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**“COMPARISON OF SUBLINGUAL NITROGLYCERIN  
SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING  
THE PRESSOR RESPONSE TO EXTUBATION: A ONE  
YEAR HOSPITAL BASED RANDOMISED CONTROLLED  
TRIAL”**

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**By**

**REG NO. BA0117005**

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**Submitted to the**

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**In Partial Fulfillment of the requirements for the degree of**

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**in**

**ANAESTHESIOLOGY**

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

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**APRIL – 2020**

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

**ENDORSEMENT BY THE HOD/PRINCIPAL/  
HEAD OF THE INSTITUTION**

This is to certify that the dissertation entitled“**COMPARISON OF SUBLINGUAL NITROGLYCERIN SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR RESPONSE TO EXTUBATION: A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL**” is a bonafide research work done by **REG NO. BA0117005.**

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Sir/Madam,

The softcopy of thesis entitled "COMPARISON OF SUBLINGUAL NITROGLYCERIN SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR RESPONSE TO EXTUBATION – A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROLLED 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 7% (Seven percentage) which is within the acceptable limits of 10% as per the guidelines given by UGC.

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## LIST OF ABBREVIATIONS

<b>HR</b>	-	<b>Heart Rate</b>
<b>SBP</b>	-	<b>Systolic Blood Pressure</b>
<b>DBP</b>	-	<b>Diastolic Blood Pressure</b>
<b>MAP</b>	-	<b>Mean Arterial Pressure</b>
<b>SpO2</b>	-	<b>Percentage of oxygen saturation</b>
<b>NTG</b>	-	<b>Nitroglycerin</b>
<b>NS</b>	-	<b>Normal Saline</b>
<b>CBC</b>	-	<b>Complete Blood Count</b>
<b>RBS</b>	-	<b>Random Blood Sugar</b>
<b>ECG</b>	-	<b>Electrocardiogram</b>
<b>CXR</b>	-	<b>Chest X- Ray</b>
<b>NIBP</b>	-	<b>Non Invasive Blood Pressure</b>
<b>PACU</b>	-	<b>Post Anaesthesia Care Unit</b>
<b>ASA</b>	-	<b>American Society of Anaesthesiologist</b>
<b>S.D</b>	-	<b>Standard Deviation</b>
<b>mg</b>	-	<b>milligram</b>
<b>PR</b>	-	<b>Pulse Rate</b>
<b>RR</b>	-	<b>Respiratory Rate</b>
<b>Temp</b>	-	<b>Temperature</b>
	-	<b>alpha</b>
	-	<b>Beta</b>

## **ABSTRACT**

### **Introduction**

The pressor response to extubation is seen in the form of increased HR, SBP, DBP and MAP. This effect may be well tolerated in ASA I patients but have deleterious effects on patient with history of cardiac diseases, CVA, Hypertensive individuals. Various methods have been tried to attenuate the response to extubation such as non pharmacological methods like extubation in deeper plane of anesthesia , using supra glottis airway devices and pharmacological methods such as Magnesium sulphate, dexmedetomidine, clonidine, fentanyl, remifentanyl, NTG etc.

### **OBJECTIVES**

To compare the efficacy of one puff of sublingual NTG spray V/s one puff of NS spray to attenuate pressor response to extubation.

### **METHODOLOGY**

The present study was conducted at, KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi 590010 on 60 patients between the age group of 18-60 years of either gender belonging to ASA I and II undergoing elective surgeries under GA were included in the study and randomized to 2 groups. Group A received one puff of Sublingual NTG spray (0.4 mg) and Group B received one puff of NS spray 1 minute after neuromuscular reversal was given. HR, SBP, DBP, MAP and SpO2 were recorded before reversal (TR) and at the time of reversal(To) and thereafter every minute till 10 minutes. Time of extubation was noted. Side effects like hypotension were noted.

## **RESULTS**

It was observed that there was increase in heart rate, systolic blood pressor and diastolic blood pressure during extubation but NTG group had better hemodynamic stability as compared with NS group. This attenuation of pressor response to extubation ( SBP, DBP, MAP) in group A when compared to group B which was statistically highly significant with p value being <0.0001. Tachycardia was observed in both the groups. NTG is known to cause reflex tachycardia but in our study it was not that significant.

## **CONCLUSION**

1 puff(0.4 mg) of sublingual NTG spray is effective in attenuating pressor response to extubation which is easy to administer, safe and cost effective.

## **KEYWORDS:**

General anaesthesia, Laryngoscopy, Pressor response to extubation, NTG spray

## TABLE OF CONTENTS

<b>SL NO.</b>	<b>SECTIONS</b>	<b>PAGE NO.</b>
<b>1</b>	<b>INTRODUCTION</b>	<b>1-2</b>
<b>2</b>	<b>OBJECTIVES</b>	<b>3</b>
<b>3</b>	<b>REVIEW OF LITERATURE</b>	<b>4-10</b>
<b>5</b>	<b>METHODOLOGY</b>	<b>11-15</b>
<b>6</b>	<b>RESULTS</b>	<b>16-27</b>
<b>7</b>	<b>DISCUSSION</b>	<b>28-33</b>
<b>8</b>	<b>CONCLUSION</b>	<b>34</b>
<b>9</b>	<b>SUMMARY</b>	<b>35</b>
<b>10</b>	<b>BIBLIOGRAPHY</b>	<b>36-40</b>
<b>11</b>	<b>ANNEXURES</b>	
	<b>ANNEXURE I - INFORMED CONSENT</b>	<b>41-43</b>
	<b>ANNEXURE II – ETHICAL CLEARANCE</b>	<b>44</b>
	<b>ANNEXURE II - PROFORMA</b>	<b>45-47</b>
	<b>ANNEXURE III - PHOTOGRAPHS</b>	<b>48-51</b>
	<b>ANNEXURE IV - KEY TO MASTER CHART</b>	<b>52</b>

## LIST OF TABLES

TABLE NO	DESCRIPTION	PAGE NO
1	Demographic data for mean age	17
2	Demographic data percentage of male and female	18
3	ASA physical status	19
4	Heart Rate	20
5	Systolic Blood Pressure	22
6	Diastolic Blood Pressure	24
7	Mean Arterial Pressure	26

## LIST OF GRAPHS

TABLE NO	DESCRIPTION	PAGE NO
1	Demographic data for mean age	17
2	Demographic data percentage of male and female	18
3	ASA physical status	19
4	Heart Rate	21
5	Systolic Blood Pressure	22
6	Diastolic Blood Pressure	24
7	Mean Arterial Pressure	26

### LIST OF FIGURES

FIGURES NO	DESCRIPTION	PAGE NO
1	Nerve supply of larynx	28

### LIST OF PHOTOGRAPHS

PHOTOGRAPHS	DESCRIPTION	PAGE NO
1	NTG Spray Fig 1	47
2	NTG Spray Fig 2	48
3	NTG Spray VS. Normal Saline spray	49

## INTRODUCTION

Extubation is one of the most crucial part of general anaesthesia as there are marked hemodynamic changes to extubation<sup>(1)</sup> such as increase in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure to mention few. These changes even though transient may be troublesome in some individuals like people who are hypertensive, with past history of cerebrovascular accident, myocardial ischemia sometimes leading to arrhythmia and cardiac arrest.

The exact mechanism of extubation response<sup>(2)</sup> is not known but it is believed to involve both sympathetic and parasympathetic systems. The sympathetic response involves polysynaptic pathway with Glossopharyngeal and Vagus nerve forming afferent arc to the sympathetic nervous system via brain stem and spinal cord. This causes firing of adrenergic mediators such as norepinephrine and epinephrine which leads to increase in HR and blood pressure. Parasympathetic reflex is monosynaptic and is more common in children.

This hemodynamic response to extubation can be attenuated by number of non-pharmacological methods such as extubation in deeper planes of anaesthesia or by using laryngeal mask airway<sup>(3)(4)(5)</sup> and pharmacological methods such as topical anaesthesia using lignocaine<sup>(6)</sup> or pre-treatment with beta blockers<sup>(7)</sup>, fentanyl<sup>(8)(9)(10)</sup>, dexmedetomidine<sup>(10)(11)(12)(13)</sup>, remifentanyl<sup>(14)</sup>, prostaglandins<sup>(30)</sup>, magnesium sulphate<sup>(31)</sup> or nitroglycerin<sup>(15)(16)(17)(18)</sup>.

Ideal agent to attenuate hemodynamic response to extubation should be readily available, easy to administer, cost effective with fast onset of action and peak with minimal side effects.

Nitroglycerin is one of the most widely used drug to control intra-operative rise in blood pressure. Nitroglycerin is potent vasodilator, predominantly acting on

venules than arterioles by generating nitric oxide<sup>(19)(20)(8)</sup> (NO) in vascular smooth muscle.

Sublingual Nitroglycerin spray is used to treat acute hypertensive crisis and acute anginal attack which is simple and easy to use.

There are many studies showing the effect of sublingual Nitroglycerin spray to attenuate hemodynamic changes to intubation however very few have studied its effect during extubation.

Hence in our study we have observed the effect of sublingual NTG spray and compared it with normal saline spray to attenuate hemodynamic response to extubation.

## **OBJECTIVES**

### **Primary objective:**

To compare the effect of 1 puff of sublingual nitroglycerin spray versus 1 puff of normal saline spray in attenuating pressor response to extubation.

### **Secondary objective:**

To study side effects if any.

## REVIEW OF LITERATURE

Tracheal extubation after general anaesthesia requires skill and judgment learned through experience. Extubation is associated with increase in heart rate, increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure. Various methods have been tried to decrease this stressor response to extubation such as non pharmacological methods like using laryngeal mask airway<sup>(4)(3)(5)</sup> or extubation in deeper planes of anaesthesia and pharmacological methods such as pre-treatment with beta blockers<sup>(21)</sup>, fentanyl<sup>(8)(9)(10)</sup>, remifentanyl<sup>(14)</sup>, magnesium sulphate<sup>(31)</sup> or nitroglycerin.<sup>(15)(16)(17)(18)</sup>

In the study done by KatsuyaMikawa, Makato Hasegawa, Takeshi Suzuki<sup>(17)</sup> in the year 1991, where they assessed efficacy and safety of I.V Nitroglycerin to attenuate hypertensive response to laryngoscopy and intubation. Study was randomized controlled and double blind. In this study 30 patients belonging to ASA I posted for elective surgeries were randomized into three groups having 10 patients in each group. Group I patients received 1.5mcg/kg of Nitroglycerin whereas, Group II received 2.5 mcg/kg of NTG and group C received saline, administered through intravenous route, with start of laryngoscopy (lasting 30 seconds) which was attempted 2 minutes after administration of Thiopental sodium(5 mg/kg) and Vecuronium (0.2 mg/kg). Study concluded that Nitroglycerin is effective in attenuating hypertensive response to tracheal intubation.

Another study done by MohammadrezaSafavi, AzimHonarmand, NedaAzavi<sup>(16)</sup> titled “Attenuation of pressor response to tracheal intubation in severe preeclampsia: relative effectiveness of Nitroglycerin infusion, Sublingual Nifedepine and Intravenous Hydralazine” was undertaken in 2011. A total number of 120 patients who were undergoing elective caesarian section were randomized into three groups.

Each group received one of the following drugs before intubation\_ Nitroglycerin group receiving 5mcg/min infusion (Group NTG n=40), Nifedepine group receiving 10 mg sublingual tablet (Group NIF n=40), Hydralazine group receiving 5-10 mg Intravenous Hydralazine (Group H n=40). Patient were pre-oxygenated for 5 min and received the study drug following which anesthesia was induced with inj.Thiopentone 5mg/kg and Scoline 1.5mg/kg was given and Rapid sequence intubation was done after 100 seconds of giving the study drug. Heart rate, systolic arterial pressure, diastolic arterial pressure and mean arterial pressure were recorded pre induction, pre intubation and at 1, 3, 5 and 10 minute after intubation. This study concluded that attenuation of the pressor response to tracheal intubation was better with Nitroglycerin infusion in severe pre eclampsia.

A study titled “Attenuation of pressor response following intubation: Efficacy of nitroglycerin sub lingual spray done in the year 2016 by Indira Kumari, UdithaNaithani, Vinod Kumar Dadheech, D.S Pradeep, KhemrajMeena, DevendraVerma<sup>(22)</sup>”, 90 patients of ASA I and II, between 18-60 years scheduled for surgeries under general anesthesia were included. Study was prospective randomized controlled trial where patients were randomized to 3 groups with Group C (control group) receiving no Nitroglycerin spray while Group N1 receiving 1 puff of NTG spray whereas Group N2 receiving 2 puffs of NTG spray one minute prior intubation. Patients were pre oxygenated for 3 minutes and intubation was done as per standard general anesthesia technique. Immediately following induction Nitroglycerin spray was administered as one metered spray in Group N1 (400 mcg) and two metered sprays (800 mcg) in group N2 and group C did not receive any drug. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded at T1 : baseline (before premedication), T2 : just before intubation (60

seconds after induction and nitroglycerin spray), T3: just after intubation, T4: 1 min after after intubation, T5: 2min after intubation, T6: 5 min after intubation, T7: 10 min after intubation. The study concluded that Nitroglycerin both in a dose of 1 spray or 2 spray which was given 1 minute prior to intubation is effective in attenuating the pressor response in normotensive ASA I and II patients.

