	126	126	122	122	100	98	110	100	98
7	1039507	F	25	45	1	128	106	98	102	120	120	120	120	114	112	110	109
8	1039801	F	30	65	1	114	120	120	110	110	118	94	96	97	104	104	102
9	1039867	F	34	45	1	120	110	106	100	90	90	94	90	90	96	110	112
10	1078111	F	31	70	1	130	125	130	125	125	130	118	119	113	107	108	96
11	1076181	F	21	45	1	116	114	114	109	121	103	109	98	95	103	112	111
12	1079748	F	33	45	2	118	107	105	110	113	116	99	101	104	106	108	116
13	1080509	F	40	60	1	140	135	136	139	139	138	123	117	116	116	116	118
14	1080329	M	50	65	1	128	118	114	116	114	118	112	108	108	102	103	98
15	1081164	M	39	72	2	150	137	119	114	122	126	82	74	82	88	87	72
16	1080961	F	54	60	1	150	145	131	130	124	122	130	130	128	126	126	124
17	1083189	F	40	60	1	138	137	129	122	120	124	122	121	124	126	124	126
18	1081865	M	25	65	1	138	132	128	126	120	122	118	116	114	112	112	110
19	1081424	M	45	65	1	134	128	126	124	122	128	120	118	116	111	110	110
20	1082696	F	33	50	1	110	108	104	106	106	110	108	106	106	104	98	96
21	1083036	F	42	60	2	153	148	144	149	145	103	111	99	92	91	86	94
22	1083189	F	40	65	1	128	122	120	118	118	112	108	109	104	102	100	98
23	1083189	F	40	60	1	140	135	138	123	123	117	116	116	118	112	110	108
24	1083397	F	30	60	1	130	120	109	118	120	112	118	120	122	126	118	118
25	1077901	F	52	50	1	117	104	93	94	94	108	112	110	108	109	110	102
26	1085570	M	45	65	1	148	146	142	135	128	120	118	118	116	110	118	120
27	1084768	M	26	60	2	130	125	130	125	125	130	118	119	113	107	108	96
28	1086734	M	25	50	1	126	118	112	116	112	118	112	108	106	102	103	98
29	1086700	F	22	55	1	148	137	118	112	122	125	82	72	82	88	87	70
30	1087430	F	22	50	1	150	144	131	130	124	120	132	130	128	126	126	124
31	1087928	F	38	55	1	137	124	116	114	114	108	106	104	106	104	106	102
32	1088571	F	37	60	1	138	134	130	122	122	116	117	117	118	113	110	108
33	1086571	M	45	70	1	109	106	104	104	104	119	107	105	104	103	97	95
34	1075882	M	29	60	1	153	148	144	149	145	103	111	99	92	91	86	94
35	1081221	F	52	60	1	142	138	136	130	128	128	126	118	116	110	118	116
36	1099955	M	57	67	2	167	147	128	130	144	130	116	100	85	88	86	85
37	1080667	F	42	70	1	130	124	118	111	87	85	90	90	89	90	89	90
38	1098674	F	42	60	1	142	138	136	130	128	128	126	118	116	110	118	116
39	1078112	F	31	70	1	130	125	130	125	125	130	118	119	11	107	108	96
40	1087431	M	21	67	1	116	114	114	109	121	103	109	98	95	103	112	111
41	1084572	F	40	60	2	154	148	143	142	140	109	115	119	120	118	114	111

	DBP																	
10	BASAL	10	20	30	NDUCTIO	L-I	1	2	3	4	5	7	10	BASAL	10	20	30	INDUCTION
108	86	80	78	80	80	120	88	80	74	70	90	76	80	91	101	98	88	91
122	74	78	71	60	70	90	76	70	70	74	83	90	86	86	89	102	79	86
150	72	72	62	69	70	90	90	86	88	88	96	96	92	86	106	94	86	86
110	82	82	80	74	84	84	84	83	76	73	74	74	76	88	98	102	98	98
108	86	84	86	85	80	78	81	76	70	70	66	70	72	108	98	90	80	82
98	86	78	80	90	90	90	96	68	70	82	74	70	68	86	110	106	99	88
106	80	60	58	66	70	80	84	84	80	78	70	76	70	102	107	110	111	82
106	80	86	80	74	74	89	75	62	67	67	66	66	68	82	84	90	82	86
108	76	64	66	60	50	52	54	50	47	59	70	71	68	84	76	74	88	80
90	84	84	81	86	88	86	85	86	78	71	70	61	59	76	72	77	80	100
107	74	68	68	62	71	65	71	51	49	57	76	75	66	82	98	97	89	88
114	75	70	69	70	76	84	75	76	75	76	73	79	76	83	87	88	82	88
118	85	81	83	86	86	98	82	82	78	78	77	81	82	86	89	81	73	104
