“TO COMPARE EFFECT OF SEVOFLURANE vs TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS”

Dissertation submitted to

THE TAMI LNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE

MADRAS MEDICAL COLLEGE CHENNAI- 600003

MAY – 2020

REG.NO.201720022

CERTIFICATE

This is to certify that this dissertation **"TO COMPARE EFFECT OF SEVOFLURANE vs TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS"** submitted by Dr.S.VISHNUPRIYA in partial fulfilment for the award of the master degree of Doctor of Medicine MD in Anaesthesiology by the Tamil Nadu Dr .M. G. R .Medical University, Chennai. , is a bonafide record of the work done by her in the INSTITUTE OFANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Rajiv Gandhi Government General Hospital , during the academic year 2017 - 2020

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I

CERTIFICATE BY THE GUIDE

This to certify that the dissertation entitled "**TO COMPARE EFFECT OF SEVOFLURANE vs TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS**" submitted by Dr.S.VISHNUPRIYA in partial fulfilment for the award of the master degree of Doctor of Medicine MD in Anaesthesiology by the Tamil Nadu Dr .M. G. R .Medical University, Chennai. , is a bonafide record of the work done by her in the INSTITUTE OFANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Rajiv Gandhi Government General Hospital , during the academic year 2017 - 2020

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DECLARATION

I hereby, solemnly declare that this dissertation titled " **TO COMPARE EFFECT OF SEVOFLURANE vs TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS**" is a bonafide record of the work done by me in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Rajiv Gandhi Government General Hospital, during the academic year 2017 - 2020 under the guidance of Prof. Dr.SAMUEL PRABHAKARAN M.D. , D.A. , Professor of Anaesthesiology , Institute of Anaesthesiology and critical care, Rajiv Gandhi Govt .General Hospital and Madras Medical College, Chennai - 600003 and submitted to The Tamil Nadu Dr .M.G.R.Medical University , Guindy , Chennai –32, in partial fulfilment for the requirements for the award of the degree of MD Masters in Anesthesiology (Branch X) , examinations to be held on May 2020 .I have not submitted this dissertation previously to any university for the award of degree or diploma.

Place: Chennai S. Vishnupriya

ACKNOWLEDGEMENT

I am extremely thankful to DR.JAYANTHI, M.D, FRCP, Dean, Madras Medical College &Rajiv Gandhi Govt .General Hospital, for her permission to carry out this study.

I am immensely grateful to Prof. DR.ANURADHA SWAMINATHAN, M.D.,D.A., Director Institute of Anaesthesiology and Critical Care, Madras Medical College & Rajiv Gandhi Govt .General Hospital for her Concern and support in conducting this study .

I am extremely grateful and indebted to my guide Prof .DR.SAMUEL PRABHAKARAN M.D.,D.A., Professor of Anaesthesiology ,Institute of Anaesthesiology and critical care, Rajiv Gandhi Govt .General Hospital , for his concern, inspiration, meticulous guidance, expert advice and constant encouragement in preparing this dissertation.

I am very grateful to express my sincere gratitude to the Professors, Institute of Anaesthesiology & Critical Care, for their constant motivation and valuable suggestions.

I sincerely thank Dr. N.Sumathy M.D., Dr.Bhuvana M.D, Dr D.Shanmugapriya, M.D, Dr.Kathiravan DLO, M.D, Dr.Balaji M.D, for their advice, guidance and unrelenting support during the study.

I am extremely thankful to, Dr.Marium Shirin M.D, Dr.Asha M.D, Dr .Rukesh, M.D., for their guidance and expert advice in carrying out this study.

I am thankful to the Institutional Ethics Committee for their guidance and approval for this study.

I am thankful to all my colleagues, family and friends for their moral support, help and advice in carrying out this dissertation.

Last but not the least; I thank all the patients for helping this study.

Above all I pay my gratitude to the Lord Almighty for blessing me to complete this work.

TABLE OF CONTENTS

INTRODUCTION

Extubation is very critical part of airway management [1]. Although problems that can arise during induction and intubation, the risk for complications can be more frequent during extubation of the trachea. Because extubation significantly gets less attention than intubation. And there are no well-established strategies.

Similar to intubation, recognition of the difficult extubation and planning is important process. Despite these important factors, literature on extubation is significantly less comprehensive than intubation. Nearly one-third of reported major airway complications occurred during extubation**.**

Extubation Complications includes hypoventilation, upper airway obstruction, laryngospasm, bronchospasm, vocal cord damage, negative pressure pulmonary oedema, pulmonary aspiration, coughing and hemodynamic alterations like tachycardia, hypertension, dysrhythmias, and increased intraocular, intrathoracic, intracranial, intra-abdominal pressures.

All these complications and Hemodynamic changes are undesirable. Coughing during emergence from anaesthesia even though a protective physiological effect, this will cause significant patient's discomfort and that leads to hemodynamic alterations.

The techniques performed to minimise these effects and improve patients safety include -

1. Bailey's technique (Deep plane extubation followed by LMA exchange during emergence)

2. IV Administration of agents like Lignocaine, Remifentanil, Dexmeditomidine

3. Topical and intracuff lignocaine

All these techniques are performed during emergence; we studied how intra op maintenance of anaesthesia affects emergence. So here we compared maintenance with sevoflurane and Propofol as TIVA on extubation response.

BALANCED ANAESTHESIA

Balanced anaesthesia [2] is achieved by smaller doses of two or more agents than the usual larger dose of a single agent. The smaller doses are considered safe.

In 1926 John S Lundy from Mayo clinic coined the term called balanced anesthesia, for combination of agents and also techniques.

Premedication to reduce pre-operative anxiety, to decrease somatic and autonomic responses while manipulating the airway, for stable hemodynamics, to reduce dose requirements of inhalational agents. Opioids reduce requirements of Propofol[4] or inhalations agents, while as single anesthetic agents they produce excessive hemodynamic depression. So the phases of balanced anaesthesia as follow

1. Premedication (Anticholinergic, sedatives, opioids)
2. Induction (Intravenous or inhalational)
3. Maintenance (Inhalational or intravenous)
4. Recovery or Emergence (antisialagogue, Reversal)

With all these agents and in combination with techniques like regional anaesthesia[3] we are aiming to achieve analgesia, amnesia, muscle relaxation, abolition of autonomic reflex, maintaining heamodynamic stability.

TIVA

Total intravenous anaesthesia describes the provision of anaesthesia by intravenous infusions alone. Anaesthesia is induced and maintained either by a combination of hypnotic and analgesic agents or by infusion of a hypnotic alone.

An ideal drug for Total intravenous anaesthesia should have the following properties[5]:

1. Predictable plasma concentration according to a known pharmacokinetic model.
2. Predictable link between pharmacodynamics and pharmacokinetic effects.
3. It should not have active metabolites
4. Should have a rapid onset of action
5. It should be stable in a plastic syringe

Total intravenous anaesthesia is a strict definition that refers to the induction and maintenance of anaesthesia using intravenous agents and an Oxygen and air mixture, but nitrous oxide is sometimes used as an adjunct. The IV agents may be given by manual infusion or by an infusion device which is programmed with a pharmacokinetic model to achieve a target [6] either plasma (Target controlled infusion plasma) or brain (Target controlled effect) concentration of drug. When using an infusion of intravenous agents there is no point-of-delivery measure of the target concentration equivalent to the end-tidal monitoring of inhalational agents. A TCI will display a calculated value for plasma concentration based on the software model used and the information which we feed to the system usually patient weight, height, age and gender.

ADVANTAGES

1. Delivering anaesthesia by the inhalational route for a spontaneously breathing [7] patient has a feedback that provides autoregulation on respiration which affects the depth of anaesthesia. For example if the patient is in deep plane, the minute volume falls and delivery of the volatile agent is reduced. But if the patient is in too light plane, Minute volume increased so more volatile agent is inhaled and anaesthesia deepens. This can be avoided in TIVA.

2. Another advantage of using TIVA over conventional IV induction followed by volatile anaesthesia is that there is no twilight period between the end of intravenous induction anaesthetic effects and the onset of volatile anaesthesia maintenance.

3. Reduce contamination of OT environment by Inhalational agents.

4. Cost effective compared to inhalational anaesthesia.

LIMITATIONS

Inadvertent discontinuation of the infusion: - This will cause patient waking up. So this technique must therefore be used carefully to avoid awareness. Measure may be taken to reduce discontinuation is dedicated intravenous cannula or by a dedicated lumen of a multi-lumen catheter can be used for infusion, and it should be under vision at all times so that a disconnection, kinckig may be noticed.

Intraoperative Awareness Use of midazolam in a small dose as an adjunct to TIVA reduces the incidence of awareness. Also Co-induction with Propofol and Midazolam allows to set lower target concentration at infusion. Instead of 0xygen/Air if Nitrous oxide is used it increases anaesthetic effects

Individual variability The effect site or plasma concentrations displayed on a TCI pump is just a guide because their accuracy is within 25%. So it is important to assess individual sensitivity to intravenous agents by observing the concentrations at which patients go to sleep.This will be a guide to keep target concentration required during surgery. The patient needing a higher concentration to go to sleep is more likely to need a higher target concentration at every stage of surgery. For this individual variability and lack of measurement of plasma concentrations it is advisable to use monitors that measure depth of anaesthesia during TIVA.

TARGET CONTROLLED INFUSION

It uses microprocessors controlled infusion pump programmed with three compartments model of pharmacokinetics.

Models of TCI

DRUGS	NAME OF THE MODEL
Propofol	Modified Marsh[8] and Schnider Model
Peadiatric model	Peadfusor
Remifentanyl	Minto

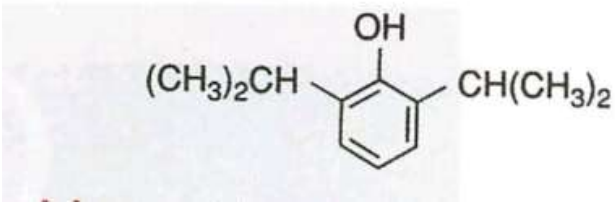
BRISTOL MODEL

This is Manual method of TIVA unlike TCI. This is simple infusion scheme of propofol. The target concentration is 3 micro gram/ml in 2 minutes and to maintain this level for the duration of surgery.

Induction is started with rate of 10mg/kg/hour which is maintained for 10 minutes then rate decreased to 8 mg/kg/hour which is maintained for next 10 minutes. Here after duration of surgery maintained by 6 mg/kg /hour. This also simply called 10-8-6 Algorithm. Anyway TCI is superior to this.

PROPOFOL

Propofol is a substituted isopropylphenol[9] (2,6-diisopropyIphenol) administrated as 1% concentration. It is an aqueous solution made of 1.2% purified egg phosphatide, 10% soybean oil and 2.25% glycerol. It produces rapid unconsciousness after administration.



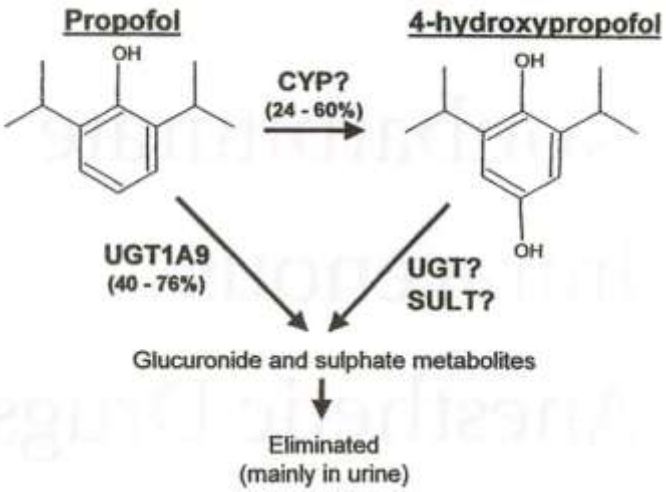
STRUCTURE OF PROPOFOL

Pharmacokinetics [10],[11]

1. pH is 7 and it is insoluble in water
2. Volume of distribution is 20–40 L and protein binding is 97%.
3. Onset is 90–100 seconds ("one arm-brain circulation"); BP drops around 200 seconds (faster with old age, hypovolemia)
4. Offset: 2-8 minutes; terminated by redistribution from the brain to other compartments.

* *Elimination*: it has Rapid plasma clearance (20 to 30 ml/kg/min) so it has elimination half-life of 3 to 24 hours. This is because a rapid central compartment clearance by hepatic metabolism and extrahepatic metabolism (so more complete recovery compared to Thiopental).

* The liver metabolizes Propofol to inactive water-soluble compounds (glucuronide, sulfate) which are excreted by kidney. The renal[12] and lung metabolism are responsible for 30%-60% of elimination so the metabolism still takes place during the anhepatic phase of liver transplant) and 3% of drug is excreted unchanged via urine and feces.