In the study “comparison of different doses of Nitroglycerin spray for attenuation of stress response to laryngoscopy” during intubation by Mona Panchal, Upasana Bhatia where 50 ASA I and II patients of either sex aged 20-60 years scheduled for elective surgery were included. Study design was randomized controlled study where patients were randomized in to , Group I (n=25) received 400 mcg and Group II (n=25) received 800mcg of intranasal nitroglycerin spray 2 minutes before laryngoscopy and endotracheal intubation. General anesthesia was administered as per standard technique and patients were observed after laryngoscopy and intubation every minute till 5 minutes for any complications. Heart rate, systolic blood pressure, diastolic blood pressure were recorded at T1: baseline (before premedication), T2: just before intubation, T3: just after intubation, T4: 1 minute after intubation, T5: 2minute after intubation, T6: 3 minute after intubation, T7:4 minutes after intubation, T8: 5minutes after intubation. Study concluded that Nitroglycerin spray in a dose of 400mcg given 2 minutes prior to induction of generalanesthesia is effective in attenuating pressor response to laryngoscopy and intubation where as 800 mcg dose does not have any extra advantage over 400 mcg of nitroglycerin spray.

In a study done by V.MadhuriGopal titled “Comparative study of pressor response to laryngoscopy and intubation with oral spray of Nitroglycerin and oropharyngeal spray of lignocaine<sup>(32)</sup>” done in the year 2017 where 60 patients belonging to either sex aged between 18-60 years belonging to ASA I and II with

Mallampati class I and II were included. Study design was prospective randomized study where study population were randomized into 30 patients in each group. Anaesthesia was induced as per general anesthesia guidelines and endotracheal intubation was done with appropriate size endotracheal tube. Group L- Lignocaine group (n=30) received oropharyngeal Lignocaine 10% spray 100mg 3 minutes before induction, Group N – Nitroglycerin group (n=30) received oral nitroglycerin spray 0.8mg 30 seconds before induction. Heart rate, systolic and diastolic blood pressure were recorded at baseline, at induction, 1, 3, 5 and 10 minute interval after laryngoscopy. The study concluded that Nitroglycerin spray group was better in attenuating pressor response to laryngoscopy and intubation without side effects compared to Lignocaine spray group.

“A comparative study to evaluate the effects of NTG and Esmolol on hemodynamic parameters in controlled hypertensive patients during emergence from anaesthesia and extubation” a study undertaken by R.Vacchani, Rahul Gulati published in 2017 in which 60 controlled hypertensives were included. Patients belonged to ASA status II and III, aged 30-65 years were randomly divided into group I (NTG infusion 0.5mcg/kg/min) and group II (Esmolol 100mcg/kg/min). After completion of surgery and before reversal, the study drug was started and continued during extubation. Data were recorded at following stages- pre-operatively, just before reversal, just after reversal, at the time of extubation, 1 and 3 minutes after extubation. Statistical comparison of drugs was done by student's t tests. It was noted that there was increase in HR in both the groups. Study concluded that intravenous Esmolol had better hemodynamic stability but both attenuate extubation response without any adverse effects and complications.

A study undertaken in 2016 by HarminderKaur, Sanjay Kumar Morwal, Fareed Ahmed and Monika Rathore titled “ A comparative study of effects of intravenous Nitroglycerin and Esmolol on hemodynamic response following tracheal extubation<sup>(18)</sup>” where study was double blind randomized comparative and interventional. A total of 100 patients belonging to ASA I, age between 20-60 years were randomized to Group A ( Esmolol group n=50) who received Intravenous Esmolol 1mg/kg and Group B (Nitroglycerin group n=50) who received intravenous Nitroglycerin 1mcg/kg. After pre medication patients were intubated as per general anesthesia protocol. Once surgery was concluded and spontaneous respiratory attempts were noted residual neuromuscular blockade was reversed and one minute after reversal of drug study drug was given over 60 seconds. Extubation was done as per criteria. Hemodynamic parameters were noted every minute till extubation from time of stoppage of Isoflurane. After extubation HR, SBP,DBP, MAP and O2 saturation were noted every 2 minutes for 10 minutes, then every 5 minutes for 30 minutes. Unpaired T test was used to test significance of means and Chi square test was used to test significance of proportions, ANOVA test was used for intra and inter group variance. This study concluded that Esmolol had better hemodynamic stability compared to Nitroglycerin but rise in systolic blood pressure, diastolic blood pressure and mean arterial pressure is significantly controlled by intravenous Nitroglycerin.

AmeyaArunTagalpallewar, Bhushan.M.Ambare, J.N.Agrawal and Monica.S.Masare carried out a study in 2017 named ‘Efficacy of sublingual nitroglycerin spray in attenuation of hemodynamics to tracheal extubation<sup>(23)</sup>’, where the study was prospective, randomized controlled, open study enrolling 60 normotensive and 60 hypertensive patients (total 120 patients).This study included ASA I and II patients, weighing 20-60 kgs who were posted for elective surgery under

general anesthesia. Both the types of patients were randomized into two groups of 30 patients in each group, where 50% received NTG spray and 50% did not receive spray. Patients were induced as per general anesthesia protocol. At the end of surgery the study group was given two puffs of NTG spray through sublingual route when spontaneous respiratory attempts were noticed. Immediately following this residual neuromuscular blockade was reversed. After extubation heart rate, SBP, DBP and oxygen saturation was noted every 2 minutes for 10 minutes and thereafter every 5 minutes. Paired t test was used to compare intra-group hemodynamic variables. Inter-group analysis of hemodynamic parameters was done by unpaired t test. In the study they observed that in normotensive and hypertensive group HR increased after NTG spray and after reversal. After NTG spray SBP, DBP and MAP were close to baseline for 2 minutes during extubation. Increase in HR along with reduction in BP seen after Nitroglycerin spray did not produce significant increase in RPP as compared to control group.

“Deepak Singh, Omprakash Sundrani, Ameya Tagalpallewar, K.K. Sahare, C.P. Bhagat, D.S. Patel in their study -The effects of NTG sublingual spray to blunt the hemodynamic response to endotracheal extubation in lumbar disc surgery<sup>(15)</sup>” done in 2015 where they performed randomized, prospective, controlled open study on 60 patients. Patients were randomly divided into group A (n=30) or group B control (n=30). Patients were induced as per general anaesthesia protocol. At the end of surgery when spontaneous respiratory attempts were noted two puffs of NTG sublingual spray was given to group A patients whereas no group B patients did not receive any drug. Hemodynamic parameters were noted before administration of drug, at the time of extubation and also at 1 minute, 3 minutes, 5 minutes, 10 minutes, 15 minutes and 20 minutes after extubation. Statistics was done for the data using SPSS

version 17.0. The study proved that sublingual NTG spray (800mcg) administered prior to extubation can prevent hypertension. The HR and Rate Pressure Product was comparable in Group A and Group B.

A study titled “A randomized controlled study of tracheal extubation response following Nitroglycerin spray in normotensive and hypertensive patients” by Dr. Sunil Tuljapure, Dr.VaishaliKotambkarIn 2015 where 120, ASA I and II normotensives ( n=60) and hypertensives(n=60) undergoing general anaesthesia with ET tube intubation were enrolled. Both type of patients were randomized to 2 groups consisting of 30 patients in each group, 50% receiving NTG spray (Group A and Group C) and 50% not receiving NTG spray (Group B andD).Standard anaesthesia techniques were used for all patients at the time of induction. When respiratory attempts were noted at the end of surgery, group A and C received 2 puffs of sublingual Nitroglycerin spray, immediately following this neuromuscular blockade was reversed. Hemodynamic parameters were noted every one minute till extubation. Patients were extubated once criteria were met. After extubation heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation were noted every 2 minutes for 10 minutes (0,2,4,6,8,10) there after every 5 minutes every (15,20,25,30) in all patients. Statistical analysis was done for the data using appropriate study design. This study concluded that Nitroglycerin spray is effective in attenuating extubation response in both hypertensive and normotensive patients.

## **MATERIAL AND METHODS**

Present study titled “Comparison of Sublingual Nitroglycerin Spray vs. Normal saline Spray in Attenuating The Pressor Response to Extubation: A One Year Hospital Based Randomized Controlled Trial” was undertaken in the “Department of Anaesthesiology, KLE’S Dr. Prabhakar Kore Hospital, Belagavi during the period of January 2018 to December 2018”.

### **Source of data:**

Participants in the study 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 intubation in tertiary hospital at Nehru Nagar, Belagavi between January 2018 to December 2018 were included.

### **Type of study:**

A one year randomized controlled trial.

### **Study duration:**

One year from January 2018 to December 2018.

### **Criteria for selecting patients were:**

#### **Inclusion Criteria:**

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

**Exclusion Criteria:**

- Hypertensive patients.
- ASA grade III and IV
- Patients allergic to study drug
- Patients with difficult airway

**Sample size:**

Total sample – 60

Group A - 30

Group B - 30

**Sample size calculation:**

Type I error rate = 0.05

Type II error rate = 0.02

And power of study being 80% and using the formula:

$$n = \frac{2(Z_{\alpha} + Z_{\beta})^2 p(1-p)}{(p_0 - p_1)^2}$$
$$n = \frac{2(1.96 + 0.84)^2 (75)(25)}{(5.5 - 14.5)^2}$$

n=19.2

n= sample size

Z<sub>α</sub> = 1.96

Z<sub>β</sub> = 0.84

P<sub>0</sub> = 5.4

$P_1=14.5$

For sake of consistent results sample size has been taken as 60. There are two groups of 30 each.

**Methods:**

Approval from ethical committee and written informed consent was obtained. A total of 60 patients undergoing surgery under general anaesthesia with endotracheal intubation were included in the study.

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

**Group A:** where patients received 1 puff of sublingual nitroglycerin spray 1 minute after administration of reversal.

**Group B:** where patients received 1 puff of sublingual normal saline spray 1 minute after administration of reversal.

A thorough pre-anaesthetic evaluation was done on day before surgery. Detailed medical history was elicited and detailed physical examination was carried out. Patients were kept nil per orally for 8 hours prior to surgery. Preoperatively investigations like CBC, RBS and Sr. Creatinine were done. ECG and CXR were done if patient was more than 40 years of age.

On the day of surgery 18G intravenous line was secured in the pre-operative recovery room and IV fluids were started. Once patient was shifted to operation theatre standard monitors (i.e. Pulse oxymeter, ECG, NIBP) were attached.

Patients were preoxygenated with 100% Oxygen for three minutes. Patients were premedicated with Inj. Glycopyrrolate 0.005mg/kg and Inj. Midazolam 0.05mg/kg and Inj. Fentanyl 2mcg/kg.

Patient was induced with Inj.Thiopentone 5 mg/kg followed by Inj. Succinylcholine 2mg/kg. With the onset of neuromuscular blockade laryngoscopy was done and endotracheal intubation was done with appropriate size endotracheal tube.

Intraoperatively patients were maintained with Oxygen, Nitrous oxide and Isoflurane. Inj.Vecuronium in a dose of 0.1 mg/kg and maintenance with 1/4<sup>th</sup> of loading dose was given for neuromuscular blockade.

At the end of the procedure patients were reversed with Inj.Glycopyrrolate 0.01mg/kg and Inj Neostigmine 0.05mg/kg.

One minute after administration of reversal drug, Group A patient received one puff of NTG spray (GTN spray, Medley pharmaceuticals, India, 1 puff= 0.4mg) sublingually and group B patient received one puff of Normal Saline spray sublingually. Blinding was achieved by using identical spray bottles. The anaesthesiologist administering the spray and recording the various parameters was blinded to the drug.Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean blood pressure and SpO<sub>2</sub> were recorded at the time of administration of reversal (TR), at the time of administration of spray (T<sub>0</sub>) and subsequently every minute till 10 minutes. Patients were extubated when spontaneous respiratory attempts were adequate, patient obeyed to verbal commands and criteria for extubation were met. Time of extubation was also noted.

Incidences such as arrhythmia, hypotension or tachycardia or any other side effects were noted. Patients were kept in PACU for 2 hours after extubation and were

followed up for side effects or adverse events if any. Patients were removed from the study if there were extensive hemodynamic alteration intraoperatively and if patients required post - op ventilation.

**Statistical Analysis:**

The data was tabulated and master chart was prepared. Microsoft Excel was used to tabulate data and SPSS 22.0 and R environment version 3.2.2 was used to analyze data. The categorical data was tabulated as ratios and percentages and continuous data was presented mean  $\pm$  standard deviation. Student t test was used to find significance of study parameters on continuous data between two groups. A p value of  $< 0.05$  was considered statistically significant. The data was represented in tables and appropriate charts.