100	82	72	76	80	78	72	70	69	71	72	72	68	72	77	78	81	76	80
85	97	91	78	73	82	85	58	53	56	58	58	51	56	64	65	67	61	95
120	93	88	87	88	82	80	84	86	80	84	82	84	82	71	84	87	81	99
124	77	801	80	72	76	74	78	78	82	84	80	76	78	100	101	96	90	84
110	92	86	84	82	82	80	84	76	78	76	78	80	74	83	83	73	78	76
108	84	82	84	82	82	86	78	68	66	70	72	76	70	88	78	84	67	68
92	74	76	68	66	68	70	64	62	60	58	58	58	56	72	88	87	80	58
93	123	112	108	112	102	60	85	61	64	60	62	56	51	88	96	84	87	90
99	82	78	64	72	78	72	68	69	70	72	68	70	68	84	86	90	92	80
110	85	80	76	82	82	82	78	78	81	82	70	68	72	104	111	96	94	90
112	74	78	71	60	70	70	74	70	86	90	94	78	70	93	94	90	88	86
100	84	74	70	76	74	70	82	70	78	79	76	70	68	80	82	78	79	82
122	98	96	92	88	90	85	76	75	72	70	72	74	78	95	99	66	68	65
90	85	84	81	86	88	86	85	86	78	71	70	61	59	99	86	92	94	100
100	80	74	76	80	78	72	70	68	70	72	68	72	72	90	88	92	94	82
85	98	90	78	73	82	84	58	53	56	58	58	50	56	84	74	64	70	94
120	92	86	87	87	80	80	84	86	80	84	82	82	84	72	78	74	76	98
100	84	80	76	74	76	70	68	66	65	66	68	69	66	76	76	78	74	76
111	84	82	78	80	84	80	76	78	80	81	72	69	72	68	69	64	70	98
91	72	67	65	66	66	70	62	62	60	54	55	57	58	74	68	66	76	56
93	123	112	108	112	102	60	85	61	64	60	62	56	51	64	58	66	64	90
112	90	86	84	82	78	78	76	78	80	81	72	69	72	90	91	78	68	98
95	89	88	77	80	86	82	70	63	62	59	56	56	62	88	80	98	88	105
90	80	78	72	62	51	62	64	62	59	59	64	68	70	92	84	78	78	68
112	90	86	84	82	78	78	76	78	70	68	68	68	70	80	84	78	80	6
90	84	84	81	86	88	86	85	86	78	71	70	61	59	100	101	96	97	90
107	74	68	68	62	71	65	71	51	49	57	76	75	66	88	78	84	67	70
108	94	90	92	90	84	75	72	70	76	78	81	82	76	100	98	96	84	82

MAP								HR											
L-I	1	2	3	4	5	7	10	BASAL	10	20	30	INDUCTION	L-I	1	2	3	4	5	7
136	101	98	88	79	102	86	89	70	70	68	62	62	110	100	98	98	99	94	86
106	94	86	84	88	98	102	98	68	89	70	64	68	88	86	82	78	76	80	79
110	106	99	102	107	110	110	111	70	68	50	58	70	90	83	77	74	80	77	80
100	96	94	89	87	86	85	88	83	100	88	97	94	106	96	93	90	96	93	91
84	90	82	84	76	74	88	80	60	62	60	58	58	60	62	68	66	70	72	68
84	86	72	76	80	76	72	77	100	86	88	88	88	90	91	95	94	92	79	88
97	98	97	89	83	87	83	87	70	68	54	60	64	79	80	80	78	82	69	66
89	81	73	77	79	79	77	81	100	103	99	100	106	100	88	89	91	85	82	79
65	67	64	61	71	84	87	81	82	78	78	70	68	65	62	60	60	58	57	56
101	96	97	90	83	83	73	69	98	95	93	88	99	106	109	107	110	88	88	86
78	84	67	64	72	88	87	80	101	78	72	78	78	97	85	80	80	75	69	69
95	83	85	84	86	85	91	90	90	94	88	90	100	129	87	85	83	85	87	90
111	96	94	91	91	90	93	94	83	79	78	79	87	77	87	111	101	106	92	85
82	82	78	79	76	79	80	82	62	60	58	57	57	66	64	64	62	60	64	62
99	66	60	65	68	68	58	66	77	75	72	63	75	69	62	59	58	56	54	55
86	92	94	90	88	92	94	92	86	76	77	74	74	78	74	76	74	70	68	70
74	64	68	70	72	78	74	76	68	65	61	57	58	59	60	60	59	58	60	62
76	78	74	74	68	64	68	66	84	78	74	72	75	80	76	72	68	69	70	72
69	64	70	74	74	68	66	58	78	69	64	64	69	74	68	66	64	66	68	64
60	58	56	57	56	52	54	56	80	76	76	74	74	76	72	70	68	66	68	64
69	91	71	68	67	66	65	61	92	86	86	88	86	78	77	79	76	73	69	67
80	76	72	73	70	68	64	69	84	72	68	70	70	68	69	64	66	70	64	62
90	91	91	93	86	74	64	68	83	76	78	76	72	76	74	72	70	68	72	70
84	88	86	98	102	88	80	84	64	68	62	60	62	72	70	76	72	68	68	70