. **METABOLISM OF PROPOFOL**

* It is Stable at room temperature and not sensitive to light

* Can be diluted with 5% Dextrose, Dextrose with normal saline or Ringer lactate solution, but dilution less than 2 mg/ml may crack the emulsion and degrade the Propofol.

* Context-sensitive half time of Propofol[13] is 20 minutes even after 6 hours of infusion.

* Concentration-dependent inhibition of cytochrome P-450 which may alter drug metabolism.

Mechanism of action [14];- Propofol potentiates GABA receptor[15],[16] binding by attaching to the beta subunit of the GABA A receptor. Since GABA is an inhibitory neurotransmitter it hyperpolarizes the cell membrane (increases Chloride ion conductance),that will prevent depolarization with resultant neurotransmission.

-It involves inhibition of Ach release in the prefrontal cortex and hippocampus and also causes inhibition of NMDA in CNS;

-Direct depressant effect on neurons of the spinal cord.

- Antiemetic effect caused by decreasing serotonin levels in the area postrema. It also increases Dopamine level in Nucleus accumbens that explain abusive property.

DOSING:-

. CP50 for Propofol is defined as the blood concentration needed for 50% of subjects to not respond to a defined stimulus in the absence of any other drug. The value is 2.3 to 3.5 mics/ ml. Cp50 is reduced by administration of other sedatives with Propofol. This concept is equivalent to MAC of inhalational agents [17].

. *Induction* dose is 1 to 2.5 mg/kg IV bolus. Dose is reduced in elderly patients [18],[19] (smaller Vd), with reduced cardiovascular reserve and when premedicated with benzodiazepines, opioids, or lidocard.

Pediatric induction dose is 2.5 to 3.5 mg/kg iv because of larger Vd.

Sedation dose is 25 to 100 mcg/kg/min IV, titrated according to the effect

Opioid	Alfentanil EC_{50}-EC_{95} (90-130 ng/mL)	Fentanyl EC_{50}-EC_{95} (1.1-1.6 ng/mL)	Sufentanil EC_{50}-EC_{95} (0.14-0.20 ng/mL)	Remifentanil EC_{50}-EC_{95} (4.7-8.0 ng/mL)
Bolus	25-35 μg/kg in 30 sec	3 μg/kg in 30 sec	0.15-0.25 μg/kg in 30 sec	1.5-2 μg/kg in 30 sec
Infusion 2	50-75 μg/kg/hr for 30 min 30-42.5 μg/kg/hr thereafter	1.5-2.5 μg/kg/hr for 30 min 1.3-2 μg/kg/hr up to 150 min	0.15-0.22 μg/kg thereafter	13-22 μg/kg/hr for 20 min 11.5-19 μg/kg/hr thereafter
Infusion 3		0.7-1.4 μg/kg/hr thereafter		
Propofol	**Propofol EC_{50}-EC_{95} (3.2-4.4 μg/mL)**	**Propofol EC_{50}-EC_{95} (3.4-5.4 μg/mL)**	**Propofol EC_{50}-EC_{95} (3.3-4.5 μg/mL)**	**Propofol EC_{50}-EC_{95} (2.5-2.8 μg/mL)**
Bolus	2.0-2.8 mg/kg in 30 sec	2.0-3.0 mg/kg in 30 sec	2.0-2.8 mg/kg in 30 sec	1.5 mg/kg in 30 sec
Infusion 1	9-12 mg/kg/hr for 40 min	9-15 mg/kg/hr for 40 min	9-12 mg/kg/hr for 40 min	7-8 mg/kg/hr for 40 min
Infusion 2	7-10 mg/kg/hr for 150 min	7-12 mg/kg/hr for 150 min	7-10 mg/kg/hr for 150 min	6-6.5 mg/kg/hr for 150 min
Infusion 3	6.5-8 mg/kg/hr thereafter	6.5-11 mg/kg/hr thereafter	6.5-8 mg/kg/hr thereafter	5-6 mg/kg/hr thereafter

INTRAVENOUS AGENTS INFUSION DOSES

TIVA maintenance (sole): 200 to 350 mcg/kg/min IV. Dose reduced when coadministered with other anesthetics (75 to 120 mcg/kg/min IV + remifentanil 0.1 5--0.2 mcg/kg/min IV or with nitrous oxide 100 to 200 mcg/kg/min IV)

Women may require a higher dose than men because of larger Vd and high clearance rate.

Nausea and vomiting: 10 to 20 mg IV produces antiemetic effect

Emergence delirium: I0 to 20 mg IV boluses

CLINICAL USES

1. It is a rapid acting IV hypnotic agent with faster onset and also faster psychomotor recovery than Thiopental. It is utilized as a single agent to produce differential levels of consciousness, from a light sedation to induction and maintenance of general anesthesia

2. A component of balanced anesthesia. It decreases concentrations of volatile agents/nitrous oxide. Can also be used with opioids and benzodiazepines for Monitored anesthesia care or TIVA techniques

3. Treatment for ICP: Causing cerebral vasoconstriction thus reducing ICP,neuro protection and burst suppression .

4. Treatment of Emergence delirium (compared to benzodiazepines which have longer duration and can have paradoxical reaction)

5. Sedation for procedures and ventilated patients (quick onset, quick recovery)

6. It does not trigger malignant hyperthermia

7. Used as a Anticonvulsant for its burst suppression activity

8. Nausea and vomiting; reduces incidence of PONV when used for maintenance or even in sub anesthetic doses

9. Antipruritic effects, for pruritus caused by opioids and cholestatic liver disease

10. Blunting airway response compared to thiopental. Hence preferred for Asthmatic patients.

ADVERSE EFFECTS

1. Emulsions support bacterial growth despite additives. So the solutions should be used as soon as possible and maximum < 6 hours after opening the vial, sepsis and death may occur due to contamination

2. Potential cross-allergic reactions can occur due to soybeans and egg yolk.

3. *Propofol infusion syndrome.* It is a potentially fatal complication characterized by metabolic acidosis(lactic acidosis), rhabdomyolysis of cardiac and skeletal muscle, arrhythmias like bradycardia, Atrial fibrillation, ventricular tachycardia and Supra ventricular tachycardia, bundle branch block, and asystole, Congestive cardiac failure, renal failure, Hepatomegaly, subsequently leading to death. Laboratory reports may reveal myoglobinuria, ST-segment elevation, increased Creatine kinase, troponin, hyperkalemia, and azotemia. This happens in critically ill patients, children and adults, and long duration surgeries when doses exceed 4-5 mg/kg/h for 48hours. Mechanism behind this may be mitochondrial toxicity, mitochondrial defects, impaired tissue oxygenation, and carbohydrate deficiency. Treatment is immediately discontinuing of infusion, cardiac support, and metabolic acidosis correction

4. It may increase serum triglycerides which is usually associated with pancreatitis.

5. Caution should be taken in pregnancy as it decreases MAP and crosses placenta rapidly and will lead to neonatal depression.

6. Pain on injection. This can be reduced by premedication with opioid or co administration with Lidocaine as 1 ml of Lignocard per 10 ml of Propofol dilution and use of larger veins can reduce pain

PROPOFOL AND TCI

Propofol can be used both for induction and maintenance of anaesthesia, because of its favourable ‘wake up’ profile. To use Propofol as infusion requires some understanding of kinetic model. Propofol is a sterically hindered phenol. The potentially active hydroxyl group in this phenol ring is shielded by the electron clouds and surrounding attached isopropyl groups, which reduces its reactivity. So unlike phenol, propofol is insoluble in water but highly soluble in fat. Hence prepared as a lipid emulsion. Because of high lipid solubility, after long duration infusions there is risk of accumulation in fatty tissues. There are no active metabolites of Propofol. Because of high lipid solubility and insignificant ionisation once Propofol distributes into fat it will redistribute back into plasma slowly. Propofol has extremely large volume of distribution this accounted for mainly by the third compartment. An induction dose of Propofol is extensively bound to albumin (98%) following intravenous injection. After the bolus dose there is rapid loss of consciousness as the lipid tissue of the CNS takes up the highly lipophilic drug. After next few minutes Propofol distributes to peripheral tissues and the concentration in the CNS falls. With absence of further doses of drug the patient will wake up. Its distribution half-life is 1–2 minutes which accounts for the rapid fall in plasma levels and a short duration of action. The very rapid elimination of Propofol by hepatic and extra-hepatic metabolism also contributes to rapid reduction in plasma concentration and wake up profile. But the terminal elimination half-life is very much longer (5–12 hours) because of relatively slow redistribution from the fatty tissues. But this plays an insignificant role in onset of clinical action after a bolus dose. The pharmacodynamic

profile of propofol lags behind concentration in plasma due to the short delay in access to and from the CNS. Time-to-peak effect of propofol is around 1.7 min this explains the brain concentration of propofol is lower than that of plasma on induction but higher during the elimination phase. Modelling this lag-time requires use of depth of anaesthesia monitoring; usually the bispectral monitor will be useful to measure the brain (effect compartment) concentration. Anaesthesia with propofol can be induced and maintained by delivering the drug according to a three-compartment kinetic model with an effect compartment that equilibrates with the central compartment.

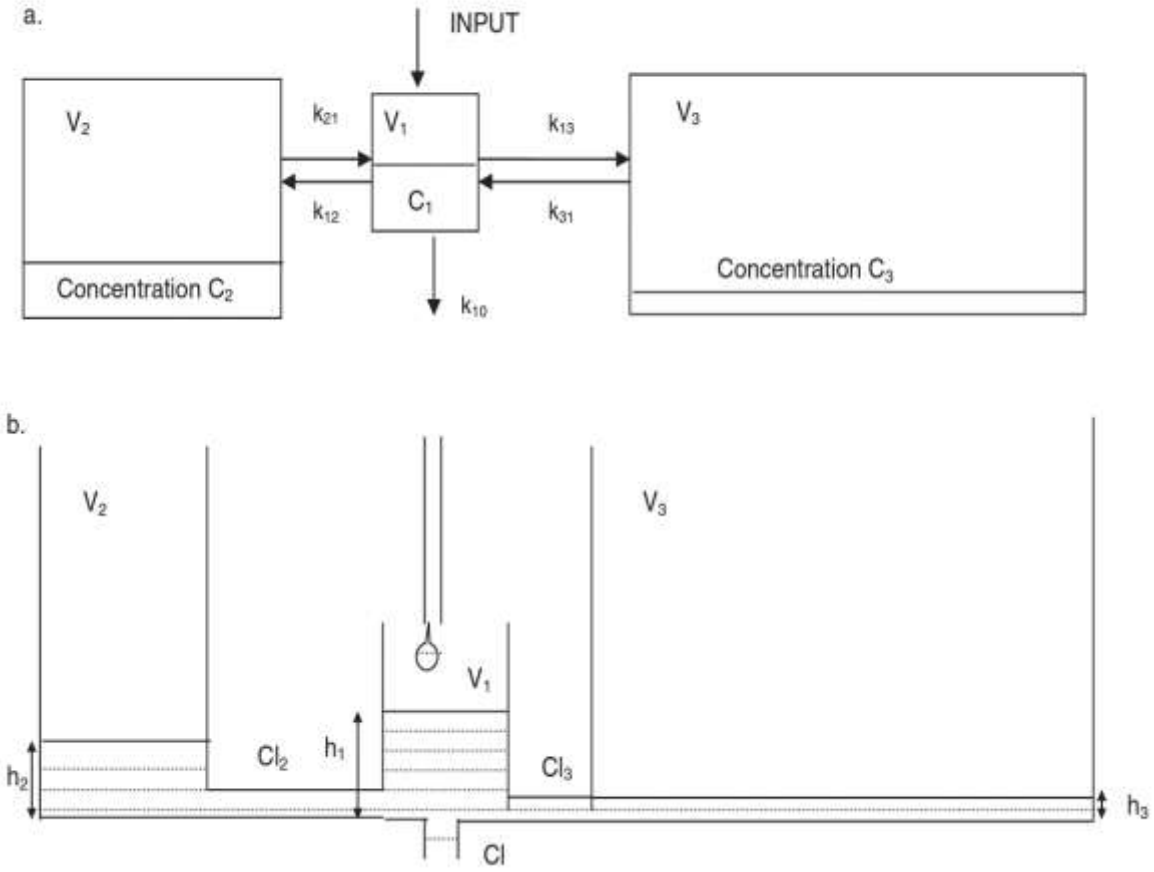
The two commonly used models for Propofol TCI are

1. Marsh model

2. Schnider model

The Marsh model for propofol was originally developed to target plasma concentration. On the other hand the Schnider model was specifically designed for concentration of targeting effect site. However, in modern TCI pumps either model can be selected so one can choose the target plasma or effect compartment. Both model designed to deliver time to peak effect time of 1.7 minutes. But a major difference is dose of delivery in first minute. Schnider model has small fixed central compartment while Marsh model has three times bigger compartment. So the drug dose delivered by Marsh model at 1st minute is three times larger than Schnider model.