## RESULTS

This study titled “Comparison of sublingual nitroglycerin spray versus normal saline spray in attenuating the pressor response to extubation: a one year hospital based randomized control trial” was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Medical College, KAHER, Belagavi from January 2018 to December 2018. 60 patients were enrolled in the study after having met inclusion and exclusion criteria. Written informed consent in the vernacular language was taken from the patients. Patients were randomized into two groups consisting of 30 patients in each group using computer generated randomization table.

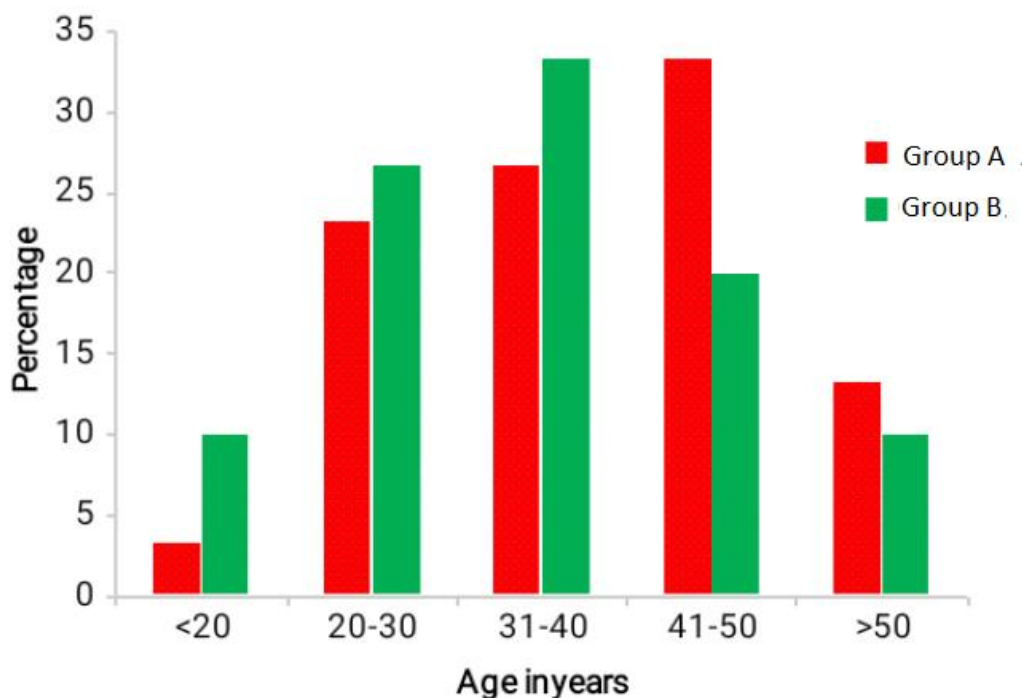
The data was tabulated on Microsoft Excel which was represented as Mean and Standard for all sets of data. Students “t” test has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameter. “Chi-square/ Fisher Exact test” has been used to find the significance of study parameters on categorical scale between two or more groups, Non parametric setting for Qualitative data analysis. Software: The statistical software namely “SPSS 22.0, and R environment ver.3.2.2” was used for data analysis and graphs and tables were generated using Microsoft Excel and Word.

**AGE DISTRIBUTION:**

The minimum age group was 19 years and maximum was 55 years in Group A. In Group B minimum age group was 19 years and maximum was 58 years. The mean age in Group A was 39.2 years and yielded a standard deviation of 11.74, in Group B the mean age was 35.9 years and yielded a standard deviation of 11.26. The p value was 0.266 which made age distribution in two groups comparable.

<b>GROUP A</b>	<b>GROUP B</b>
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Maximum	Minimum	Mean	S.D	Maximum	Minimum	Mean	S.D	P Value	Inference
55	19	39.23	11.74	58	18	35.90	11.26	0.2663	ns



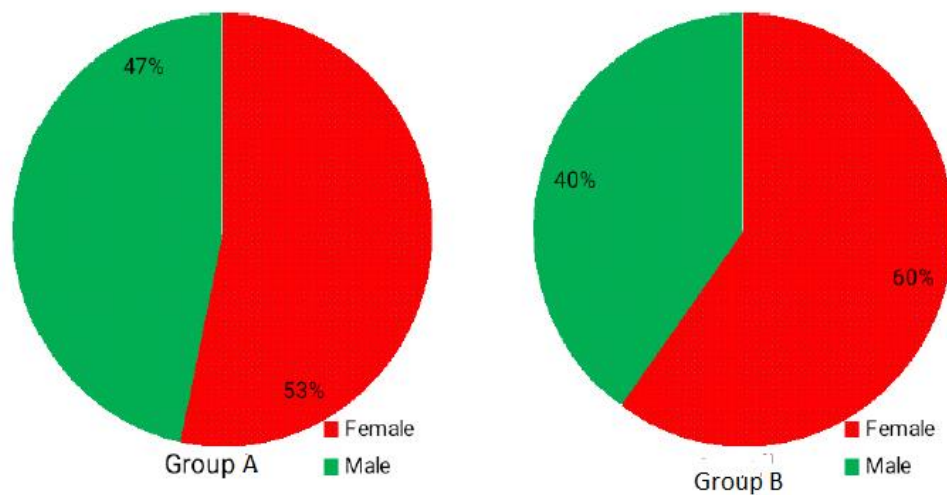
**GENDER DISTRIBUTION:**

In Group A there were 16 females and 14 males. In Group B there were 18 females and 12 males. The distribution of gender across both the groups was comparable with p value 0.602.

**GENDER DISTRIBUTION OF THE SAMPLE**

	<b>GROUP A</b>	<b>GROUP B</b>	<b>TOTAL</b>
<b>FEMALE</b>	16	18	34
<b>MALE</b>	14	12	26
<b>TOTAL</b>	30	30	60

GENDER DISTRIBUTION IN PERCENTAGE

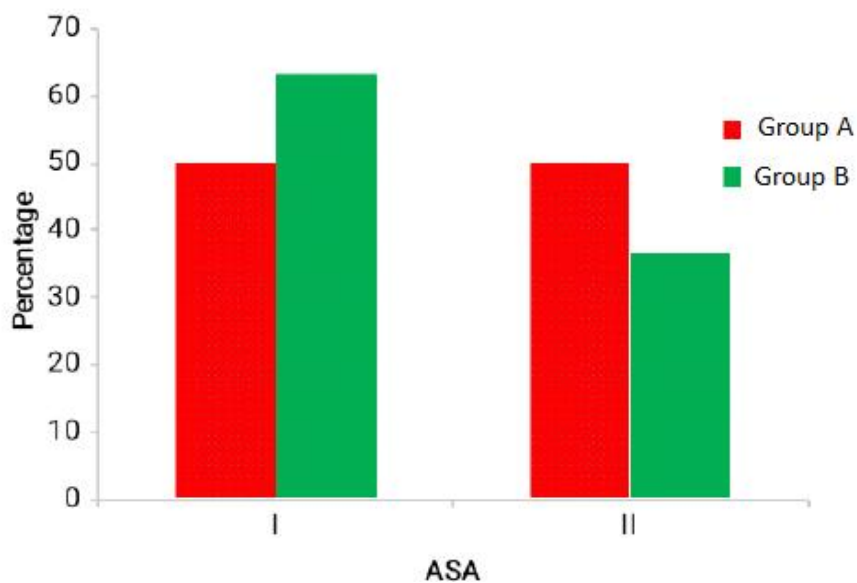


**ASA STATUS:**

There were 15 patients in Group A who were ASA I patients where as 15 patients were ASA II. Where as group B had 19 patients who were ASA I while 11 were of ASA II status. When compared, difference was statistically not significant with p value 0.297

**DISTRIBUTION OF ASA**

	<b>GROUP A</b>	<b>GROUP B</b>	<b>TOTAL</b>
<b>ASA I</b>	15	19	34
<b>ASA II</b>	15	11	26
<b>TOTAL</b>	30	30	60



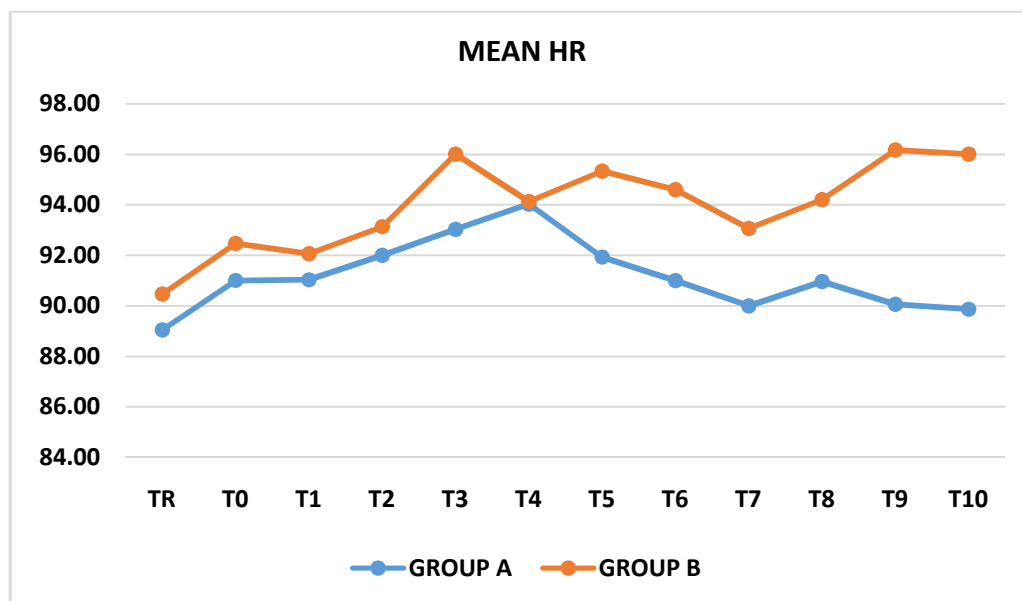
PERCENTAGE DISTRIBUTION OF ASA STATUS

After the surgery, 1 minute after the reversal of neuromuscular blockade, patients in Group A received 1 puff of sublingual Nitroglycerin while Group B patients received 1 puff of sublingual saline. Heart rate, SBP, DBP , MAP was recorded at the time of administration of reversal(TR), at the time of administration of spray (T0) and subsequently at one minute interval till 10 minutes.

Time of extubation was also noted. Time of extubation in both the groups was 3-4 minutes from the time of administration of reversal (TR).

**HEART RATE:****FOR HR**

	<b>GROUP A</b>		<b>GROUP B</b>		<b>P VALUE</b>	<b>INFERENCE</b>
	<b>MEAN</b>	<b>S.D.</b>	<b>MEAN</b>	<b>S.D.</b>		
<b>TR</b>	89.05	12.67	90.47	5.36	0.5730	NS
<b>T0</b>	91.01	12.66	92.47	5.35	0.5630	NS
<b>T1</b>	91.03	11.88	92.07	4.57	0.6582	NS
<b>T2</b>	92.00	9.50	93.13	4.29	0.5536	NS
<b>T3</b>	93.03	9.73	96.00	3.45	0.1209	NS
<b>T4</b>	94.03	10.49	94.13	3.79	0.9610	NS
<b>T5</b>	91.93	10.54	95.33	3.91	0.1030	NS
<b>T6</b>	91.00	10.34	94.60	4.01	0.0807	NS
<b>T7</b>	90.00	9.71	93.07	3.54	0.1097	NS
<b>T8</b>	90.97	9.30	94.20	3.84	0.0836	NS
<b>T9</b>	90.07	9.68	96.17	4.22	0.0112	S
<b>T10</b>	89.87	9.78	96.00	5.48	0.0340	S



### In Group A-

Mean HR at the time of administration of reversal was  $89.05 \pm 12.67$  (TR) and at the time of administration of NTG spray was  $91.01 \pm 12.66$  (T0).

Maximum increase in HR was seen at 4 minutes which was  $94.03 \pm 10.49$ . The HR subsequently reduced gradually reaching baseline at 10 minutes.