84	86	76	82	89	80	76	72	94	90	86	80	82	84	78	76	76	78	72	74
68	58	66	70	66	58	68	60	85	75	70	76	68	70	74	75	70	68	66	62
101	96	97	90	89	83	73	69	98	95	93	88	99	105	106	107	110	88	88	86
80	802	80	78	76	78	80	83	64	60	58	50	57	66	62	64	62	60	64	60
99	66	60	65	66	68	58	66	76	75	72	63	75	68	64	59	58	54	54	55
86	92	94	90	90	92	94	92	76	69	64	62	72	78	72	76	74	70	66	70
78	84	68	64	68	66	70	72	84	79	77	76	74	72	64	68	68	72	72	68
96	90	91	94	96	84	74	70	82	74	77	78	70	74	74	71	70	66	70	70
60	57	56	57	57	53	55	56	80	74	76	74	75	77	72	71	67	65	68	64
69	91	71	68	67	66	65	61	92	86	86	88	86	78	77	79	76	73	69	67
96	90	91	94	84	74	70	76	82	74	77	78	70	74	74	71	70	66	70	70
98	85	75	69	68	66	65	73	76	75	71	90	76	91	84	82	83	80	75	75
69	72	71	69	69	72	70	75	77	70	70	77	65	65	60	61	58	58	58	60
65	67	64	62	71	84	87	81	82	78	78	70	68	65	62	60	60	58	57	56
100	101	96	97	90	83	84	78	98	95	9	88	99	105	109	107	110	88	88	86
64	72	88	87	80	70	78	68	101	78	72	78	78	97	85	80	80	75	69	69
76	78	72	78	79	80	76	74	100	92	94	82	84	78	74	78	76	77	72	68

	SPO2												
10	BASAL	10	20	30	INDUCTION	L-I	1	2	3	4	5	7	10
90	98	99	99	99	100	100	100	100	100	100	100	100	100
78	99	99	99	99	100	100	100	100	100	100	100	100	100
86	99	99	99	99	100	100	100	100	100	100	100	100	100
94	99	99	99	99	100	100	100	100	100	100	100	100	100
68	99	99	99	99	100	100	100	100	100	100	100	100	100
80	99	99	99	99	100	100	100	100	100	100	100	100	100
68	99	99	99	99	100	100	100	100	100	100	100	100	100
77	99	99	99	99	100	100	100	100	100	100	100	100	100
60	99	99	99	99	100	100	100	100	100	100	100	100	100
97	99	99	99	99	100	100	100	100	100	100	100	100	100
70	99	99	99	99	100	100	100	100	100	100	100	100	100
88	99	99	99	99	100	100	100	100	100	100	100	100	100
80	99	99	99	99	100	100	100	100	100	100	100	100	100
66	99	99	99	99	100	100	100	100	100	100	100	100	100
58	99	99	99	99	100	100	100	100	100	100	100	100	100
70	99	99	99	99	100	100	100	100	100	100	100	100	100
64	99	99	99	99	100	100	100	100	100	100	100	100	100
70	100	100	100	100	100	100	100	100	100	100	100	100	100
64	97	98	98	98	100	100	100	100	100	100	100	100	100
68	98	99	99	99	100	100	100	100	100	100	100	100	100
65	100	100	100	100	100	100	100	100	100	100	100	100	100
64	99	99	98	98	100	100	100	100	100	100	100	100	100
72	100	100	100	100	100	100	100	100	100	100	100	100	100
72	99	99	99	99	100	100	100	100	100	100	100	100	100
70	100	100	100	100	100	100	100	100	100	100	100	100	100
68	98	98	99	99	100	100	100	100	100	100	100	100	100
97	98	99	99	98	100	100	100	100	100	100	100	100	100
66	99	99	99	99	100	100	100	100	100	100	100	100	100
58	99	99	98	99	100	100	100	100	100	100	100	100	100
70	99	98	98	99	100	100	100	100	100	100	100	100	100
66	99	98	97	98	100	100	100	100	100	100	100	100	100
72	99	98	98	99	100	100	100	100	100	100	100	100	100
69	99	99	98	99	100	100	100	100	100	100	100	100	100
65	100	100	100	100	100	100	100	100	100	100	100	100	100
72	100	100	100	100	100	100	100	100	100	100	100	100	100
72	100	100	100	100	100	100	100	100	100	100	100	100	100
67	100	100	100	100	100	100	100	100	100	100	100	100	100
60	98	98	97	99	100	100	100	100	100	100	100	100	100
97	100	100	100	100	100	100	100	100	100	100	100	100	100
70	98	99	99	99	100	100	100	100	100	100	100	100	100
64	98	98	99	99	99	100	100	100	100	100	100	100	100