Parameters	*Marsh model(modified)*	*Schinder*
V1	*Weight (lean body mass)*	*Fixed(actual weight, age, gender are taken)*
V2	*Weight*	*Age*
V3	*Weight*	*Fixed*
k12 &k21	*Fixed*	*Age*
k13 &k31	*Fixed*	*Fixed*
Ke0 min	*1.21 min*	*0.456 min*
Clearance	*Weight*	*Weight ,height ,gender*



THE THREE COMPARTMENT MODEL

V1 - Central compartment [21]

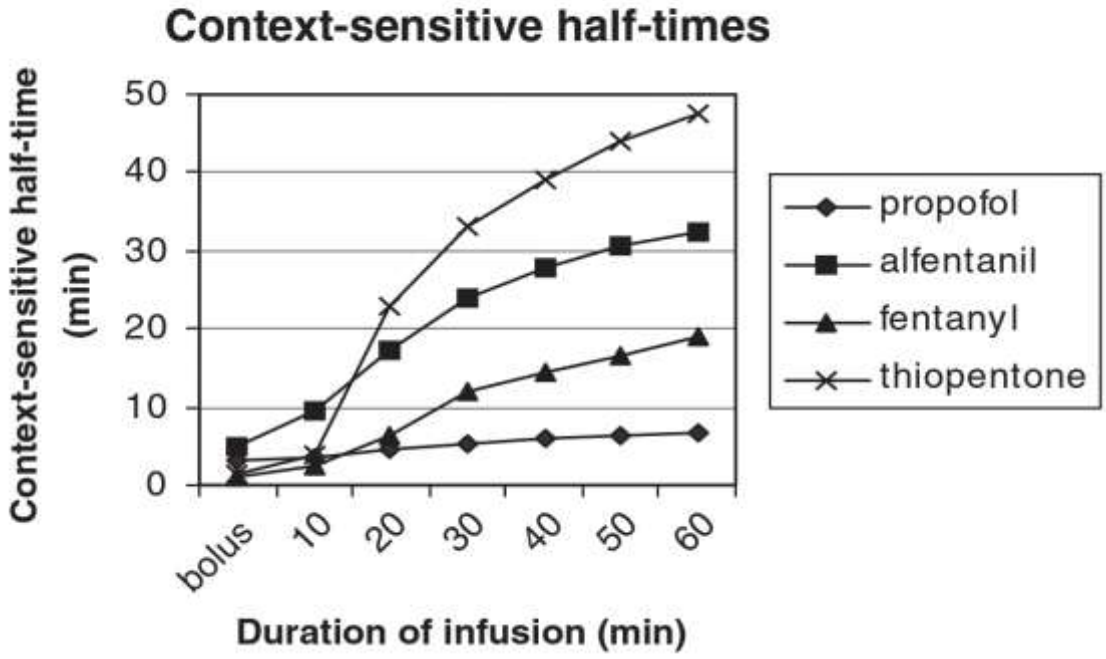
V2 & V3 - Peripheral Compartments

k10 Elimination

k12 and k13 distribution to 2 and 3 compartments

k21 and k31 redistribution back to central compartment

Cl clearance



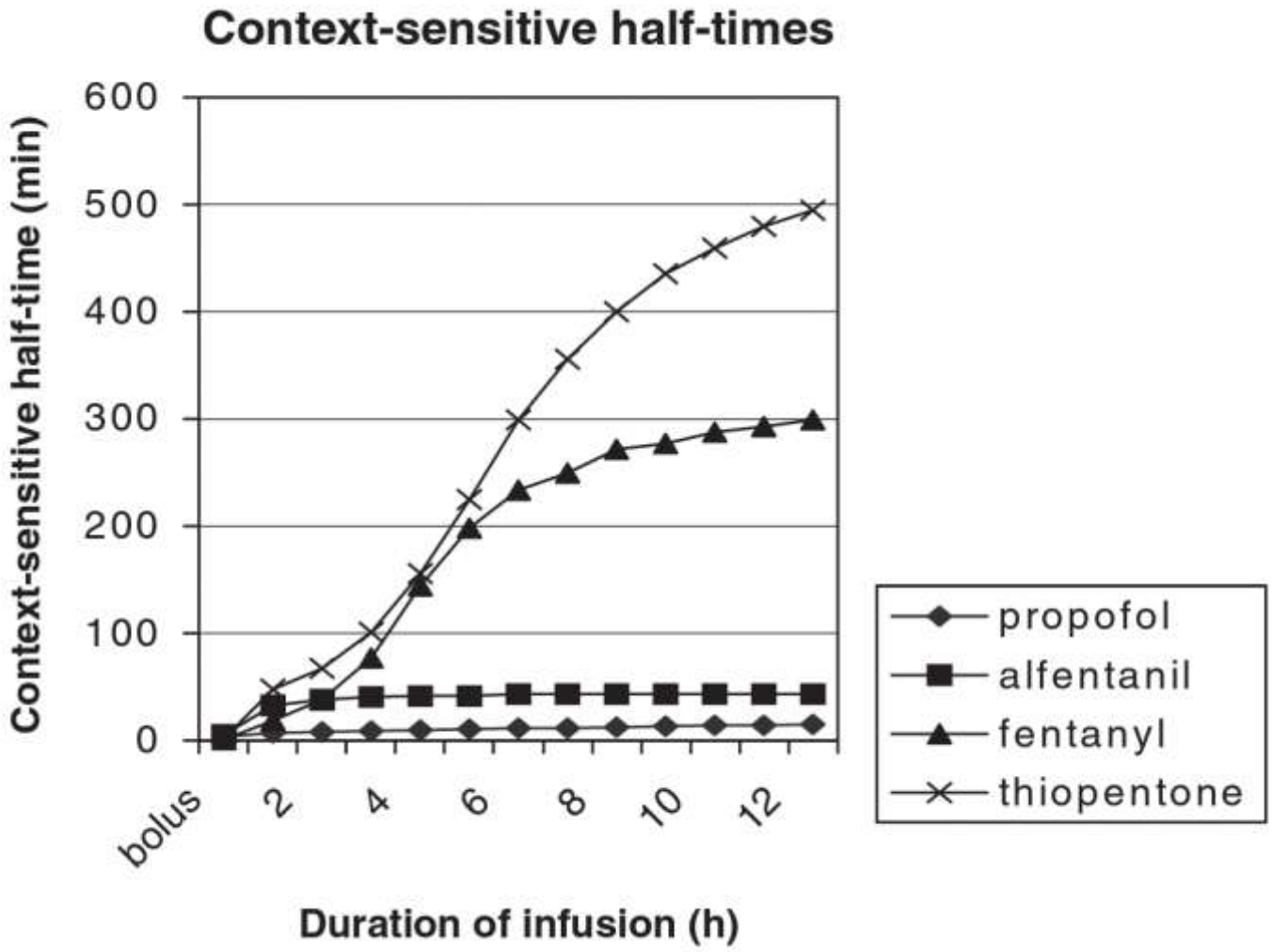
CSHT FOR SHORT DURATION

CONTEXT SENSITIVITY HALF TIME

CSHT refers time to fall in the concentration of drug in plasma to reduce 50% after stopping the infusion. $T_{1/2}$ half-life which denotes duration of actions of different drugs. But for infusions decrease in concentration of drugs depend upon duration of infusion. So concept of CHST arises. For a given drug when Clearance due to distribution is exceeds Clearance due to elimination will increase CSHT. For example Fentanyl has Clearance due to elimination which is one fifth of Clearance due to distribution. So prolong duration of infusion increases the plasma concentration of the drug, hence CSHT of fentanyl is high.

But for Propofol ,

Clearance due to elimination = Clearance due to distribution. So CSHT of Propofol is short.



CSHT FOR LONGER DURATION

Drug	Maximum possible CSHT
Fentanyl	300 minutes
Remifentanyl	8 minutes
Propofol	20 min

CSHT OF COMMONLY USED IV AGENTS

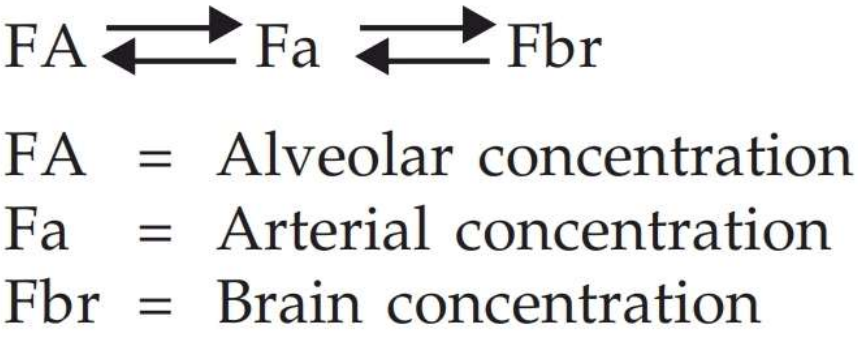
DECREMENTAL TIME

Decremental time defined as predicted time of Propofol concentration reduce from initial concentration to 1.2 mcg/ ml. This 1.2 mcg/ml correlate with wake up profile for the patient. This time may be prolonged in addition of opioid. Some TCI pumps display this.

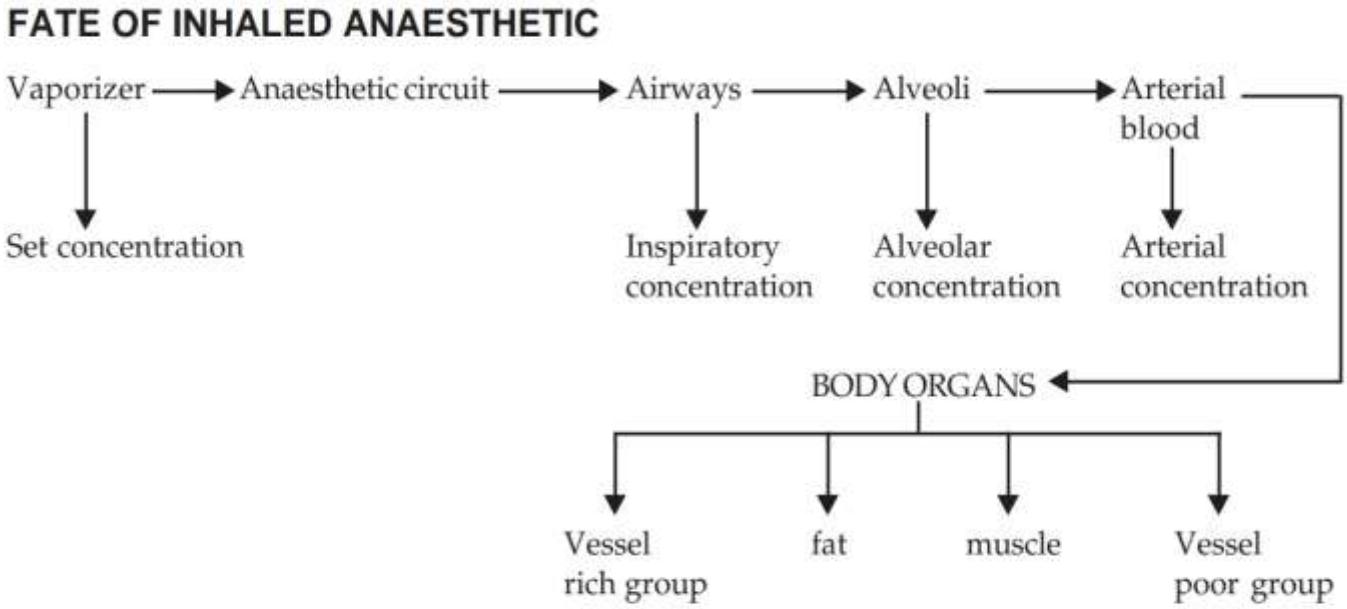
INHALATIONAL ANAESTHESIA

Volatile anaesthetic agents [23] administered in vapor form to the patient via Pulmonary route. Inhalational agents used mainly for maintenance but can also be used for induction under certain circumstances. These agents move down a concentration gradient from the vaporizer to the body organs. The movement of the molecules of anaesthetic agent depends on various factors, the most important factor is relative solubility between two phases ie between alveolar gad and blood. Initially the alveolar concentration equilibrates with the inspired concentration of inhaled anesthetic agent, which in turn equilibrates with arterial concentration and finally the brain concentration of the drug equilibrate with arterial concentration. The rate of equilibrium is established between the two phases depend upon relative solubility of the inhaled drug in the respective phases (i.e. Alveolar gas to blood and blood to brain etc.). The unit of this relative solubility is called as partition coefficient. All body organs do not equilibrate at the same rate with arterial concentration. On this basis the organs are divided into four groups as (vessel rich group, vessel poor group, fat, muscles,). Out of these groups vessel rich group is the first one to equilibrate with arterial concentration. The target organ of inhaled anaesthetic i.e. brain, will come under this group. Once equilibrium is established between all these three phases i.e. alveolar gas, blood and brain, alveolar

Concentration of the agent becomes an indirect measure of concentration in the brain. By controlling alveolar concentration we can control the brain concentration of the anaesthetic agent.