### In Group B-

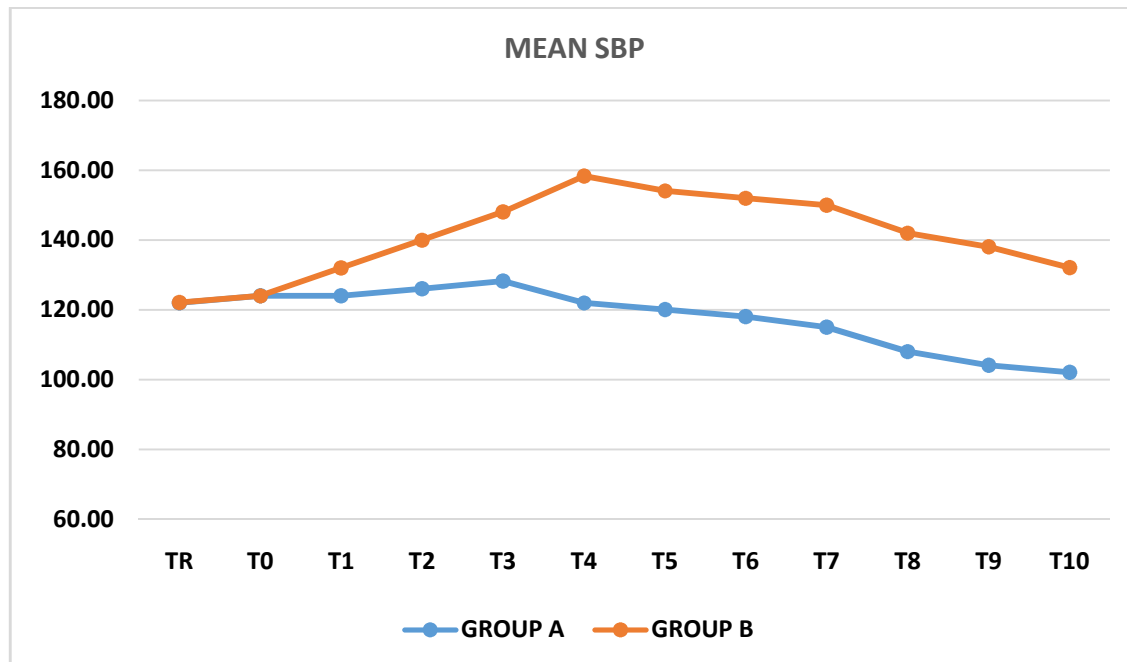
Mean HR at the time of administration of reversal was  $90.47 \pm 5.36$  (TR) and at the time of administration of saline spray (T0) was  $92.47 \pm 5.35$ .

Subsequently HR increased with maximum increase in HR seen at 3 minutes, with mean HR being  $96.00 \pm 3.45$ .

The HR remained high till 10 minutes and when compared with Group A the increase in HR was found to be statistically insignificant till 8 minutes.

**SYSTOLIC BLOOD PRESSURE:**

FOR SBP						
	GROUP A		GROUP B			
	MEAN	S.D.	MEAN	S.D.	P VALUE	INFERENCE
<b>TR</b>	122.00	8.67	122.03	3.55	0.9845	NS
<b>T0</b>	124.00	8.67	124.03	3.55	0.9845	NS
<b>T1</b>	124.00	5.41	132.00	3.66	< 0.0001	HS
<b>T2</b>	126.03	6.70	140.00	3.79	< 0.0001	HS
<b>T3</b>	128.20	6.29	148.03	3.04	< 0.0001	HS
<b>T4</b>	122.02	4.87	158.27	2.38	< 0.0001	HS
<b>T5</b>	120.03	4.73	154.13	3.64	< 0.0001	HS
<b>T6</b>	118.03	4.67	152.00	4.18	< 0.0001	HS
<b>T7</b>	115.00	4.35	149.97	3.60	< 0.0001	HS
<b>T8</b>	108.07	4.50	142.00	4.07	< 0.0001	HS
<b>T9</b>	104.07	4.04	138.00	4.25	< 0.0001	HS
<b>T10</b>	102.07	3.91	132.03	4.45	< 0.0001	HS



**In Group A –**

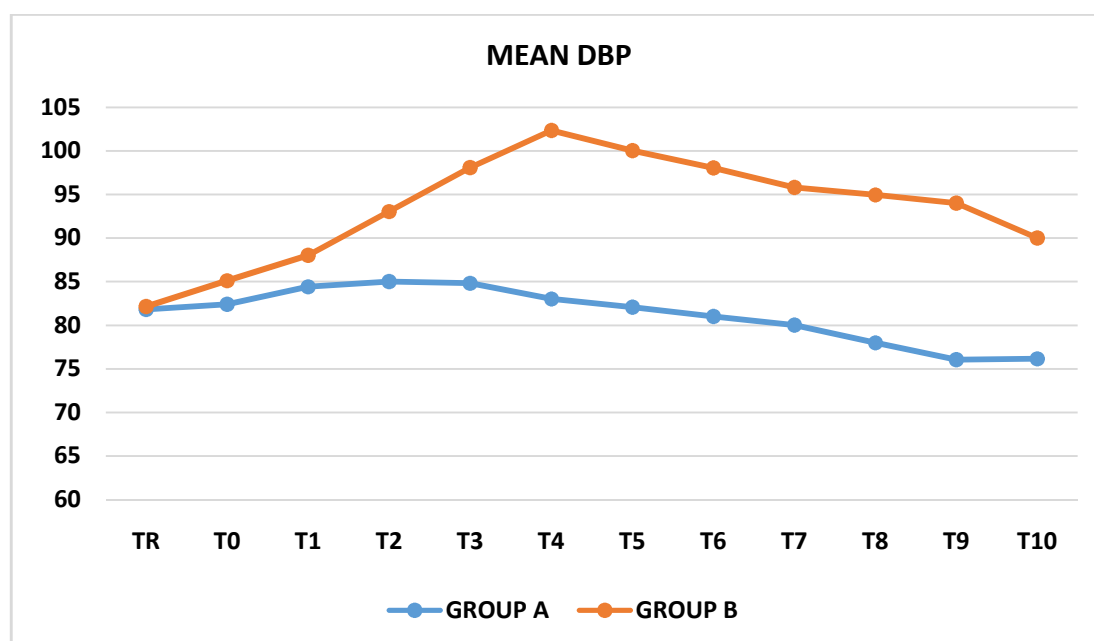
Mean SBP at the time of reversal (TR) was  $122.00 \pm 8.67$  and at the time of administration of NTG spray (T0) was  $124.00 \pm 8.67$ . The SBP increased till 3 minutes when the maximum mean BP was  $128.20 \pm 6.29$ . This SBP subsequently reduced gradually till 10 minutes (T10) which was  $102.07 \pm 3.91$ .

**Group B -**

Mean SBP at the time of reversal (TR) was  $122.03 \pm 3.55$  and at the time of administration of NTG spray (T0) was  $124.03 \pm 3.55$ . The SBP increased till 4 minutes (T4) when the maximum mean BP was  $158.27 \pm 2.38$ . This SBP remained high till 10 minutes. This increase in SBP when compared with that of group A was statistically highly significant.

**DIASTOLIC BLOOD PRESSURE:****FOR DBP**

	GROUP A		GROUP B		p VALUE	INFERENCE
	MEAN	S.D.	MEAN	S.D.		
<b>TR</b>	81.8	5.86	82.13	4.81	0.8106	NS
<b>T0</b>	82.40	8.14	85.13	4.81	0.1189	NS
<b>T1</b>	84.43	5.60	88.00	4.85	0.0107	S
<b>T2</b>	84.99	5.19	93.07	4.09	< 0.0001	HS
<b>T3</b>	84.83	6.64	98.07	3.47	< 0.0001	HS
<b>T4</b>	83.03	7.24	102.33	3.41	< 0.0001	HS
<b>T5</b>	82.07	5.81	100.03	4.49	< 0.0001	HS
<b>T6</b>	81.00	5.86	98.03	4.81	< 0.0001	HS
<b>T7</b>	80.00	6.31	95.80	4.21	< 0.0001	HS
<b>T8</b>	78.00	5.29	94.97	3.61	< 0.0001	HS
<b>T9</b>	76.03	3.41	94.00	3.05	< 0.0001	HS
<b>T10</b>	76.17	3.59	90.00	3.73	< 0.0001	HS



**In Group A –**

Mean DBP at the time of reversal (TR) was  $81.80 \pm 5.86$  and at the time of administration of NTG spray (T0) was  $82.40 \pm 8.14$ . The DBP increased till 3 minutes when the maximum mean BP was  $84.83 \pm 6.64$ . This DBP subsequently reduced gradually till 10 minutes (T10) with the mean being  $76.17 \pm 3.59$ .

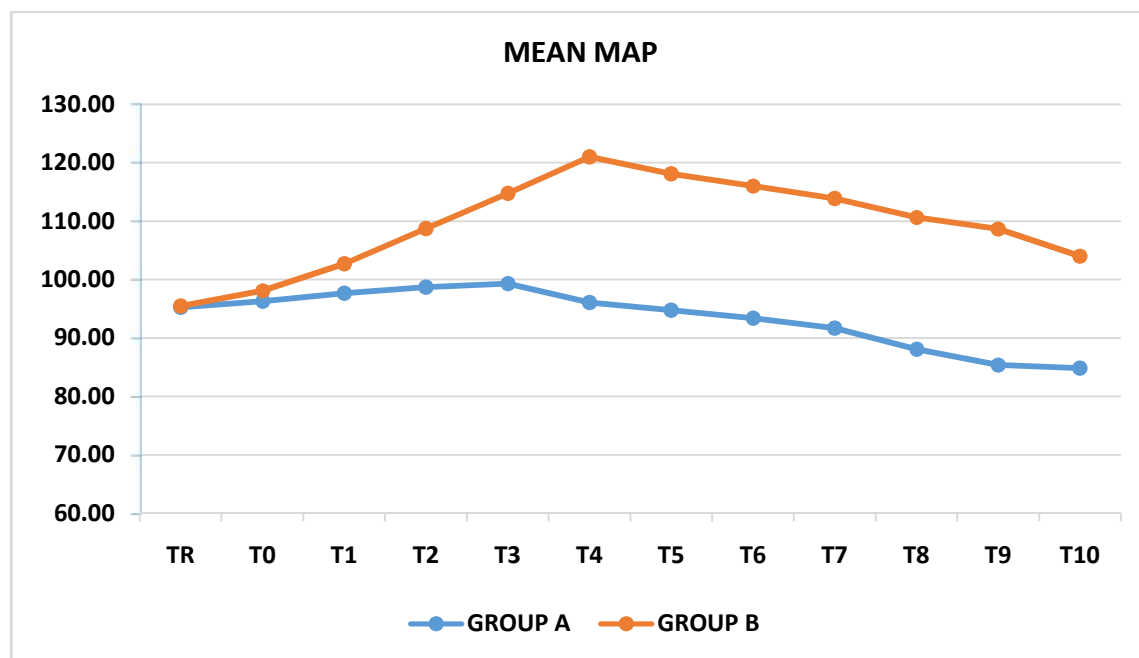
**In Group B –**

Mean DBP at the time of reversal (TR) was  $82.13 \pm 4.81$  and at the time of administration of saline spray (T0) was  $85.13 \pm 4.81$ . The DBP increased till 4 minutes (T4) when the maximum mean BP was  $102.33 \pm 3.41$ . When compared this increase in DBP was statistically highly significant, p value being  $< 0.0001$ . This DBP remained high till 10 minutes.

**MEAN ARTERIAL PRESSURE:**

**FOR MAP**

	GROUP A		GROUP B		P VALUE	INFERENCE
	MEAN	S.D.	MEAN	S.D.		
<b>TR</b>	95.20	5.68	95.43	3.06	0.8437	NS
<b>T0</b>	96.27	7.48	98.10	3.60	0.2313	NS
<b>T1</b>	97.62	4.79	102.67	3.54	< 0.0001	HS
<b>T2</b>	98.67	4.25	108.71	2.85	< 0.0001	HS
<b>T3</b>	99.29	4.15	114.72	2.47	< 0.0001	HS
<b>T4</b>	96.03	4.67	120.98	2.80	< 0.0001	HS
<b>T5</b>	94.72	3.78	118.07	3.69	< 0.0001	HS
<b>T6</b>	93.34	3.88	116.02	4.13	< 0.0001	HS
<b>T7</b>	91.67	4.17	113.86	3.39	< 0.0001	HS
<b>T8</b>	88.02	3.55	110.64	3.12	< 0.0001	HS
<b>T9</b>	85.38	2.31	108.67	2.48	< 0.0001	HS
<b>T10</b>	84.80	2.60	104.01	3.32	<0.0001	HS



**In Group A –**

Mean MAP at the time of reversal (TR) was  $95.20 \pm 5.68$  and at the time of administration of NTG spray (T0) was  $96.27 \pm 7.48$ . The MAP increased till 3 minutes when the maximum mean BP was  $99.29 \pm 4.15$ . This MAP subsequently reduced gradually till 10 minutes (T10) with the mean being  $84.80 \pm 2.60$ .

**In Group B –**

The mean MAP at the time of reversal (TR) was  $95.43 \pm 3.06$  and at the time of administration of saline spray (T0) was  $98.1 \pm 3.60$ . The MAP increased till 4 minutes (T4) when the maximum mean BP was  $120.98 \pm 2.80$ . This MAP remained high till 10 minutes. This increase in MAP when compared was statistically highly significant with p value of  $<0.0001$ .