EQULLIBRIUM OF INHALED AGENT CONCENTRATION



DISTRIBUTION OF INHALATION AGENTS

IMPORTANT DEFINITIONS

Minimum Alveolar Concentration:-

Minimum concentration of anaesthetic agent in alveoli that is required to produce immobility in 50% patients for painful surgical stimuli.

MAC awake: - minimum alveolar anaesthetic agent concentration that produces 50% of patients voluntarily respond (eye opening) to commands.

MAC95 (MAC of 1.3):- minimum alveolar anaesthetic agent concentration for which 95% of patients do not respond to skin incision

MAC BAR (MAC of 1.6): minimum alveolar anaesthetic concentration for which 50% of patients have a block of sympathetic response (HR, BP, noradrenaline levels) to surgical stimulation

MAC Intubation (-1.3): minimum alveolar concentration required to produce laryngeal response for intubation.

MAC BAR > MAC intubation > MAC skin incision > MAC laryngoscopy

PARTITION COEFFICIENTS

Blood gas coefficient:-

High blood gas coefficient indicates that agent is more soluble in blood than gas. So

$$\text{Blood/gas coefficient} = \frac{\text{Affinity of agent for blood}}{\text{Affinity of agent for gas}}$$

induction and recovery take longer time for agents with high blood partition coefficient.

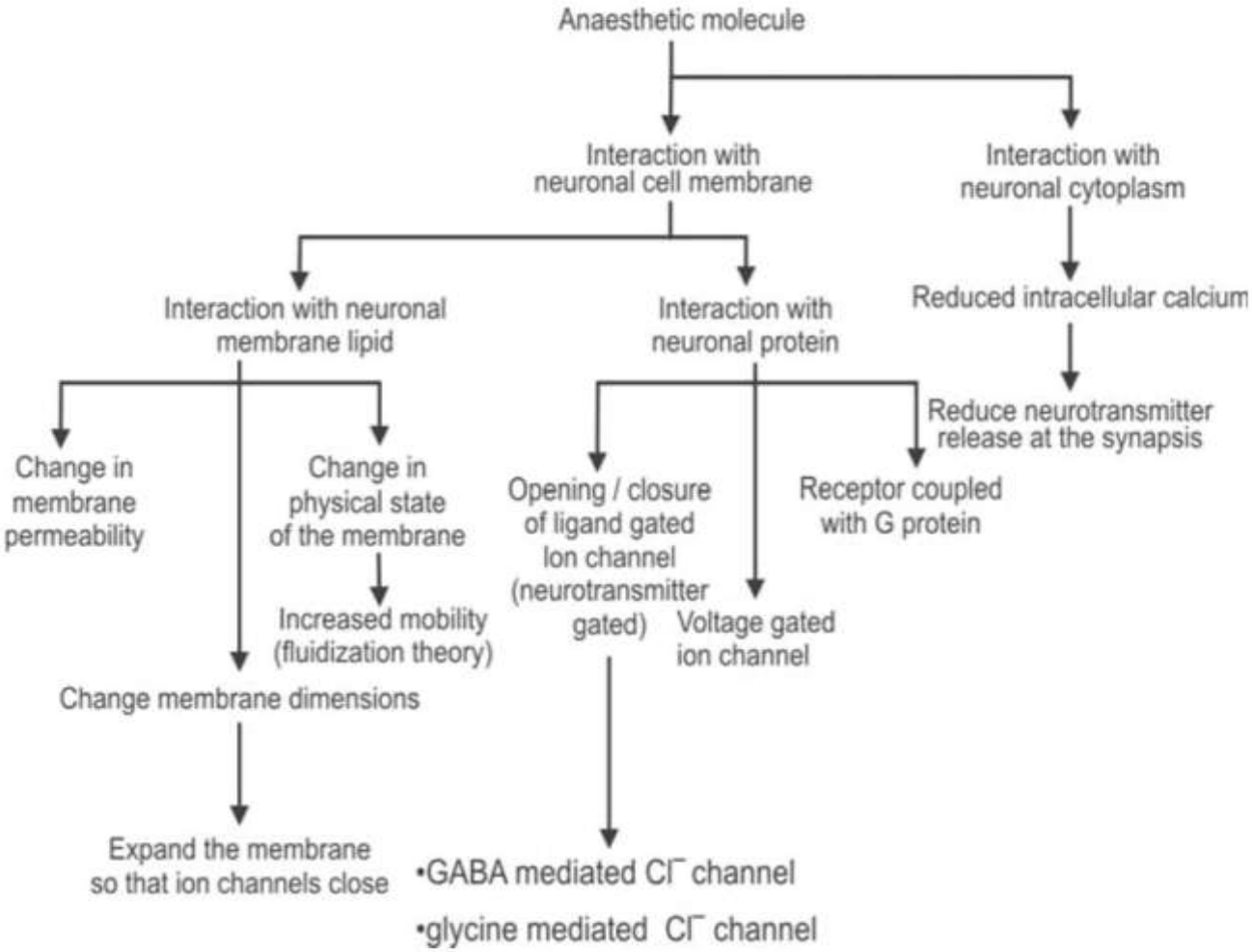
Oil gas coefficient:-

Anesthetic potency of any inhalational agent is directly proportional to its lipid solubility (so called oil gas partition coefficient). This is called as Meyer Overton rule. According to this all anaesthetic agents are lipid soluble. However exceptions to this are

1. All lipid soluble agents do not produce anesthesia but most of them can even produce convulsions.

2. As per this rule all isomers of same agent should have same potency. But this is not true. For example Isoflurane, enflurane and desflurane in spite of being isomers have different potencies.

3. Also It was very well proven that anesthetic agents are not only bind to lipophilic (lipid soluble site) site, but they also bind to hydrophilic (lipid insoluble) sites.

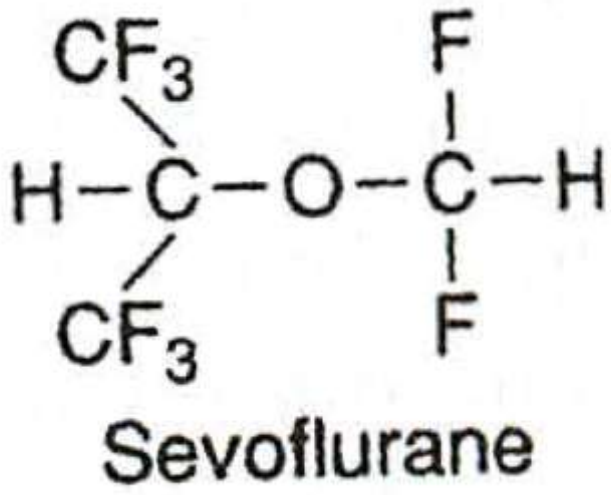


MECHANISM OF ACTION OF INHALATIONAL AGENTS

SEVOFLURANE

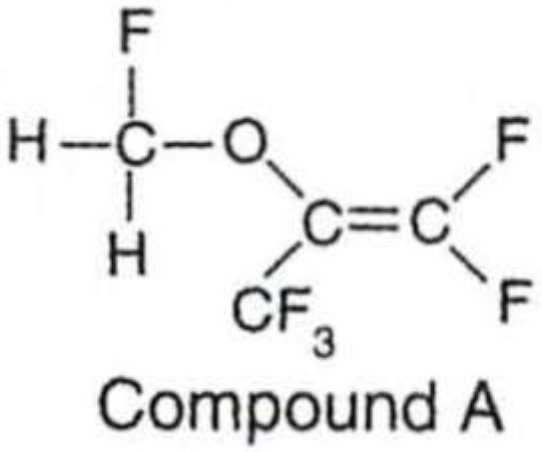
Sevoflurane is fluorinated methyl isopropyl ether. It was introduced to clinical

Practice at the year of 1981.The saturated vapor pressure of sevoflurane close to that of halothane and isoflurane this permitting delivery of this anesthetic via a conventional unheated vaporizer.



STRUCTURE OF SEVOFLURANE

Sevoflurane is a non-pungent anesthetic agent, it has minimal odour. It produces bronchodilation similar in degree to isoflurane, and it causes the least degree of airway irritation among the currently available volatile anesthetics. For these



STRUCTURE OF COMPOUND A

Reasons Sevoflurane is acceptable for inhalation induction of anesthesia and choice of induction in pediatric patients. Of all volatile agents available Sevoflurane is least likely to form carbon monoxide [24] with carbon dioxide absorbents. But sevoflurane breaks down in the presence of the strong bases present in carbon dioxide absorbents to form compounds that are nephrotoxic in animals. The principal degradation product is fluoromethyl-2, 2-d ifluoro-1-(trifluoromethyl) vinyl-ether called compound A. This found to be nephrotoxic in rodents.

PROPERTIES OF SEVOFLURANE

Molecular weight	200
Boiling point	58.6 c
Density g/ml	1.50
Vapor pressure in mm Hg	157
Oil /gas partition coefficient at 37 c	47 -57
Blood / gas partition coefficient at 37 c	0.65
MAC immobility	2.05
MAC Awake	0.63

VAPORIZERS

Inhalational agents used at present are liquid at atmospheric pressure and room temperature and it should be converted in to vapours before administered to patients. A Vaporizer is a device which converts liquid anaesthetic agents to vapour at clinically significant concentration for controlled admission with fresh gas flow via a breathing system to patients.

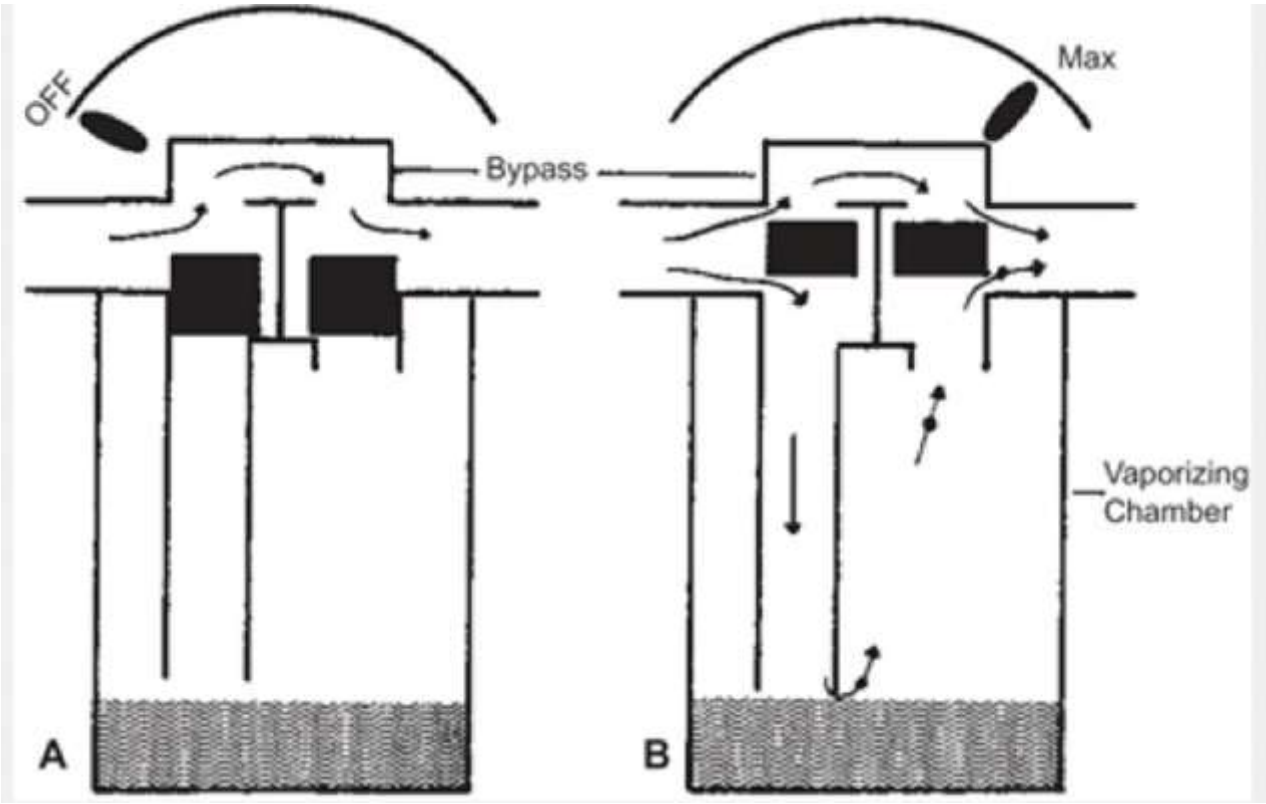
Classification of Vaporizer

A vaporizer may be Draw over or Plenum type according to pressure of fresh gas flow needed. In view of vaporization method injection, with or without wicks, bubble through, flow over types. Also if we classify on the basic of regulating vaporizer output it is classified as variable bypass or measured flow. Placement of vaporizer in circuit may be inside (VIC) or outside (VOC).

DESIGN OF A VAPORIZER

Basic design consists of

1. Concentration Dial
2. Variable Chamber
3. Bypass chamber



A ON AND B OFF POSITION

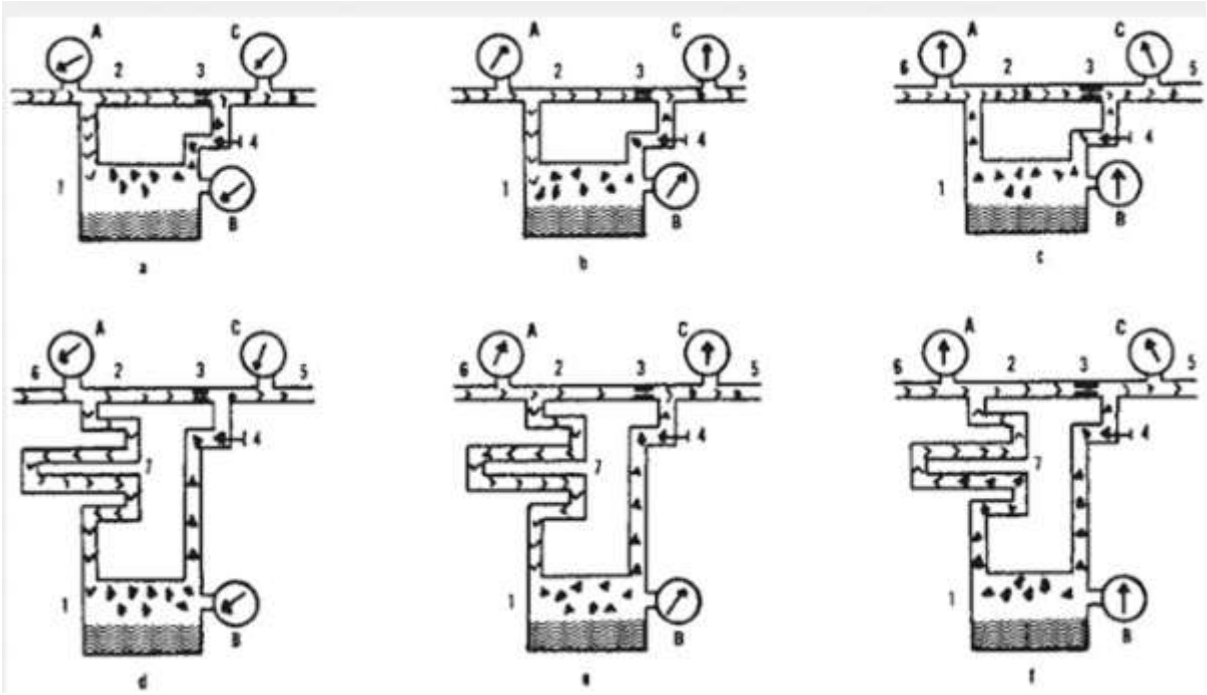
Problem with a basic system is

1. High flow decreases the output
2. Drop in Temperature with use
3. Pumping effect
4. Pressurizing effects

These draw backs are overcame in modern day vaporizers.

MODIFICATIONS

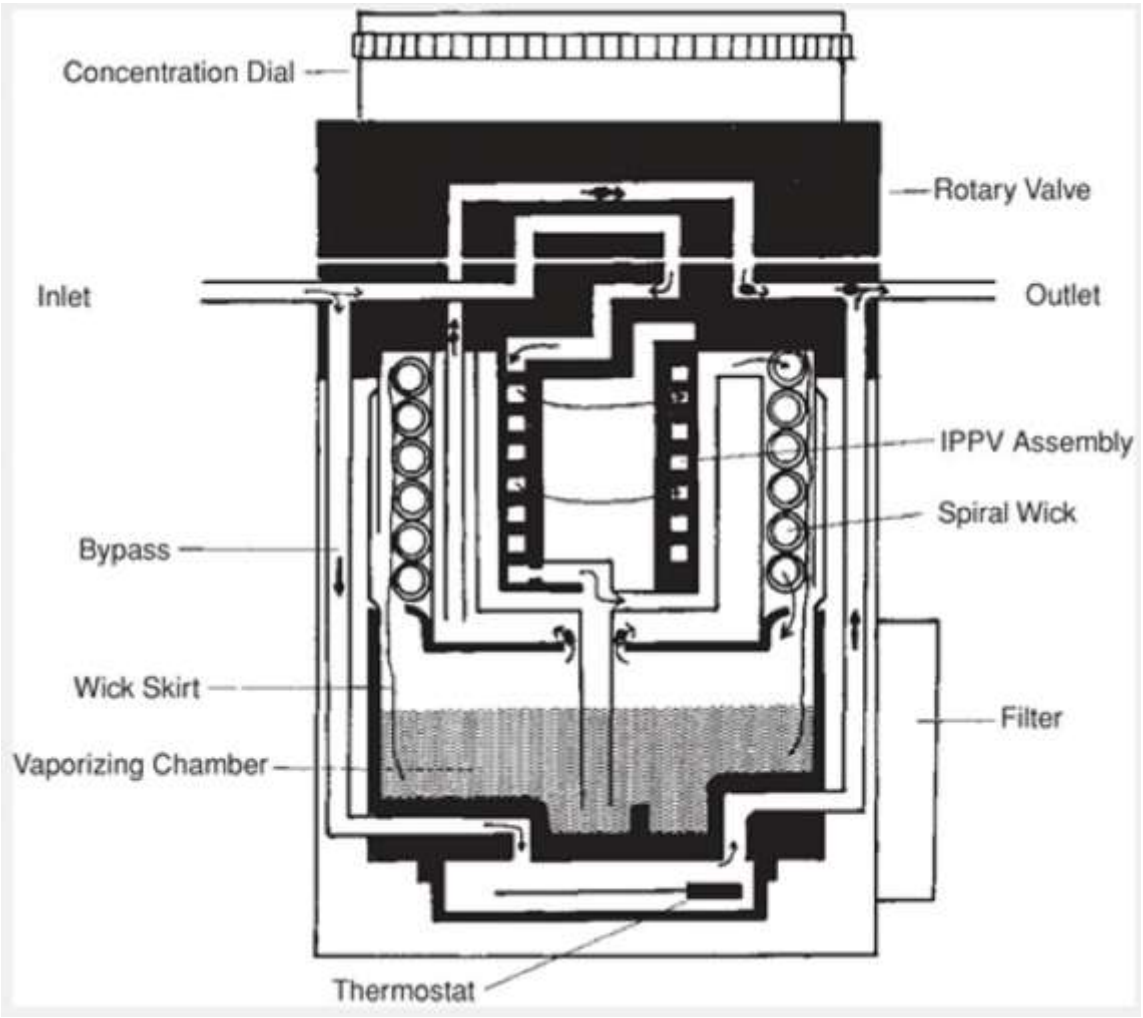
1. Wicks are included to increase the surface area in a flow over vaporizer in sake of managing output in high flow conditions. For a bubble through vaporizer bubbles will improve the surface area.
2. Temperature can be compensated by Bi metallic strips in TEC vaporizer, Supplying heat, or making the vaporizer chamber with a metal that has high latent heat capacity and good conductivity. Water filled bellows can also be used.
3. Pumping effect[25] can be reduced by keeping the vaporizer chamber size small, long, large diameter or spiral lead to chamber, exclude wicks from the junction between inlet tubes joining vaporizer chamber. A check valve can be kept at machine outlet but upstream to oxygen flush.



PUMPING EFFECT

TEC 5 VAPORIZER

We used TEC5 Vaporizer[26] for our study. TEC series means temperature compensated.



TEC 5

TEC5 Vaporizers designed for use of halothane, Isoflurane, Enflurane and Sevoflurane. This is concentration calibrated, variable bypass, and flow over, thermo compensated vaporizer. There are two filling system[27] for this vaporizer which are the key filling system and the funnel filling system. The thermostat is a bi metallic strip.

OPERATIVE FUNCTION OF TEC 5

When the dial is in zero position all fresh gas goes to bypass chamber to circuit. When the dial crosses the zero position the fresh gas split in to two and pass through bypass and vaporizing chambers.

On the path to vaporizer chamber the gas pass over the bi metallic strip. When temperature inside vaporizer drops the strip allows more flow to vaporizing chamber to maintain the constant output and vice versa.

So when the gas flows through the vaporizing chamber it first passes through central part of the rotatory valve then directed to helical channel after that it passes through the wicks which contact with the volatile agent. Finally the gas with vapour leaves the chamber in concentration of value set by the dial.

ANAESTHETIC CONSIDERATIONS IN SPINE SURGERY

Preoperative evaluation:[28] **-** Complete evaluation of respiratory, cardiovascular and neurological systems should be done as all the systems can be affected in spine pathology. Spine pathology possess difficult airway and cervical spine stability should be maintained during airway manipulation. Restrictive lung pathology is common in these patients. PFT is indicated in such case and it will predict post-operative recovery. Severe restrictive lung pathology may be associated with pulmonary hypertension. Echocardiography should be done when indicated.

Positioning [29]**: -** depend on level of approach. Patients may be transitioned between supine, lateral and prone positions. Goals are

1. Adequate padding on pressure points protects Peripheral nerves. Avoid abdominal compression during positioning. Raised intra-abdominal pressure may lead to increased blood loss in field.

2. To avoid displacement of fractures while positioning.

3. To make ensure low venous pressure to minimize the blood loss in field.

Blood loss:- frequency of transfusion in spine surgery higher. Main loss due to number of vertebral segments involved, spinal instrumentation and decortication. Rarely due to trauma of major vessels like vena cava, aorta and iliac vessels. Preoperative cross matching and adequate reservation of blood is important.

Spinal cord monitoring and injury [30]**:-** wake up test can be performed intraoperatively. But it has its own limitations. Somatosensory evoked potential,

motor evoked potential are other methods. These tests are affected by various anesthetic agents and should be monitored cautiously. Post-operative paraplegia may occur in spite of normal monitoring. Higher level like C3, C4 injury associated with respiratory depression as it supplies diaphragm. Injury above T5 associated with physiological sympathectomy.

Pain relief and post-operative care:- opioid , non-opioid like NSAIDS, steroids, acetaminophen, regional as epidural can be used. Opioid can be administered with patients controlled anesthesia devices. In indicated cases post-operative mechanical ventilation may be required. Spirometry and other respiratory muscle exercises help to improve pulmonary functions.

AIMS AND OBJECTIVE

To compare the effects of Sevoflurane vs Propofol as TIVA on extubation response and hemodynamic changes during general anaesthesia in spine surgery patients.

Primary Objectives:-

1. To compare Maximum Mean Arterial Pressure During Emergence
2. To compare Maximum Heart rate during Emergence
3. To compare Presence and absence of Cough

Secondary Objectives:-

1. To assess Intraoperative and postoperative haemodynamics.
2. To evaluate intra operative Neuro Muscular Agents dosage

REVIEW OF LITERATURE

M. Hohlrieder1, W et al.[31] Compared TIVA and balanced anesthesia on effect of cough during emergence in spine surgery patients. It is a randomized prospective study. They also compared maximum MAP, HR and lowest Spo_2 during emergence. Effect of smoking and duration for emergence also compared. This study has sample size of 60, and 26 in TIVA group 24 in balanced anesthesia group. They concluded that maximum MAP, Maximum HR, and coughs during extubation are significantly lower in TIVA group (<0.05 p value). And there is no significance for lowest Spo_2 and smoking effects.