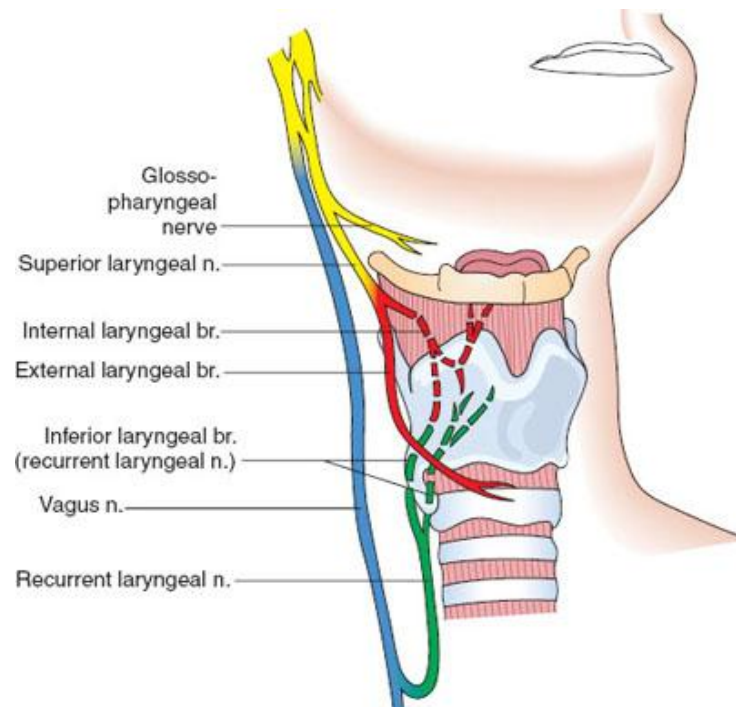
**PERCENTAGE OF OXYGEN SATURATION**

The saturation remained between 98-100% throughout the study period in both the groups.

## DISCUSSION

Laryngoscopy and extubation is the most crucial part of general anaesthesia. It was in 1940; Reid and Brace<sup>(35)</sup> first described hemodynamic changes to intubation. This led to a large number of studies to attenuate the stress response to intubation. Extubation is associated with patient awakening, pain, anxiety and airway irritation which causes similar increase in heart rate and blood pressure as during intubation what is known as pressor response to extubation. This Pressor response to extubation may be well tolerated in ASA I patients but is deleterious in patients with history of cardiovascular disease, hypertension and arrhythmias.

Pressor response to extubation<sup>(1)</sup> causes transient increase in “heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure” due to increased sympathoadrenergic activity caused by epipharyngeal and laryngopharyngeal stimulation.



### Nerve supply of larynx

Numerous methods were tried to attenuate this response to extubation such as non pharmacological methods like\_ extubation in deeper planes of anesthesia, using supraglottic airway devices<sup>(4)(3)(5)</sup> etc, Various drugs such as magnesium sulphate, preservative free lignocaine , beta blockers such as esmolol<sup>(18)(24)(11)(14)</sup>, calcium channel blockers such as verapamil<sup>(25)(26)(27)(28)</sup>, diltiazam<sup>(29)</sup>, remifentanyl<sup>(14)</sup>, fentanyl<sup>(8,9,10)</sup>, dexmedetomidine<sup>(10,11,12,13)</sup> and nitroglycerin<sup>(15,16,17,18)</sup> have been used to attenuate hemodynamic response to extubation.

Extubation in deeper planes of anesthesia causes decreased cardiovascular stimulation as there is reduced incidence of coughing and straining on the tube. However, there is chance of respiratory complication which is found to be greater after extubation under deep anesthesia, irrespective of the type of surgery where as supraglottic airway devices insertion might be difficult in some patients. Fentanyl, Remifentanyl and Dexmedetomidine even though effective, have sedating effect due to which even though we can use them during intubation but these cannot be used to attenuate pressor response during extubation as following extubation an awake patient capable of maintaining patent airway is of paramount importance.

Intravenous nitroglycerin is commonly used in anesthesia to treat hypertension while NTG spray was basically used to abort anginal attack.NTG relaxes vascular smooth muscles, predominantly venous dilatation over arterial dilatation.

Hemodynamic response to extubation increases HR, BP which in turn increases myocardial oxygen demand. Activation of sympathetic nervous system during extubation causes coronary vasoconstriction which in turn reduces coronary blood flow.NTG dilates coronary vessels thereby increases blood flow of coronaries and thus improving oxygen delivery(20) to myocardium which is an added advantage.

NTG has faster onset of action (2-3 minutes) and shorter duration of action with plasma half life 4 – 5 minutes. Sublingual Nitroglycerin spray is cost effective as well as can be easily administered.

Present study titled “Efficacy of sublingual nitroglycerin spray versus normal saline spray in attenuating pressor response during extubation: A one year hospital based randomized controlled trial” attempted to study the effects of sublingual nitroglycerin spray to attenuate pressor response to extubation. In this study 60 patients who belonged to ASA physical status I and II were randomized into Group A and Group B with 30 patients in each group. Group A received 1 puff of sublingual nitroglycerin spray 1 minute after reversal of neuromuscular blockade whereas Group B received 1 puff of sublingual normal saline spray 1 minute after reversal of neuromuscular blockade. Heart rate, systolic blood pressure,, diastolic blood pressure and mean blood pressure, oxygen saturation were noted before intervention (T0) and there after every minute i.e “ T1, T2, T3, T4, T5 ,T6, T7, T8,T9 and T10” till 10 minutes. Time of extubation was noted.

The minimum age in Group A was 19 years and maximum was 55 years. In Group B, the minimum age was 19 years and maximum was 58 years. When compared the difference was statistically not significant with p value of 0.2663. In Group A there were 16 females and 14 males, in Group B there were 18 females and 12 males. 15 patients were of ASA I whereas 15 patients were of ASA II status in Group A. There were 19 patients of ASA I & 11 patients were of ASA II status in Group B. Thus age, gender distribution and ASA physical status was comparable between the two groups.

General anaesthesia technique was standardized between the two groups with the average duration of surgery being 90-120 minutes in both the groups.

Onset of action of NTG spray is 2-3 minutes with peak action at 4 minutes. As most patients in our study were extubated at 3-4 minutes, action of NTG spray coincided with stimulus.

Though not much of the data is available on use of NTG during extubation, however it is effectively used as rescue drug by many authors during tracheal intubation with a wide dose variation (0.3 – 1.2 mg). Satisfactory results were obtained with 0.4-0.8 mg of NTG. In the study done by Indira Kumari et al titled “Attenuation of pressor response following intubation: Efficacy of nitroglycerin lingual spray<sup>(22)</sup>” concluded that 1 puff (0.4 mg) or 2 puffs (0.8 mg) of sublingual spray given 1 minute prior intubation is effective. In another study done by Upasana Bhatia et al titled “Comparison of different doses of Nitroglycerin spray for attenuation of stress response to laryngoscopy” where they compared 0.4 mg versus 0.8 mg of sublingual nitroglycerin spray 2 minute before induction of general anesthesia it was found that 0.8 mg of sublingual NTG spray does not offer any extra advantage over 0.4 mg of sublingual NTG spray. Hence use of 0.4 mg (1 puff) of sublingual NTG spray in our study is justified.

Nitroglycerin is known to produce reflex tachycardia due to sympathetic stimulation however in our study none of the patient showed any significant tachycardia. In the study done by Deepak Singh et al named “Effect of Nitroglycerin spray to blunt the hemodynamic response to endotracheal extubation in lumbar disc surgery<sup>(15)</sup>”, concluded that tachycardia was insignificant in NTG group. Similarly study by “Anant S et al and Dich-Niels et al<sup>(34)</sup>” found that following intranasal NTG spray there was attenuated pressor response to laryngoscopy and intubation without significant increase in heart rate. “Firoozbaksh et al<sup>(33)</sup>” also found that there was no significant increase in heart rate following use of intravenous

nitroglycerin during intubation. Our study also confirms similar hemodynamic changes, there was tachycardia in Group A but it was not statistically significant .

In our study, there was a small insignificant increase in SBP, DBP and MAP in the NTG group till 3 minutes. Subsequently SBP, DBP and MAP reduced till 10 minutes remaining lower than baseline (TR).

In NS group SBP, DBP and MAP markedly increased with maximum values seen at 4 minutes. SBP, DBP and MAP remained high till 10 minutes. This shows that NTG spray is considerably effective in attenuating pressor response to extubation. The results were similar to a study undertaken by Ameya A Tagalpallewar et al and as well Deepak Singh et al.

Nitroglycerin is most commonly used rescue antihypertensive in anesthesia practice. A study undertaken by Sunil Tuljapure, Vaishali Kotambkar et al in their study titled “A randomized controlled study of tracheal extubation response following nitroglycerine (NTG) sublingual spray in normotensive and hypertensive patients<sup>(36)</sup>” concluded that NTG is effective to attenuate pressor response to extubation, the effect of which started after 3 minute of sublingual NTG spray, our study also showed similar result. It is noted that onset of action of sublingual NTG is 2-3 minute hence a time gap of 3 minute was required for its action. In our study we found that “systolic blood pressure, diastolic blood pressure and mean arterial pressure” were under control within four minutes and remained to baseline during extubation in Group A where as in Group B it remained constantly high during extubation and returning to baseline thereafter 8-10 minutes post extubation. Intravenous NTG is also used during tracheal intubation to study its effect on attenuation of pressor response by Firoozbaksh et al<sup>(33)</sup> also showed similar result so as also S Kumara et al in their study on effect of 2% NTG ointment which was rubbed on the forehead of patients before

intubation found that increase in blood pressure was significantly low when compared with control group. Similar result was found in study done by Ameya et al<sup>(23)</sup> in their study on efficacy of sublingual nitroglycerin spray in attenuation of hemodynamics to tracheal extubation.

The present study was aimed at determining efficacy of 1 puff of sub lingual NTG (0.4 mg) spray versus 1 puff of normal saline spray in attenuating the pressor response during extubation. We have successfully established that 1 puff of sublingual Nitroglycerin spray is effective, practical, easy to administer and safe in attenuating pressor response to tracheal extubation.

Our study was undertaken in patients belonging to ASA I and II, these results may not be applicable in hypertensive patients who may still show pressor response to extubation . Hence further evaluation of the effectiveness of NTG spray in controlled as well as uncontrolled hypertensive patients is required.

In our study patient received 1 puff (0.4mg) which resulted in a small although insignificant increase in BP till 3 minutes. It may be possible to attenuate this small increase in BP by using higher dose of NTG spray instead of 0.4mg and requires further evaluation. It was observed that there was tachycardia as Injection Glycopyrrolate was given just before intervention since, both the groups received the same drug it will not act as bias.

## **CONCLUSION**

The conclusion drawn from study is that 1 puff (0.4mg) of sublingual Nitroglycerin spray is effective in attenuating pressor response to extubation. Sublingual NTG spray is easy to administer with rapid onset of action. It is also cost effective and can safely be used.

## **SUMMARY**

The present study entitled **“COMPARISON OF SUBLINGUAL NITROGLYCERIN SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR RESPONSE TO EXTUBATION: A ONE YEAR HOSPITAL BASED RANDOMIZED CONTROL 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, 60 patients of ASA I and II between age group 18-60 years were randomized to two groups having 30 patients in each Group.

Group A- Participants were given 1 puff of sublingual NTG spray (n=30) 1 minute after reversal of neuromuscular blockade.

Group B- Patients received 1 puff of sublingual saline spray (n=30) 1 minute after reversal of neuromuscular blockade.

General anaesthesia was induced as per standard technique. HR, SBP, DBP, MAP and SpO<sub>2</sub> were recorded in both the groups from the time of reversal of neuromuscular blockade, every minute till 10 minutes. Patients were extubated once criteria for extubation were achieved. The demographics were identical in both the groups.

We observed that HR, SBP, DBP, MAP increased till 3<sup>rd</sup> minute in Group A and thereafter had better hemodynamic control of pressor response to extubation compared to baseline and returning to baseline after 9 minutes. Whereas in Group B, HR, SBP, DBP and MAP increased progressively till 10 minutes. This increase in hemodynamic response was statistically significant.

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**INFORMED CONSENT FOR PARTICIPATION IN RESEARCH**

**STUDY**

Mr/Mrs/Miss. \_\_\_\_\_ we are requesting you to enrole you in study titled **““COMPARISON OF SUBLINGUAL NITROGLYCERIN SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR RESPONSE TO EXTUBATION: A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRAIL.”**, conducted by Dr. \_\_\_\_\_ 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 research is to know whether the study will be helpful in evaluating the efficacy of NTG spray during extubation for attenuation of pressor response to endotracheal extubation.

**Procedure Involved:**

If you agree to enrol 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 1 puff of nitroglycerin spray during endotracheal extubation, while Group B patients will receive 1 puff of sublingual saline spray during endotracheal extubation.

**Risks:**

There is almost no risk involved with using NTG sublingual spray.

**Benefits:** Attenuation of pressor response to endotracheal extubation.

**Voluntary Participation/Withdrawal:**

Taking part in the study is voluntary. You may choose not to enrol 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 KLES Hospital and MRC, Belagavi. There is no compensation or payment for such medical treatment by law. If you get injured you may contact Dr. Zakia Sultana M Tenagi at Department of Anaesthesiology, KLES Hospital and MRC or by Ph. No: 7411064138.

**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 Dr. \_\_\_\_\_

Department of Anaesthesiology, KLES Hospital and MRC, Belagavi Dr.

Professor, Dept. Of Anaesthesiology, KLES Hospital and MRC,  
Belagavi.

If you have any queries about your rights as a study subject, you may call Dr.Roopabellad, 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.

ANNEXURE II – ETHICAL CLEARANCE



K.L.E.UNIVERSITY'S  
**JAWAHARLAL NEHRU MEDICAL COLLEGE,**  
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)  
(Accredited 'A' Grade by NAAC)

Website: <http://www.jnmc.edu>  
E-Mail : [dome@jnmc.edu](mailto:dome@jnmc.edu)

Phone: (+ 91-(0)831 Office : 2471350  
Principal: 2471701  
Fax No. -91 (0)831 - 2470759

Ref: MDC/DOME/57

Date: 22/11/2017

To,

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

**“COMPARISON OF SUBLINGUAL NITROGLYCERIN SPRAY VS  
NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR  
RESPONSE TO EXTUBATION: A ONE YEAR HOSPITAL BASED  
RANDOMISED CONTROLLED TRIAL”** is ethical and justifiable.

The proposed research project has been cleared by the JNMC Institutional Ethics

Committee on Human Subjects Research.

(Dr. Arathi Darshan)  
Member Secretary

JNMC Institutional Ethics Committee  
on Human Subjects Research,  
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)  
Chairman,

JNMC Institutional Ethics Committee  
on Human Subjects Research,  
J.N.Medical College, Belagavi.

**PROFORMA**

**Title: “COMPARISON OF SUB LINGUAL NITROGLYCERIN SPRAY VS NORMAL SALINE SPRAY IN ATTENUATING THE PRESSOR RESPONSE TO EXTUBATION: A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRAIL.”**

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

***Chief complaints :***

***H/OPI:***

***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 (<sup>0</sup>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:**
- ASA physical status 1 and 2.
- Age between 18 to 60 years.
- Patients undergoing elective surgeries under general anaesthesia.
- Provides Consent
- **Exclusion Criteria :**
- Patients on antihypertensives
- ASA grade III and IV patients
- Patient allergic to study drug

**Methodology**

After obtaining the approval of ethical committee and written informed consent, a total of 60 patients undergoing surgery under general anaesthesia will be included in the study.

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

**Group A:** Patients will receive 1 puff of nitroglycerin spray after administration of reversal

**Group B:** Patients will receive 1 puff of sublingual normal saline spray after administration of reversal.

A thorough pre-anaesthetic evaluation will be done on the day before surgery.

On the day of surgery intravenous access is secured using 18G OR 20 G iv cannula and iv fluids started. Standard monitoring devices were attached before induction of anaesthesia, including non-invasive arterial blood pressure, ecg, and pulse oxymeter.

Patients will be Premedicated with injglycopyrrolate 0.005mg/kg and inj midazolam 0.05mg/kg and inj fentanyl 1 mcg/kg and Pre oxygenated with 100% oxygen for 3mins.

Will be induced with injthiopentone 5 mg/kg and injsuccinyl choline 2mg/kg. With the onset of neuromuscular blocked laryngoscope is done, tracheal tubes of internal diameter 7.5mm were used for women and 8.5mm for men.

Then after confirming the b/l equal air entry endotracheal tube will be secured with tapes at appropriate length and mechanically ventilated. Patients will be maintained with oxygen, Nitrous oxide, Isoflurane and inj. vecuronium 0.08mg/kg i.v.

SIGNATURE OF THE ANAESTHESIOLOGIST - \_\_\_\_\_

• SIGNATURE OF THE WITNESS - \_\_\_\_\_

• SIGNATURE OF THE PRINCIPAL INVESTIGATOR - \_\_\_\_\_

**ANNEXURE IV – PHOTOGRAPHS**



**FIG.1 NTG SPRAY**



FIG.2 NTG SPRAY



FIG.3 NTG SPRAY

NORMAL SALINE SPRAY

**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

TR – Time of Reversal

**NITROGLYCERIN SPRAY**

S.NO	NAME	AGE	SEX	ASA	HR											SBP												
					TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min
1	Nagraj N	38	M	I	76	78	82	90	95	95	89	93	87	87	92	94	127.5	130	128	125	133	125	124	122	119	110	107	107
2	Shobha N	38	F	I	72	74	76	86	89	95	95	99	93	91	86	88	129.5	132	130	123	125	113	110	114	109	106	103	103
3	Savita J	32	F	I	70	72	76	90	95	91	87	85	81	87	90	94	123.5	126	124	123	125	121	118	112	109	106	103	99
4	Drakshayani G	44	F	II	78	80	84	90	95	101	93	91	93	91	88	92	127.5	130	130	133	133	123	122	120	115	112	105	101
5	Mallinath T	65	M	II	66	68	72	78	83	91	93	93	93	93	96	90	131.5	134	130	121	135	127	124	120	113	106	103	99
6	Mukta D	21	F	I	68	70	111	107	107	109	107	107	95	95	92	92	102.5	105	114	108	115	113	111	112	109	102	101	101
7	Praveen N	31	M	I	90	92	88	92	95	95	93	97	95	99	98	98	127.5	130	124	131	129	119	116	112	111	108	101	101
8	Anil K	48	M	II	96	98	98	98	99	99	96	97	97	97	94	94	123.5	126	124	131	129	123	119	120	115	108	103	101
9	Satish W	24	M	I	112	114	111	107	107	109	105	95	93	93	92	92	102.5	105	114	108	115	111	116	114	111	102	101	99
10	Ganesh N	35	M	I	86	88	84	86	87	87	85	91	87	91	88	86	119.5	122	122	125	129	119	116	116	117	106	103	101
11	Kalyani P	26	F	I	120	122	121	112	105	103	101	90	90	89	86	82	117.5	120	122	129	131	128	123	122	123	124	117	113
12	Ashok	45	M	II	88	90	86	71	63	62	57	58	57	60	58	58	115.5	118	118	127	127	119	114	114	111	108	103	101
13	Anand K	19	M	I	90	92	90	92	93	97	93	93	93	92	92	92	127.5	130	130	119	123	117	122	120	117	108	103	99
14	Sindhu	47	F	II	88	90	86	86	83	82	80	69	68	69	68	68	127.5	130	135	120	118	115	115	114	114	110	106	106
15	Deepthi P	26	F	I	96	98	94	96	95	99	99	101	103	104	102	102	125.5	128	128	133	133	125	124	120	117	106	101	97
16	Ravi S	40	M	II	98	100	94	96	101	105	99	99	101	105	102	102	129.5	132	132	129	135	127	124	122	119	108	103	99
17	Vekanna R	38	M	II	104	106	106	106	103	107	107	110	105	103	104	100	127.5	130	124	127	125	119	118	112	109	102	101	101
18	Neha	24	F	I	96	98	98	98	101	107	107	105	101	105	108	110	117.5	120	124	131	135	121	120	120	123	112	107	107
19	Bharati D	40	F	II	86	88	84	86	87	87	89	87	87	91	88	86	127.5	130	124	129	127	123	122	120	117	108	103	103
20	Ramayya P	55	M	II	98	100	94	96	99	103	95	93	93	97	92	90	131.5	134	132	129	137	131	130	128	121	114	113	107
21	Mrutyunjaya B	50	M	II	88	90	90	92	91	91	91	95	91	91	88	86	123.5	126	126	131	135	127	126	124	119	112	105	101
22	Roopa S	52	F	II	90	92	88	90	91	91	89	91	89	91	90	90	127.5	130	124	129	133	127	128	130	121	114	113	113
23	Lata K	50	F	II	82	84	78	80	79	80	78	79	80	85	84	82	127.5	130	124	131	135	127	126	124	119	112	103	105
24	Kausar Nadaf	30	F	I	90	92	88	92	91	93	91	91	91	91	91	91	127.5	130	122	115	117	117	116	114	111	104	103	103
25	Sharada H	44	F	II	92	94	86	88	88	89	87	89	87	89	88	88	119.5	122	122	131	127	123	118	116	111	104	103	103
26	Heena kausar	22	F	I	90	92	88	92	91	93	89	91	89	91	90	88	105.5	108	118	131	135	123	120	118	113	106	101	101
27	Manjunath H	45	M	II	87	90	84	86	87	87	85	87	85	89	88	88	117.5	120	122	131	131	123	118	116	111	108	103	103
28	Gouravva G	55	F	II	79	82	76	78	79	80	77	79	79	81	78	78	127.5	130	130	121	127	121	120	120	117	106	105	105
29	Kallapa S	48	M	I	112	114	111	107	107	109	105	95	93	93	92	92	102.5	105	114	129	135	123	118	116	111	104	97	99
30	Fakiravva J	45	F	I	94	96	98	98	99	99	96	97	97	97	94	94	119.5	122	124	131	127	123	120	118	115	106	105	99
NAME	AGE	SEX	ASA	HR											SBP													
				TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	
Aradhana H	32	F	I	99	101	93	92	95	96	96	96	95	100	101	100	126.5	129	137	144	152	159	158	150	149	146	142	135	
Shrishail T	38	M	I	97	99	97	96	97	98	102	100	97	98	99	102	128.5	131	137	146	152	157	150	146	149	138	138	129	
Kalappa G	45	M	II	93	95	93	92	93	94	92	92	95	94	95	92	126.5	129	137	148	150	155	148	150	155	142	134	127	
Lakshmi K	46	F	II	89	91	89	88	91	92	92	90	87	86	91	90	122.5	125	133	142	150	155	150	146	149	140	140	137	
Rekha M	48	F	II	95	97	93	92	95	96	102	108	103	104	105	104	126.5	129	133	140	148	159	152	148	145	142	138	131	
Rehan M	19	M	I	99	101	95	98	99	94	100	98	97	98	99	102	122.5	125	133	140	148	153	148	150	151	146	138	131	
Sunil K	35	M	I	93	95	101	100	101	96	98	98	97	98	99	102	118.5	121	129	138	146	157	158	152	149	140	136	129	
Basappa P	46	M	II	95	97	99	98	99	94	96	96	95	96	101	104	124.5	127	137	144	152	159	154	152	151	140	140	137	
Sarita P	26	F	I	89	91	91	92	95	88	90	94	93	94	95	98	120.5	123	135	144	152	159	152	148	151	148	148	139	
Joseph F	32	M	I	87	89	87	88	91	94	94	92	91	96	101	100	122.5	125	135	142	148	161	154	152	151	146	144	135	
Malati B	28	F	I	83	85	85	88	93	94	94	94	93	98	99	102	118.5	121	127	138	146	157	152	156	155	144	140	131	
Bhavya S	23	F	I	85	87	87	88	91	94	94	90	89	94	99	102	116.5	119	131	140	152	157	152	150	147	136	132	125	
Asharani T	19	F	I	87	89	89	88	89	92	100	96	93	98	97	96	118.5	121	127	136	146	157	158	154	153	144	140	133	
Gurunath P	40	M	II	89	91	89	90	93	86	92	90	89	90	92	90	124.5	127	133	140	148	161	154	152	151	142	138	137	
Gargi B	20	F	I	91	93	91	92	95	88	90	90	93	94	95	94	126.5	129	137	144	152	163	154	150	149	146	138	131	
Raghavendra Y	31	M	I	93	95	93	94	97	90	90	90	89	90	95	98	120.5	123	137	148	154	157	150	152	149	140	136	129	
Habib Nadaf	39	M	II	95	97	97	98	101	98	98	98	97	96	97	98	122.5	125	131	138	144	155	150	146	145	134	128	119	
mahantesh	36	M	I	89	91	91	94	97	98	98	96	93	94	95	94	126.5	129	135	140	148	161	150	148	151	140	136	129	
Gouri K	40	F	I	79	81	83	86	91	86	86	86	85	86	87	86	124.5	127	131	140	148	161	154	150	147	142	136	129	
Shivaleela D	28	F	I	81	83	85	88	93	96	96	94	91	92	91	88	118.5	121	127	134	144	157	158	154	151	140	132	131	
Ningappa	18	M	I	83	85	89	94	97	100	100	98	95	94	95	90	124.5	127	131	138	146	159	158	160	155	144	140	133	