Liang C and Ding M et al[32] did a randomized clinical trial on classic general anesthesia patients. On General anesthesia patients they compared sevoflurane and propofol maintenance and sevoflurane in combined epidural general anesthesia. They chose 160 patients who were ASA PS 1 or 2, age between 45-65 years , and posted for elective gastrointestinal surgery under combined general/epidural anesthesia they, were allocated randomly to receive sevoflurane/propofol regimen (group SP, n = 80) and the sevoflurane maintenance regimen (group S, n = 80) or). After induction, anesthesia was maintained with sevoflurane with propofol (1.2 microgram/ml target plasma concentration) in group SP and with sevoflurane in group S. Bispectral index (BIS) values were maintained between 40-60 during the maintenance. Time for extubation, incidence of coughing and agitation, and other recovery characteristics were evaluated during emergence. The time to awakening and extubation in group SP shorter than those results in group S (P value of < 0.05). The incidence of coughing

and agitation in SP was lower than that of group S ((P value of < 0.05). BIS value, pain score, requirements of analgesics and antiemetics, and length of stay in the PACU were comparable in the groups. They concluded that co administration of Propofol and sevoflurane gives faster awakening and extubation and a low incidence of emergence coughing and agitation.

LD Mishra and SK Pradan et al[33] did a study on Comparison of Propofol based anaesthesia to conventional inhalational general anaesthesia for patients posted for spine surgery . They chose 80 (n=80) ASA PS I &II adult patients who were randomly allocated into two groups (study and control group). Patients in study received inj. Propofol for induction and same for maintenance along with N_2O +O_2. And the control group patients received inj.Thiopental for induction and Isoflurane N_2O +O_2 for maintenance. BIS monitoring was used for depth of anaesthesia monitering and titrating the anaesthetic dose adjustments in all patients. They concluded that post-operative nausea and vomiting reduced in propofol group. Also clear head awakening and orientation to place are better in propofol than isoflurane group

Chan vw, Chung FF et al did a randomized prospective study in elderly patients. To evaluate recovery and hemodynamic profiles in propofol induction and maintenance compared with Thiopentone induction and Isoflurane maintenance. They selected 60 non premedicated ASA PS I, II, and III adult elderly patients undergoing total hip replacement surgery. . Induction of anesthesia by propofol infusion (1.6 mg/kg) didn't produce significant bradycardia or hypotension. These changes were similar to induction with Thiopentone bolus injection (3.3 mg/kg). Furthermore, increases in BP and heart rate during Intubation were limited to 6% following Propofol induction

compared with 22% for Thiopentone bolus induction. During maintenance period, the decrease in MAP and HR was comparable in both groups. Postanesthetic recovery times for patient to get mental orientation, to achieve wakefulness, and a maximum modified Aldrete score (10) were significantly faster in the Propofol group, at 4 minutes, 6 minutes, and 20 minutes, respectively; but the time to discharge from the postanesthesia care unit was not different in both groups. They concluded the Induction of anesthesia by Propofol infusion in elderly patients will result in greater attenuation of cardiovascular and sympathetic response than Thiopentonel bolus induction.

Costing D Ellwood et al did a randomized control trial on Transition to propofol after sevoflurane anaesthesia to prevent emergent agitation on 230 children who underwent for MRI under general anesthesia. In this study anaesthesia maintained with sevoflurane and at the end of procedure, Propofol group received Propofol 3mg / kg over 3 minutes; the control group received no drug. With blind assessor emergence delirium assessed by PEAD scale and Watcha scale. Emergence delirium was lower in propofol group as per PEAD and Watcha scale (p value <0.001).

MATERIALS AND METHODS

Forty patients of ASA physical status I and II undergoing elective spine surgical procedures which are done General anesthesia with endotracheal tube were selected for my study.

Patient's age between 18 to 65 years of both gender taken for randomized prospective study by comparing sevoflurane and propofol as Total intravenous anaesthesia on cough and hemodynamic changes during emergence for Spine surgeries after obtaining ethical committee approval in our institution and informed consent obtained.

INCLUSION CRITERIA:

- Age: 18 to 65 years.
- ASA :I,II
- Surgery :Elective
- Body Mass Index <30
- Who have given valid informed consent.

EXCLUSION CRITERIA:

- Not satisfying inclusion criteria.
- Not willing (Patient refusal)
- Preexisting Respiratory disease like asthma ,COPD or recent respiratory tract infections
- Patients with anticipated difficult airway
- Risk of post-operative aspiration
- Allergic to drugs used
- Patients with severe cardiovascular, Endocrine, respiratory, renal, hepatic, Psychiatric diseases.

MATERIALS:

18G IV cannula

Drugs–Inj. Propofol, Inj. Glycopyrrolate, Inj. Thiopentone ,Inj. Fentanyl, Inj. Succinylcholine, Inj. Atracurium, Inj. Neostigmine, Inj. Dexamethasone, Inj. Paracetamol, Inj. Tramadol, Inj Nitroglycerin, emergency drugs and Ringer lactate, normal saline, Sevoflurane.

Monitors–ECG, NIBP, Spo_2 and $EtCO_2$.

Equipments : Vaporizer, Laryngoscope with assorted blades, Mask of appropriate size, Endotracheal tube.

METHODOLOGY

All patients who are satisfying inclusion criteria were included in this study. Routine investigations like complete hemogram, random blood sugar, blood grouping and cross matching, renal function test, ECG, Chest radiograph postero anterior view were done. All these patients were randomised in to two groups i.e. Group P and Group S and were informed about the procedure. And written informed consent obtained .Age, weight and height were recorded .All patients were premedicated with Tab.Alprazolam on the night before surgery .Inj. lycopyrrolate 0.2 mg I.M. given 45 min prior to intubation. Patients were shifted inside the operating rom. Basic monitors such as $EtCO_2$, ECG, NIBP, Spo2 were connected and baselines reading were recorded. Intravenous access obtained with 18G intravenous cannula. Inj. Fentanyl given and induced with Inj Thiopental according to patient's weight. Inj. Succinyl choline used as relaxant for intubation and Inj Atracurium used for maintenance relaxant. After intubation Group S maintained with a long with oxygen and nitrous oxide in 33:67% along with Sevoflurane. Whereas in Group P anaesthesia maintained with Inj Propofol infusion started by Bristol method as per 10- 8 - 6 rule. Per kilogram dose of 100 to 300 mics/kg/min kept. Intra op vitals, muscle relaxants consumption, Post-operative maximum heart rate, BP shoot up, lowest saturation and emergence cough incidence were noted.

METHODOLOGY

ETHICAL COMMITTEE APPROVAL

⇩

PATIENT SATISFYING INCLUSION CRITERIA

⇩

INFORMED CONSENT OBTAINED

⇩

RANDOMIZATION BY CLOSED ENVELOPE METHOD

⇩

HR, BP, MAP, SPO2, RR MONITORING

⇩

PREOXYGENATION

⇩

INDUCTION

⇩

INTUBATION WITH ENDOTRACHEAL TUBE

⇩

SURGERY PROCEEDED WITH MAINTENANCE OF ANAESTHESIA

GROUP S - SEVOFLURANE 0.5 -2%

GROUP T- PROPOFOL 100-300mcg /kg/min

END OF SURGERY

EXTUBATION

MEASUREMENT OF OTHER STUDY OUTCOME

COMPARE WITH THIS STUDY OUTCOME

EXTUBATION RESPONSE
TOTAL DOSE OF NEURO MUSCULAR BLOCKING AGENTS
COMPLICATIONS RATE

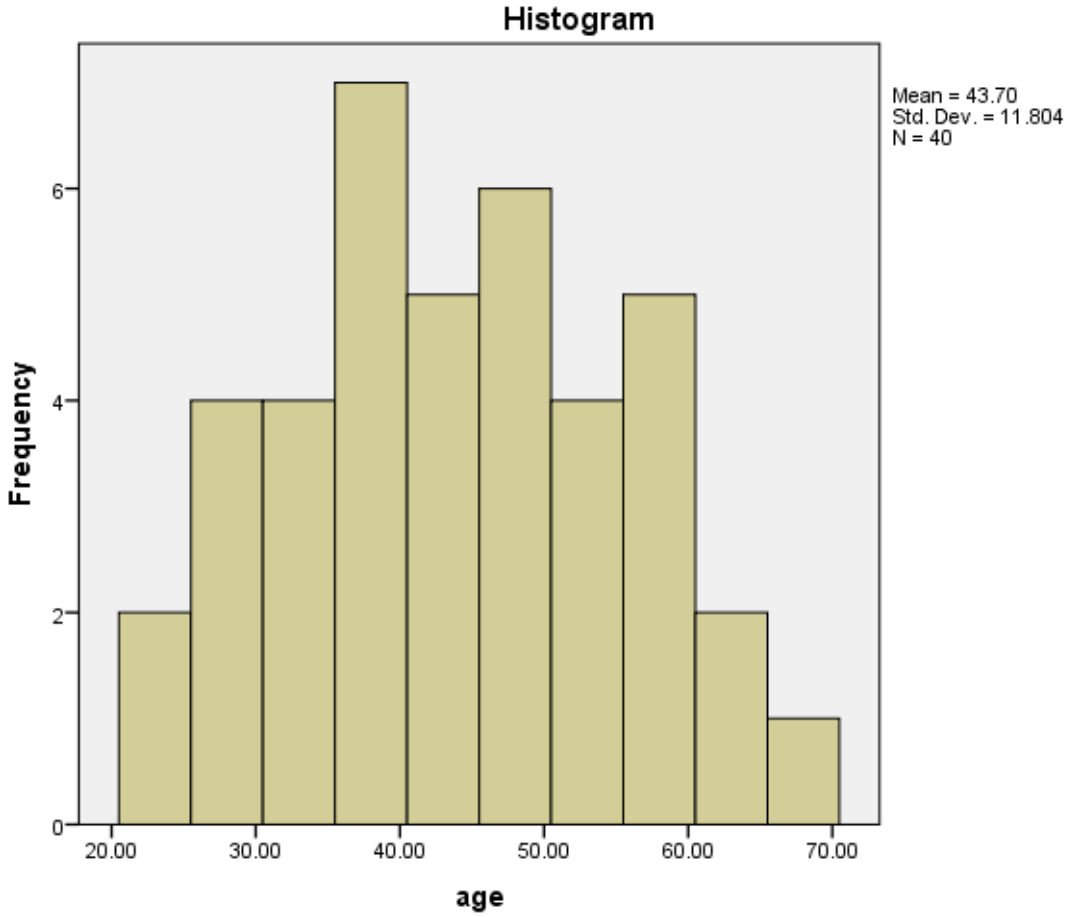
DATA COMPILATION

STATISTICAL ANALYSIS

CONCLUSION

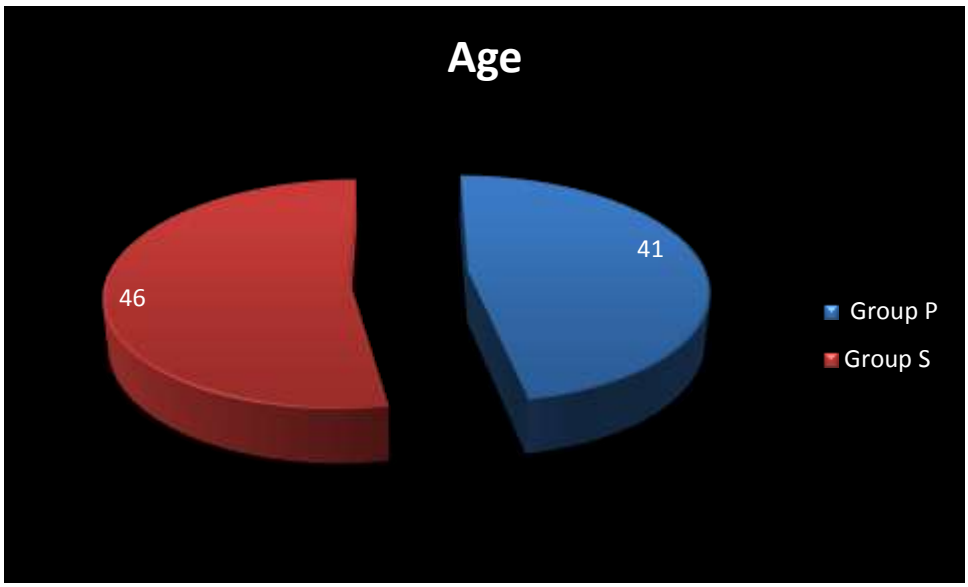
RESULTS

AGE


Histogram
Mean = 43.70
Std. Dev. = 11.804
N = 40
Frequency
0
2
4
6
20.00
30.00
40.00
50.00
60.00
70.00
age

Tests of Normality						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statstic	df	Sig.
Age	.090	40	.200*	.979	40	.643

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Age	Equal variances assumed	.005	.946	-1.411	38	.166	-5.20000	3.68639	-12.66271	2.26271
	Equal variances not assumed			-1.411	37.832	.167	-5.20000	3.68639	-12.66380	2.26380