DBP												MAP											
TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min
85	100	90.5	79.46	74	81	81	84	86	80	80	83	99	110	103	95	93	96	96	97	97	90	89	91
83	96	94.5	93.46	86	87	87	82	84	80	78	81	99	108	106	103	99	96	95	93	92	88	86	88
87	94	94.5	91.46	84	87	87	86	80	76	74	73	99	105	104	102	97	98	98	95	89	86	83	82
83	88	86.5	89.46	82	85	83	82	78	78	76	77	98	102	101	104	99	98	96	95	90	89	85	85
77	92	92.5	83.46	78	77	77	76	76	74	80	81	95	106	105	96	97	94	93	91	88	84	87	87
89	76	80.5	83.46	88	97	91	88	91	90	82	85	94	86	92	92	97	102	98	96	97	94	88	90
83	82	82.5	83.46	88	81	81	82	80	80	78	77	98	98	96	99	101	94	93	92	90	89	85	85
93	84	86.5	89.46	92	91	91	92	90	86	82	77	103	98	99	103	104	102	101	101	98	93	89	85
75	76	82.5	81.46	88	77	75	74	76	74	76	81	84	86	93	90	97	88	89	87	87	83	84	87
81	84	84.5	87.46	94	89	83	80	80	78	74	73	94	97	97	100	105	99	94	92	92	87	83	82
77	86	86.5	83.46	90	83	79	76	76	72	74	73	91	97	98	99	103	98	94	91	91	89	88	86
85	72	82.5	85.46	92	87	85	84	84	82	78	75	95	87	94	99	103	98	95	94	93	90	86	84
85	78	84.5	91.46	84	83	83	84	84	82	78	73	99	95	100	101	97	94	96	96	95	90	86	82
85	82	86.5	85.46	90	87	85	84	86	82	74	77	99	98	103	97	99	96	95	94	95	91	84	87
87	84	82.5	81.46	90	87	85	86	86	82	80	75	100	99	98	99	104	100	98	97	96	90	87	82
87	86	86.5	85.46	90	87	85	86	92	90	82	79	101	101	102	100	105	100	98	98	101	96	89	86
85	82	82.5	85.46	90	91	87	84	84	80	74	77	99	98	96	99	101	100	98	93	92	87	83	85
71	86	84.5	85.46	74	71	71	70	68	72	74	75	87	97	98	101	94	88	88	87	86	85	85	86
83	84	84.5	85.46	90	87	83	82	80	78	74	73	98	99	98	100	102	99	96	95	92	88	83	83
81	88	88.5	89.46	86	77	83	80	78	74	72	75	98	103	103	103	103	95	99	96	92	87	85	86
85	80	80.5	85.46	92	89	85	84	82	80	82	75	98	95	96	101	106	102	99	97	94	90	89	84
73	84	86.5	89.46	78	71	71	72	70	74	72	77	91	99	99	103	96	90	90	91	87	87	85	89
81	86	86.5	89.46	84	83	81	80	82	82	78	73	97	101	99	103	101	98	96	95	94	92	86	84
85	82	84.5	85.46	88	85	83	84	84	80	76	73	99	98	97	95	97	96	94	94	93	88	85	83
81	76	84.5	85.46	88	81	81	80	78	76	74	75	94	91	97	101	101	95	94	92	89	85	83	84
67	80	86.5	85.46	66	67	69	66	68	68	74	73	80	89	97	101	89	86	86	83	83	80	83	82
83	70	78.5	85.46	88	83	81	82	80	78	74	71	95	87	93	101	102	96	94	93	90	88	83	82
79	70	72.5	73.46	76	85	81	78	76	72	70	69	95	90	92	89	93	97	94	92	89	83	81	81
71	60	66.5	67.46	78	69	69	70	70	70	72	75	82	75	82	88	97	87	86	85	83	81	80	83
87	84	82.5	81.46	86	95	87	86	86	82	78	75	98	97	96	98	99	104	98	97	95	90	87	83
DBP												MAP											
TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min	TR	T0	1 min	2 min	3 min	4 min	5 min	6 min	7 min	8 min	9 min	10 min
78	83	86	91	95	100	100	94	92	94	91	86	94	98	103	108	114	120	119	113	111	112	108	102
72	79	82	87	95	98	92	88	86	88	91	90	91	96	101	106	114	118	111	107	107	105	107	103
82	83	90	93	95	98	100	98	96	92	91	90	97	98	106	111	113	117	116	115	116	109	105	102
76	77	80	87	93	98	98	92	86	88	91	90	92	93	98	105	112	117	115	110	107	106	107	105
78	89	92	97	101	106	98	94	90	92	97	92	94	102	106	111	117	124	116	112	108	109	111	105
76	91	94	97	101	100	94	92	96	98	95	88	92	102	107	111	117	118	112	111	114	114	109	102
86	83	84	91	95	102	104	102	98	96	93	88	97	96	99	106	112	120	122	119	115	111	107	101
82	81	82	91	97	106	100	98	96	94	93	94	96	96	101	108	115	124	118	116	114	110	109	108
82	75	78	87	95	102	104	98	96	94	93	94	95	91	97	106	114	121	120	115	114	112	111	109
82	87	88	93	99	106	100	98	98	96	95	96	96	100	104	109	115	124	118	116	116	113	111	109
88	81	84	89	95	100	100	104	100	98	97	92	98	94	99	105	112	119	117	121	118	114	111	105
76	87	88	95	97	102	94	92	90	88	87	82	90	98	103	110	115	120	113	111	109	104	102	96
86	77	80	89	95	100	104	102	98	94	93	88	97	92	96	104	112	119	122	119	116	111	109	103
82	85	86	93	99	106	100	98	94	96	93	88	96	99	102	108	115	124	118	116	113	112	108	104
84	89	90	97	101	108	104	100	96	94	93	88	98	102	106	112	118	126	121	117	114	112	108	102
80	89	96	101	105	98	92	96	94	92	95	88	94	100	110	116	121	118	111	115	112	108	109	101
72	83	84	89	95	98	92	88	94	94	97	90	89	97	100	105	111	117	111	107	111	108	107	99
84	93	94	97	103	106	106	100	98	96	93	86	98	105	108	111	118	124	121	116	116	111	107	100
80	91	94	97	101	108	102	96	94	92	89	88	95	103	107	111	117	126	119	114	112	109	105	101
90	85	88	95	97	102	104	106	100	98	97	92	100	97	101	108	113	120	122	122	117	112	109	105
88	87	88	91	95	98	98	104	100	98	95	90	100	100	103	106	112	118	118	123	118	114	110	104
84	83	86	93	99	106	106	100	98	96	93	86	95	95	100	107	115	124	124	119	116	112	108	100
84	89	92	99	103	106	106	100	96	92	89	88	96	100	105	110	116	122	123	120	116	110	106	104
86	85	88	95	97	102	104	102	100	104	99	98	98	98	103	110	113	121	123	122	120	119	113	110
86	83	84	89	93	100	104	102	98	96	99	98	98	96	99	105	111	120	119	117	112	108	110	108
86	81	84	91	99	106	104	102	102	96	95	90	96	93	98	106	114	123	122	119	118	113	110	105
76	95	96	101	105	100	94	92	90	94	97	92	90	104	107	112	118	119	115	113	112	111	111	105

	GROUP A				GR	
	MEAN	S.D.	MINIMUM	MAXIMUM	MEAN	S.D.
AGE	39.23	11.74	19	65	35.90	11.26

**GENDER DISTRIBUTION OF THE SAMPLE**

	GROUP A	GROUP B	TOTAL
FEMALE	16	18	34
MALE	14	12	26
TOTAL	30	30	60

**DISTRIBUTION OF ASA**

	GROUP A	GROUP B	TOTAL
I	15	19	34
II	15	11	26
TOTAL	30	30	60

**INTRA GROUP COMPARISON**

**IN THE FOLLOWING TABLES p VALUE IS CALCULATED USING STUDENT'S PAIRED t TEST**

NS - NOT SIGNIFICANT

S - SIGNIFICANT

VS - VERY SIGN



GROUP A		GROUP B	
MINIMUM	MAXIMUM	p VALUE	INFERENCE
18	58	0.2663	NS

**DURATION OF SURGERY**

GROUP A		GROUP B		p VALUE	INFERENCE
MEAN	S.D.	MEAN	S.D.		
127.00	34.00	130.00	58.07	0.4025	NS

NS - NOT SIGNIFICANT      HS - HIGHLY SIGNIFICANT

**FOR HR**

	GROUP A		GROUP B
	MEAN	S.D.	MEAN
TR	89.05	12.67	90.47
T0	91.01	12.66	92.47
T1	91.03	11.88	92.07
T2	92.00	9.50	93.13
T3	93.03	9.73	96.00
T4	94.03	10.49	94.13
T5	91.93	10.54	95.33
T6	91.00	10.34	94.60
T7	90.00	9.71	93.07
T8	90.97	9.30	94.20
T9	90.07	9.68	96.17
T10	89.87	9.78	96.00

**FOR SBP**

	GROUP A		GROUP B
	MEAN	S.D.	MEAN
TR	122.00	8.67	122.03
T0	124.00	8.67	124.03
T1	124.00	5.41	132.00
T2	126.03	6.70	140.00
T3	128.20	6.29	148.03
T4	122.02	4.87	158.27
T5	120.03	4.73	154.13
T6	118.03	4.67	152.00
T7	115.00	4.35	149.97
T8	108.07	4.50	142.00

<b>T9</b>	104.07	4.04	138.00
<b>T10</b>	102.07	3.91	132.03

**FOR DBP**

	<b>GROUP A</b>		<b>GRO</b>
	<b>MEAN</b>	<b>S.D.</b>	<b>MEAN</b>
<b>TR</b>	81.8	5.86	82.13
<b>T0</b>	82.40	8.14	85.13
<b>T1</b>	84.43	5.60	88.00
<b>T2</b>	84.99	5.19	93.07
<b>T3</b>	84.83	6.64	98.07
<b>T4</b>	83.03	7.24	102.33
<b>T5</b>	82.07	5.81	100.03
<b>T6</b>	81.00	5.86	98.03
<b>T7</b>	80.00	6.31	95.80
<b>T8</b>	78.00	5.29	94.97
<b>T9</b>	76.03	3.41	94.00
<b>T10</b>	76.17	3.59	90.00

**FOR MAP**

	<b>GROUP A</b>		<b>GRO</b>
	<b>MEAN</b>	<b>S.D.</b>	<b>MEAN</b>
<b>TR</b>	95.20	5.68	95.43
<b>T0</b>	96.27	7.48	98.10
<b>T1</b>	97.62	4.79	102.67
<b>T2</b>	98.67	4.25	108.71
<b>T3</b>	99.29	4.15	114.72
<b>T4</b>	96.03	4.67	120.98
<b>T5</b>	94.72	3.78	118.07
<b>T6</b>	93.34	3.88	116.02
<b>T7</b>	91.67	4.17	113.86
<b>T8</b>	88.02	3.55	110.64
<b>T9</b>	85.38	2.31	108.67
<b>T10</b>	84.80	2.60	104.01

<b>UP B</b>		
<b>S.D.</b>	<b>p VALUE</b>	<b>INFERENCE</b>
5.36	0.5730	NS
5.35	0.5630	NS
4.57	0.6582	NS
4.29	0.5536	NS
3.45	0.1209	NS
3.79	0.9610	NS
3.91	0.1030	NS
4.01	0.0807	NS
3.54	0.1097	NS
3.84	0.0836	NS
4.22	0.0112	S
5.48	0.0340	S

<b>UP B</b>		
<b>S.D.</b>	<b>p VALUE</b>	<b>INFERENCE</b>
3.55	0.9845	NS
3.55	0.9845	NS
3.66	< 0.0001	HS
3.79	< 0.0001	HS
3.04	< 0.0001	HS
2.38	< 0.0001	HS
3.64	< 0.0001	HS
4.18	< 0.0001	HS
3.60	< 0.0001	HS
4.07	< 0.0001	HS