Age between 18 to 65 years included in our study allotted in to Group P and Group S. It is a continuous data. Distribution analyzed with Kolmogorov-Smirnov test and Shapiro-wilk concluded normally distributed. Since it is a ordinal variable with normal distribution also a small group Unpaired student t test applied. P value is 0.946 (insignificant)

SEX

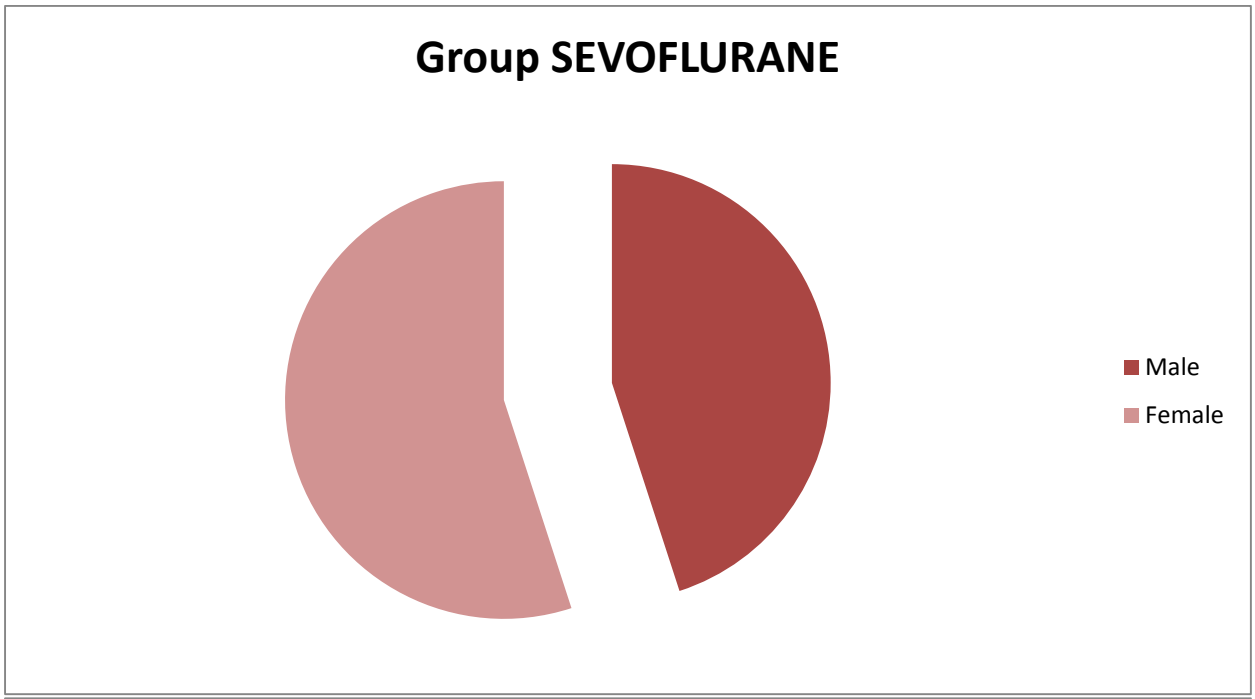
		SEX		Total	
		F	M		
	Group P	9	11	20	
	Group S	11	9	20	
Total		20	20	40	

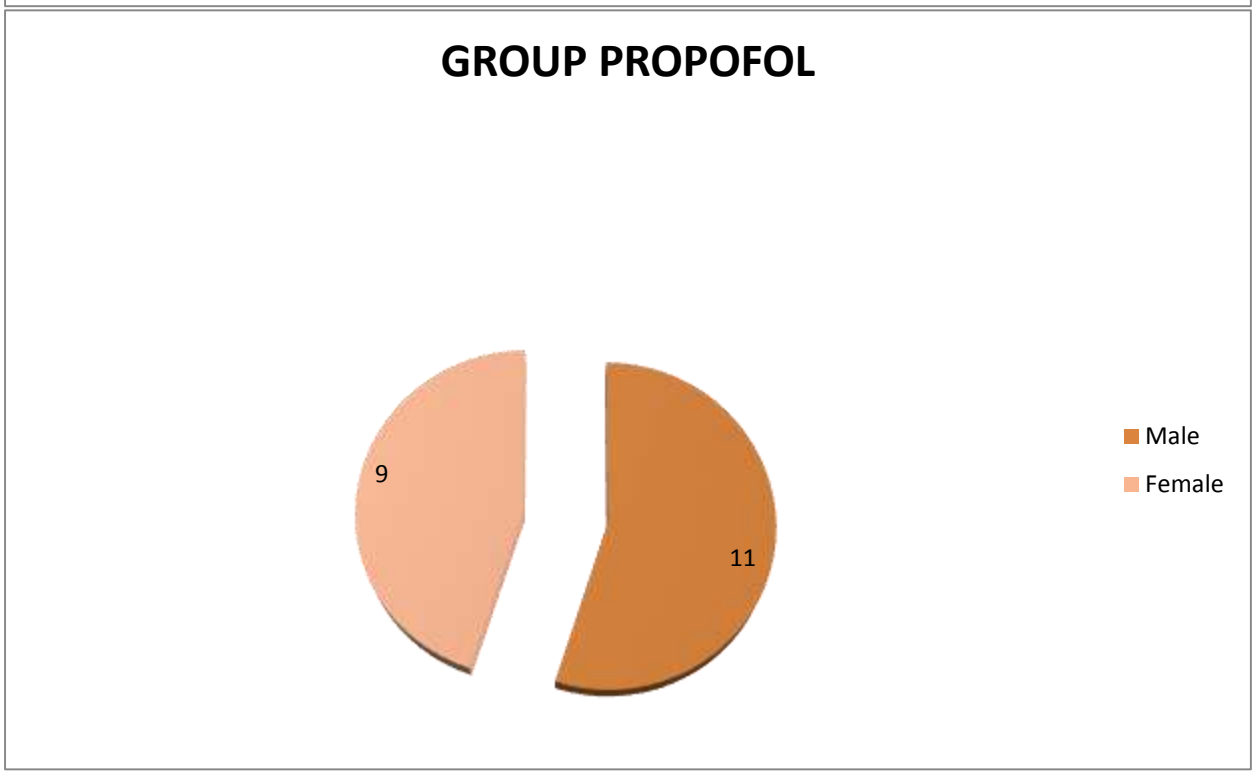
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.400[a]	1	.527		
Continuity Correction[b]	.100	1	.752		
Likelihood Ratio	.401	1	.527		
Fisher's Exact Test				.752	.376
N of Valid Cases	40				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 10.00.

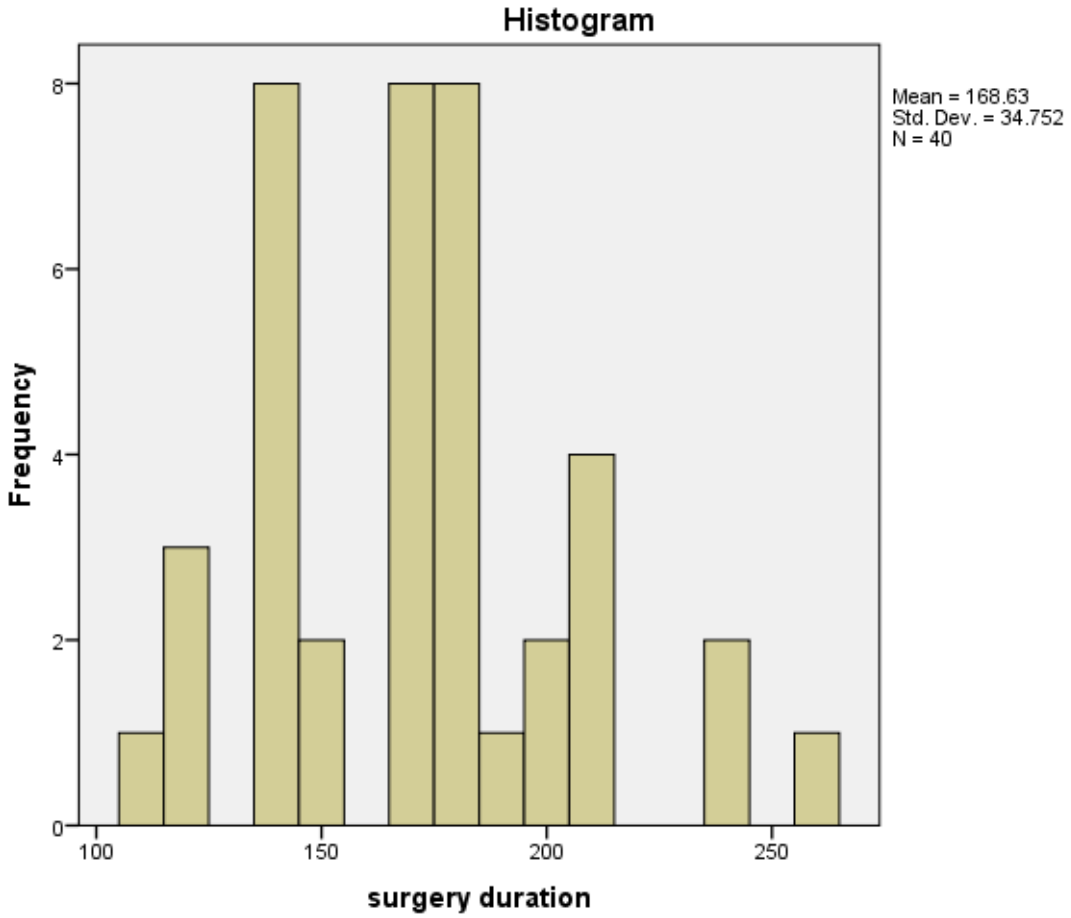
b. Computed only for a 2x2 table





Sex is a nominal data. There are 9 females and 11 males in Group P. and 11 females and 9 males in Group S. The statistical diagnostic test applies here is Fisher's exact test. P value is 0.752 which is insignificant.