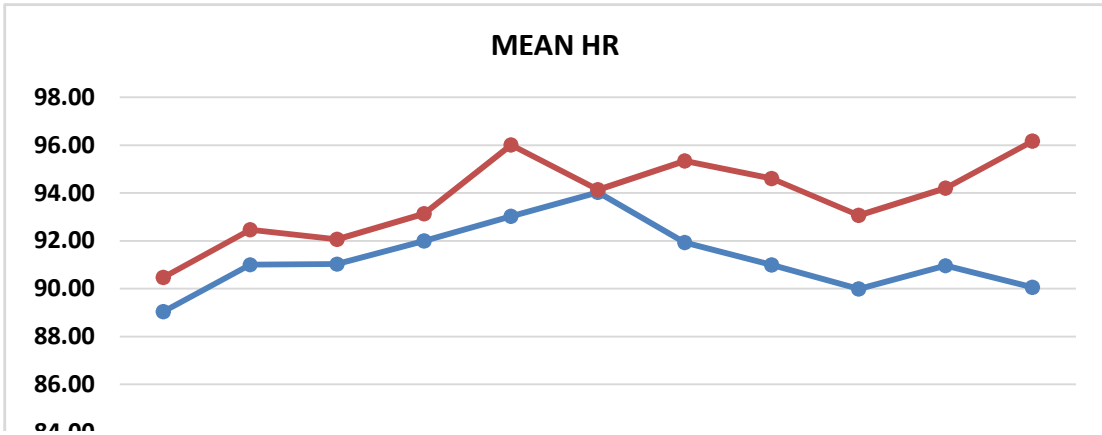
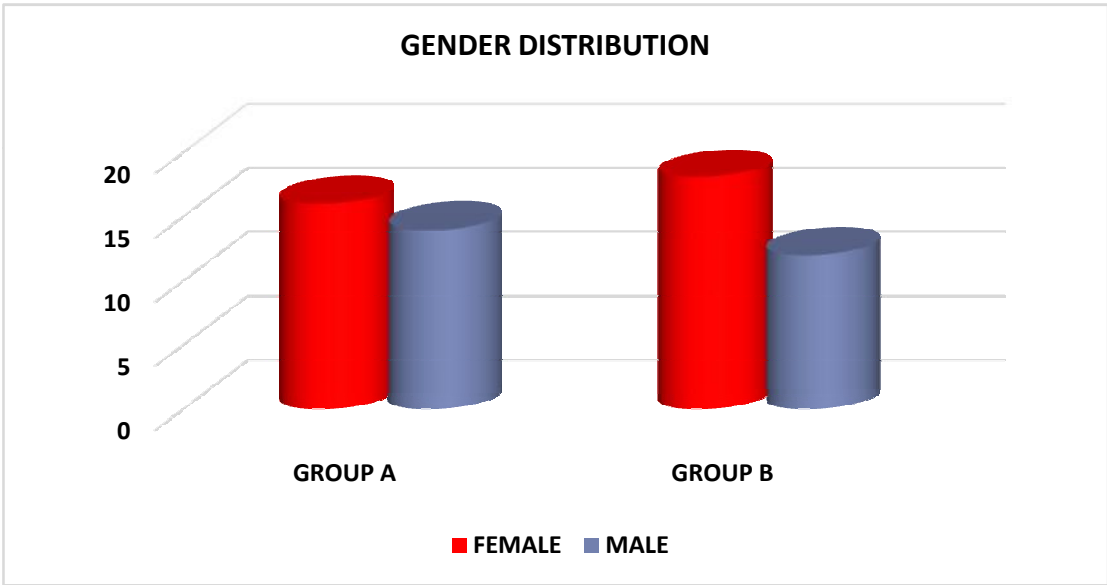
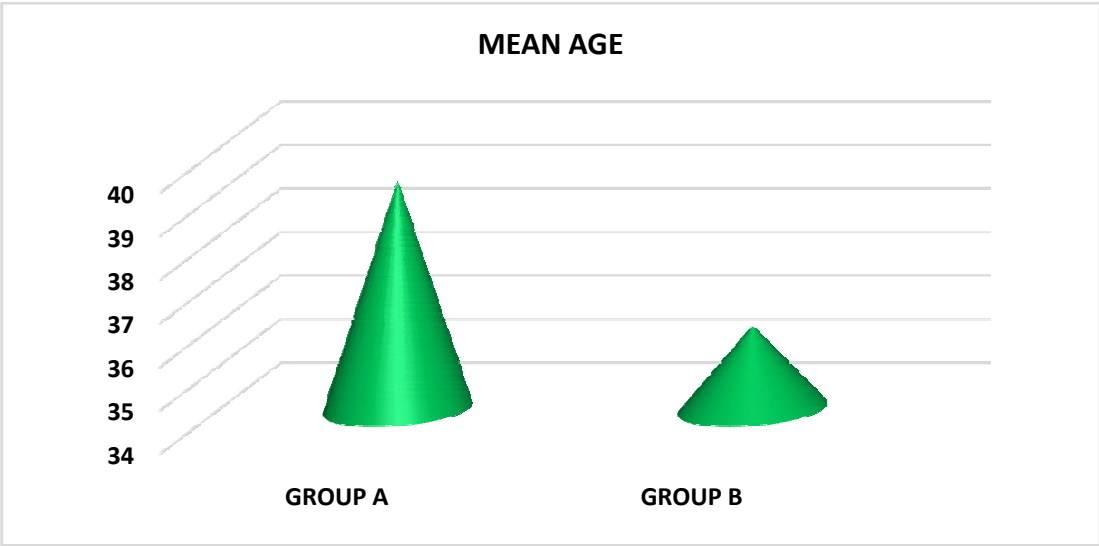
4.25	< 0.0001	HS
4.45	< 0.0001	HS

**UP B**

S.D.	p VALUE	INFERENCE
4.81	0.8106	NS
4.81	0.1189	NS
4.85	0.0107	S
4.09	< 0.0001	HS
3.47	< 0.0001	HS
3.41	< 0.0001	HS
4.49	< 0.0001	HS
4.81	< 0.0001	HS
4.21	< 0.0001	HS
3.61	< 0.0001	HS
3.05	< 0.0001	HS
3.73	< 0.0001	HS

**UP B**

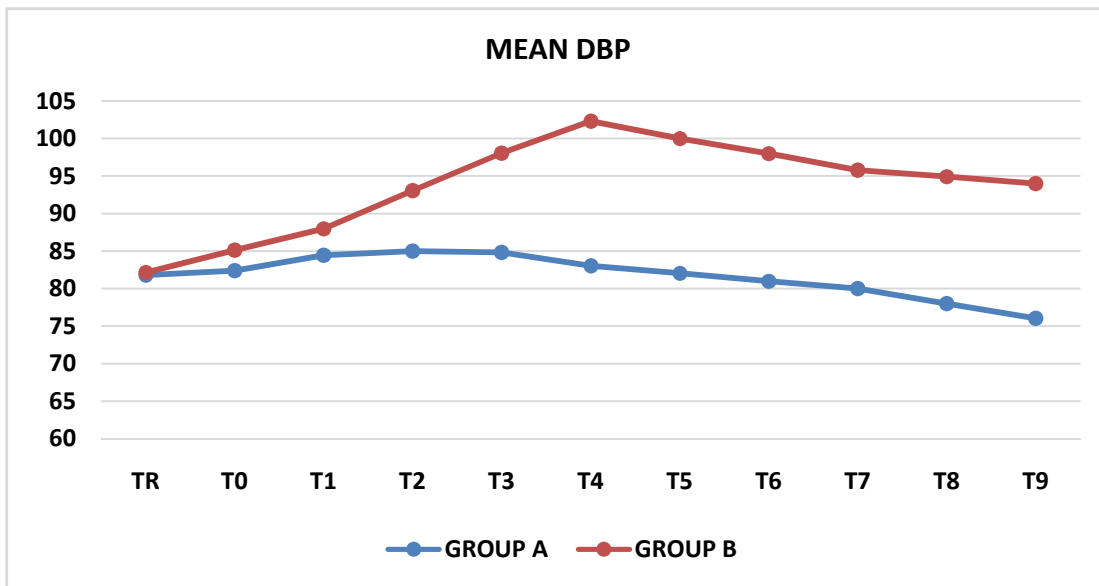
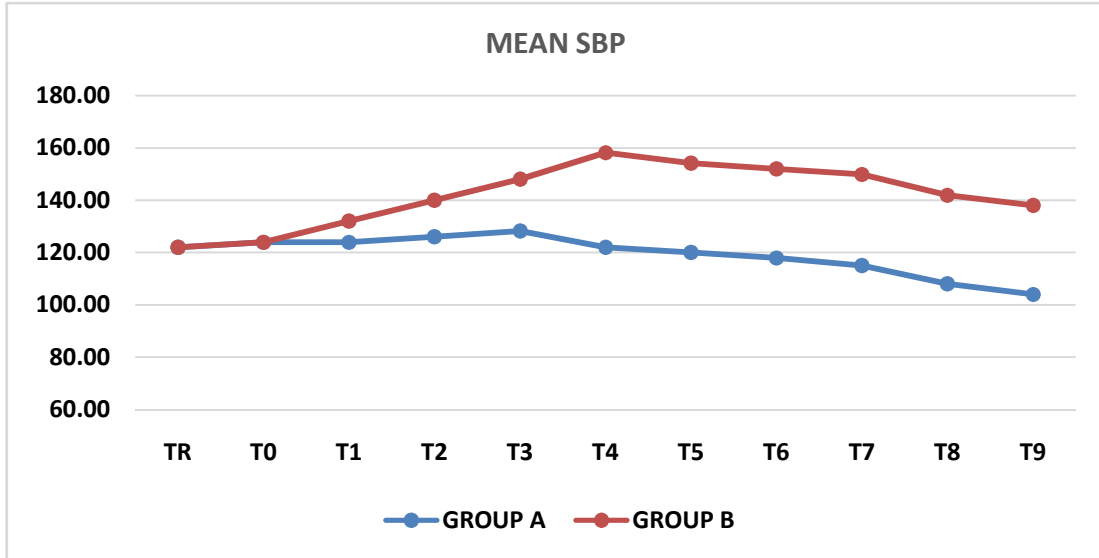
S.D.	p VALUE	INFERENCE
3.06	0.8437	NS
3.60	0.2313	NS
3.54	< 0.0001	HS
2.85	< 0.0001	HS
2.47	< 0.0001	HS
2.80	< 0.0001	HS
3.69	< 0.0001	HS
4.13	< 0.0001	HS
3.39	< 0.0001	HS
3.12	< 0.0001	HS
2.48	< 0.0001	HS
3.32	< 0.0001	HS

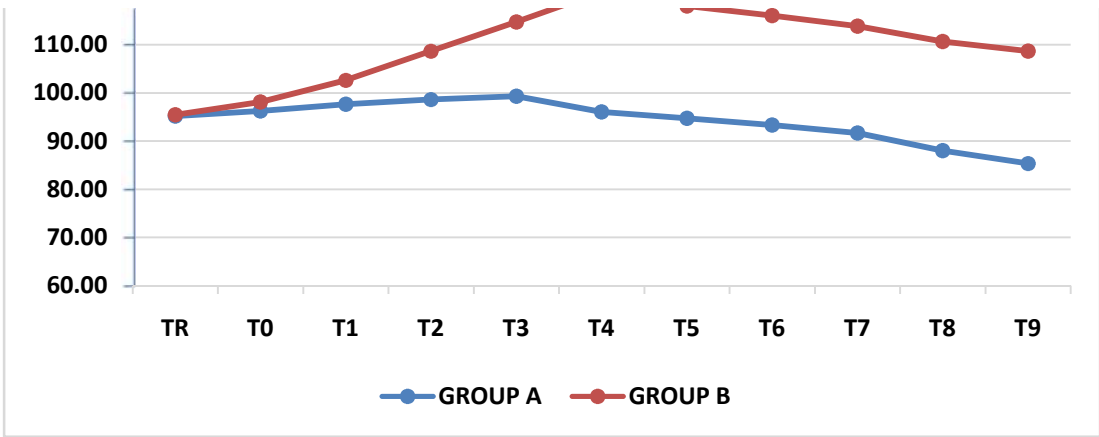


84.00

BASE 1 min 2 min 3 min 4 min 5 min 6 min 7 min 8 min 9 min 10 min

GROUP A GROUP B























HR

GROUP A    GROUP B

<b>BASE</b>	89.05	90.47
<b>1 min</b>	91.01	92.47
<b>2 min</b>	91.03	92.07
<b>3 min</b>	92.00	93.13
<b>4 min</b>	93.03	96.00
<b>5 min</b>	94.03	94.13
<b>6 min</b>	91.93	95.33
<b>7 min</b>	91.00	94.60
<b>8 min</b>	90.00	93.07

<b>9 min</b>	90.97	94.20
<b>10 min</b>	90.07	96.17
	89.87	96.00

SBP

GROUP A    GROUP B

<b>TR</b>	122.00	122.03
<b>T0</b>	124.00	124.03
<b>T1</b>	124.00	132.00
<b>T2</b>	126.03	140.00
<b>T3</b>	128.20	148.03
<b>T4</b>	122.02	158.27
<b>T5</b>	120.03	154.13
<b>T6</b>	118.03	152.00
<b>T7</b>	115.00	149.97
<b>T8</b>	108.07	142.00
<b>T9</b>	104.07	138.00
<b>T10</b>	102.07	132.03

DBP

GROUP A    GROUP B

<b>TR</b>	81.8	82.13
<b>T0</b>	82.40	85.13
<b>T1</b>	84.43	88.00
<b>T2</b>	84.99	93.07
<b>T3</b>	84.83	98.07
<b>T4</b>	83.03	102.33
<b>T5</b>	82.07	100.03
<b>T6</b>	81.00	98.03
<b>T7</b>	80.00	95.80
<b>T8</b>	78.00	94.97
<b>T9</b>	76.03	94.00
<b>T10</b>	76.17	90.00

MAP

GROUP A    GROUP B

<b>TR</b>	95.20	95.43
<b>T0</b>	96.27	98.10
<b>T1</b>	97.62	102.67
<b>T2</b>	98.67	108.71

<b>T3</b>	99.29	114.72
<b>T4</b>	96.03	120.98
<b>T5</b>	94.72	118.07
<b>T6</b>	93.34	116.02
<b>T7</b>	91.67	113.86
<b>T8</b>	88.02	110.64
<b>T9</b>	85.38	108.67
<b>T10</b>	84.80	104.01