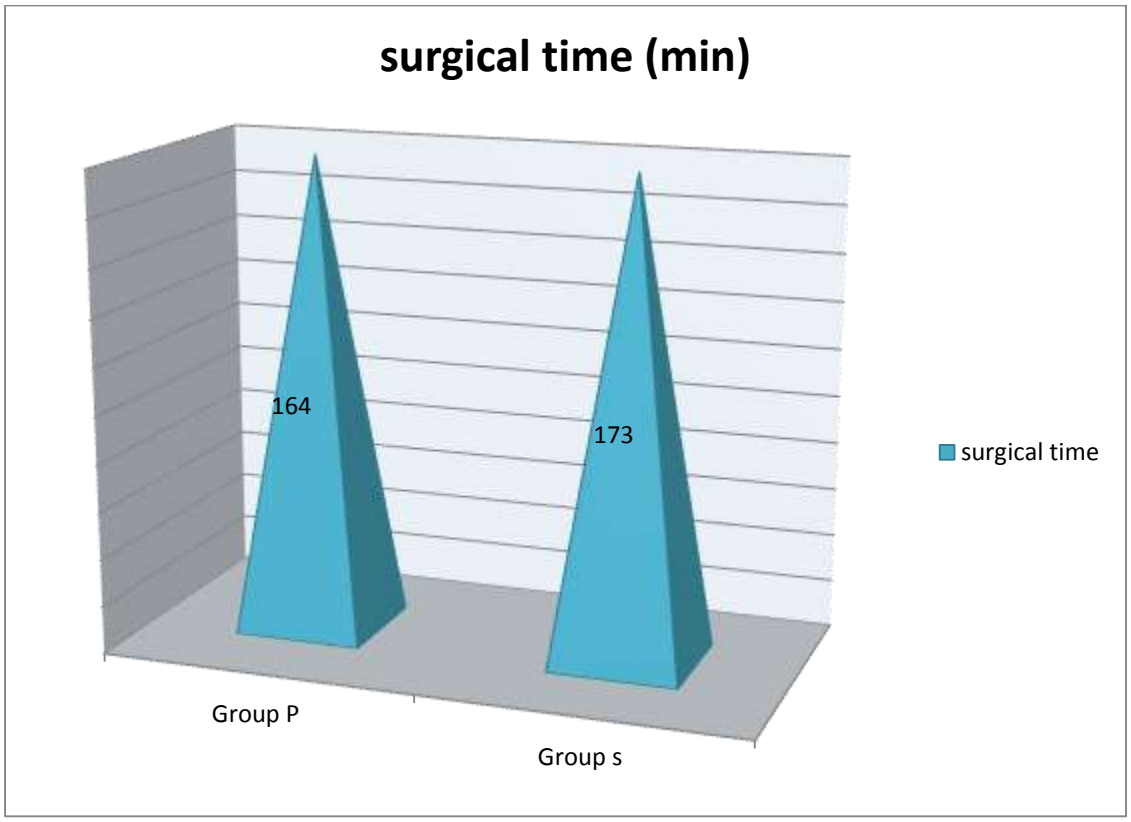
DURATION OF SURGERY



Tests of Normality

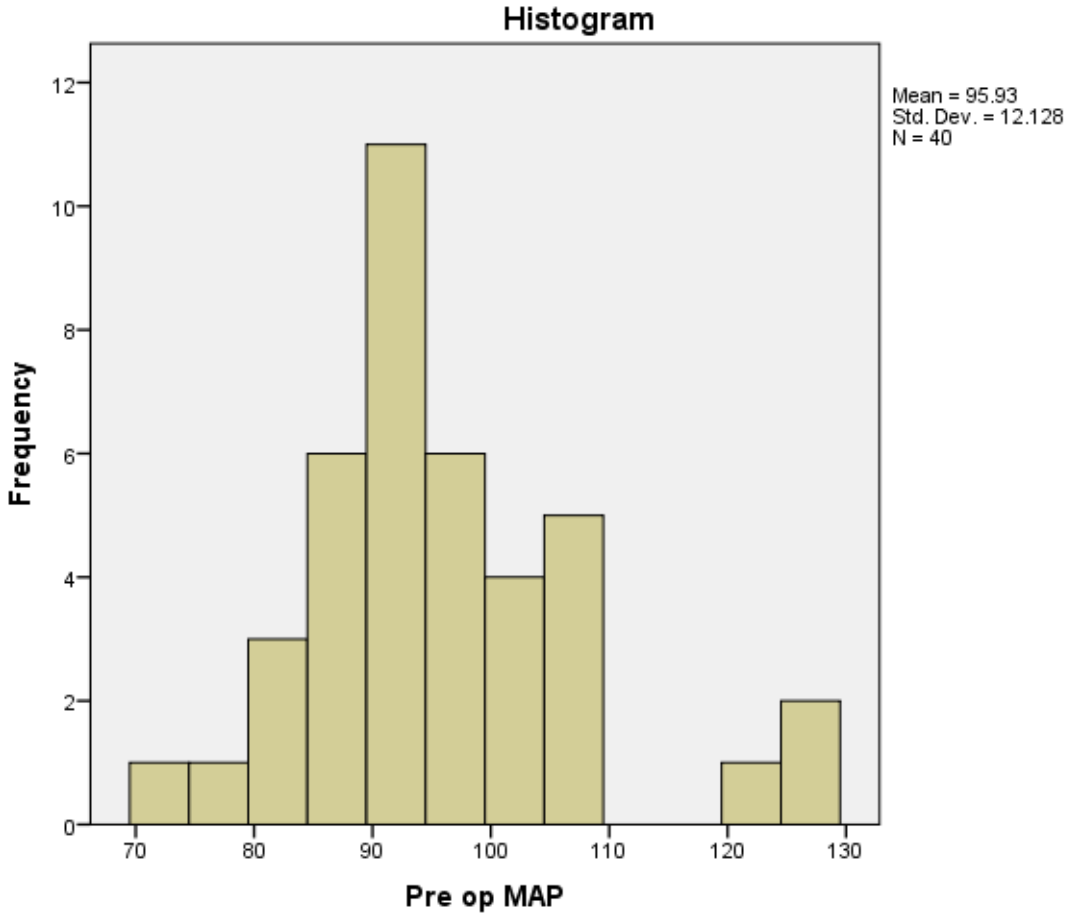
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
surgery duration	.133	40	.071	.953	40	.095

	MEAN		P Value(Student t test)
	P	S	
SURGERY DURATION	164	173	0.407



The duration of surgery is a continuous data. Using Shapiro-wilk test and Kolmogorov-smirnov test it's concluded as normally distributed. Hence unpaired student t test applied. P value is 0.407 (insignificant).

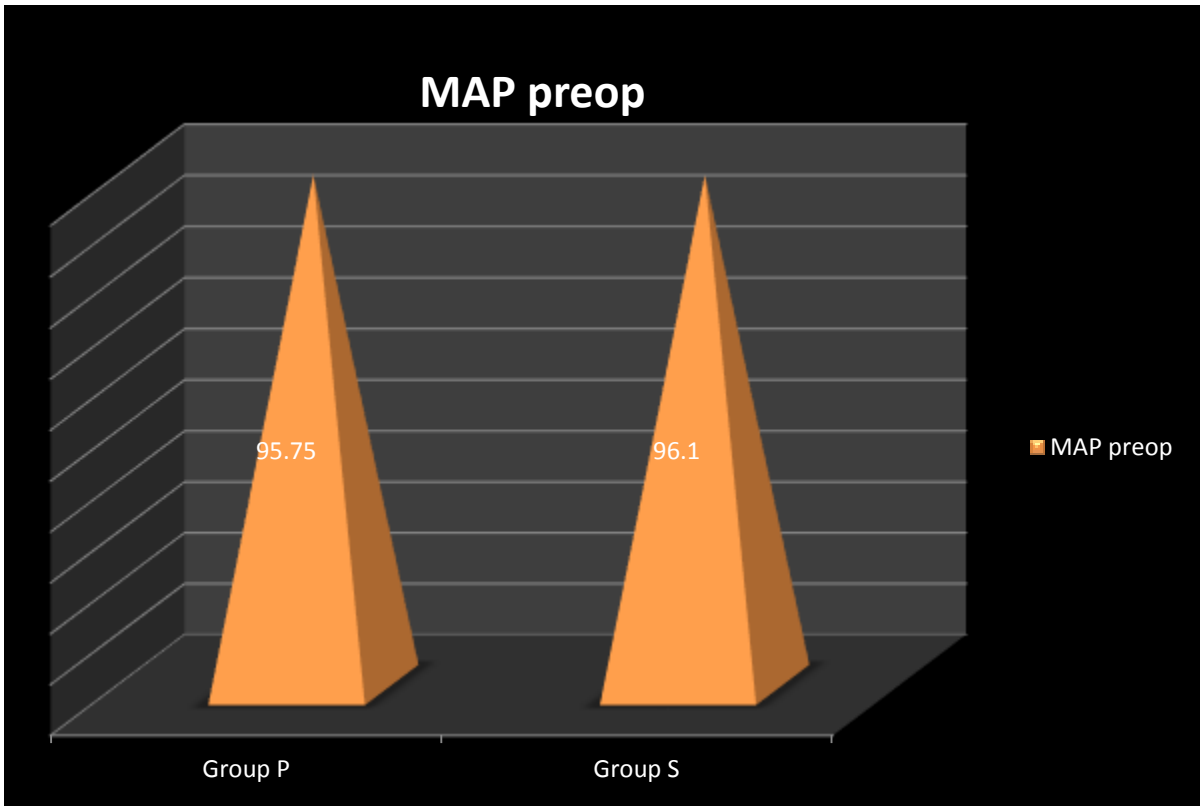
PRE OPERATIVE MAP



Tests of Normality

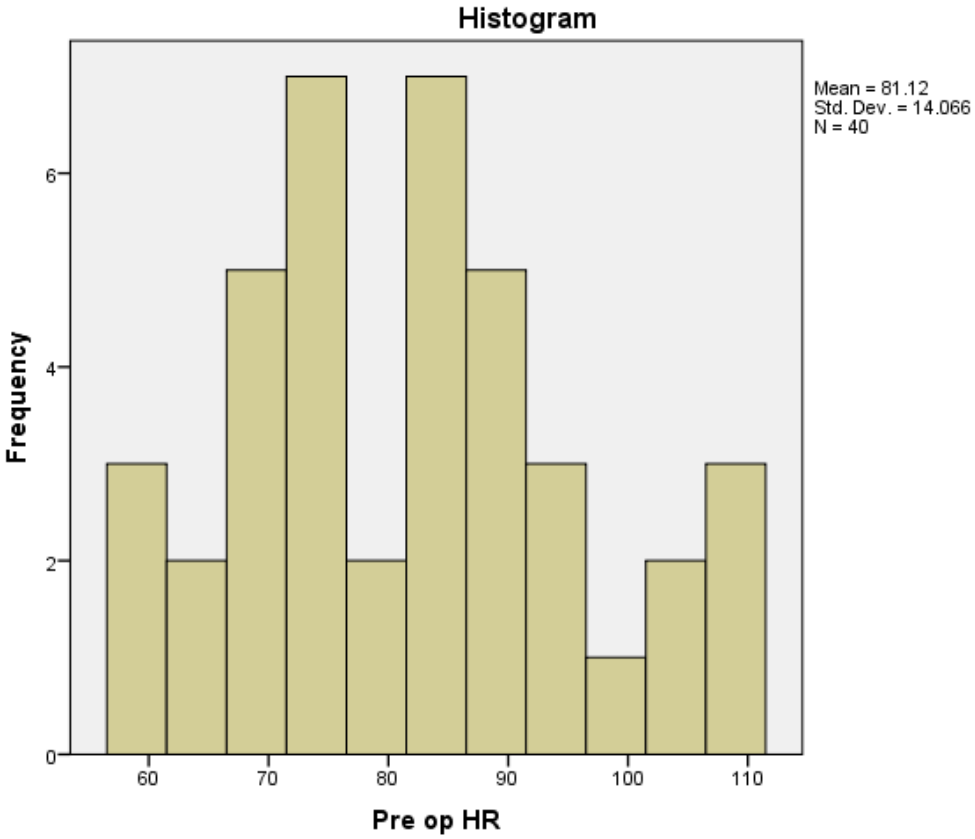
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Pre op MAP	.140	40	.048	.926	40	.012

	MEAN		P Value(Student t test)
	P	S	
PRE OP MAP	97.75	96.10	0.929



Pre-operative MAP value should be comparable to get a unbiased results. Using same normality above this concluded as normally distributed. Also it is a continuous data. Unpaired Student t test applied. P value is 0.929. Hence both groups are comparable.

PREOPERATIVE HR

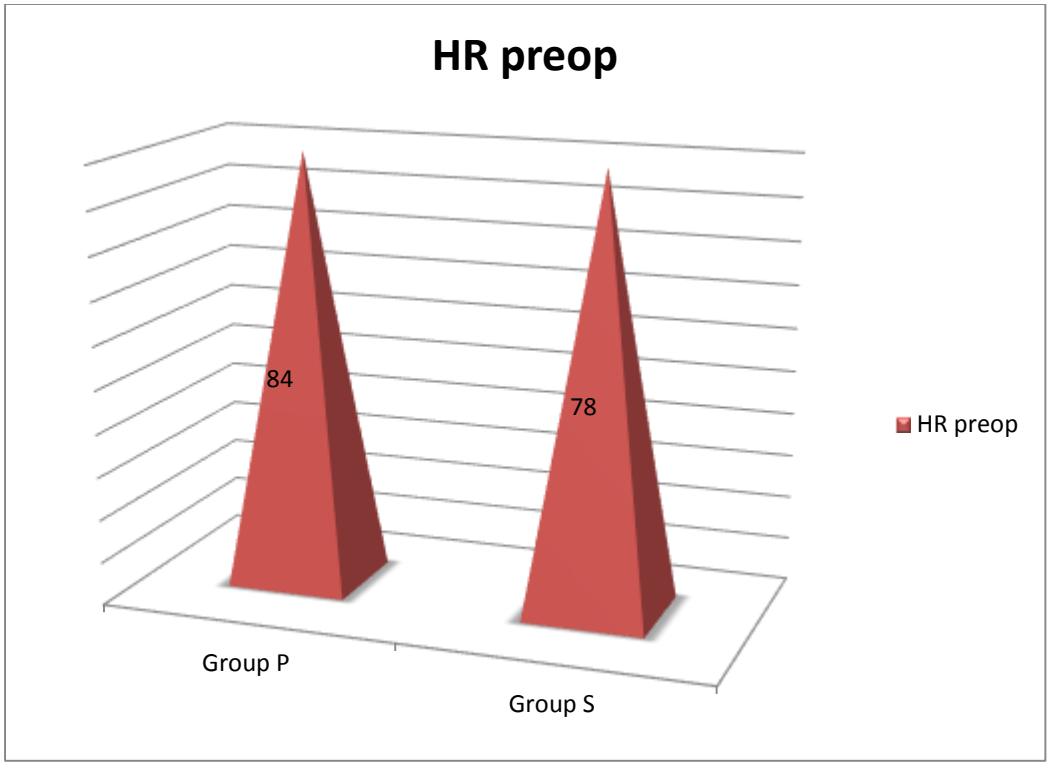


Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Pre op HR	.142	40	.042	.954	40	.105

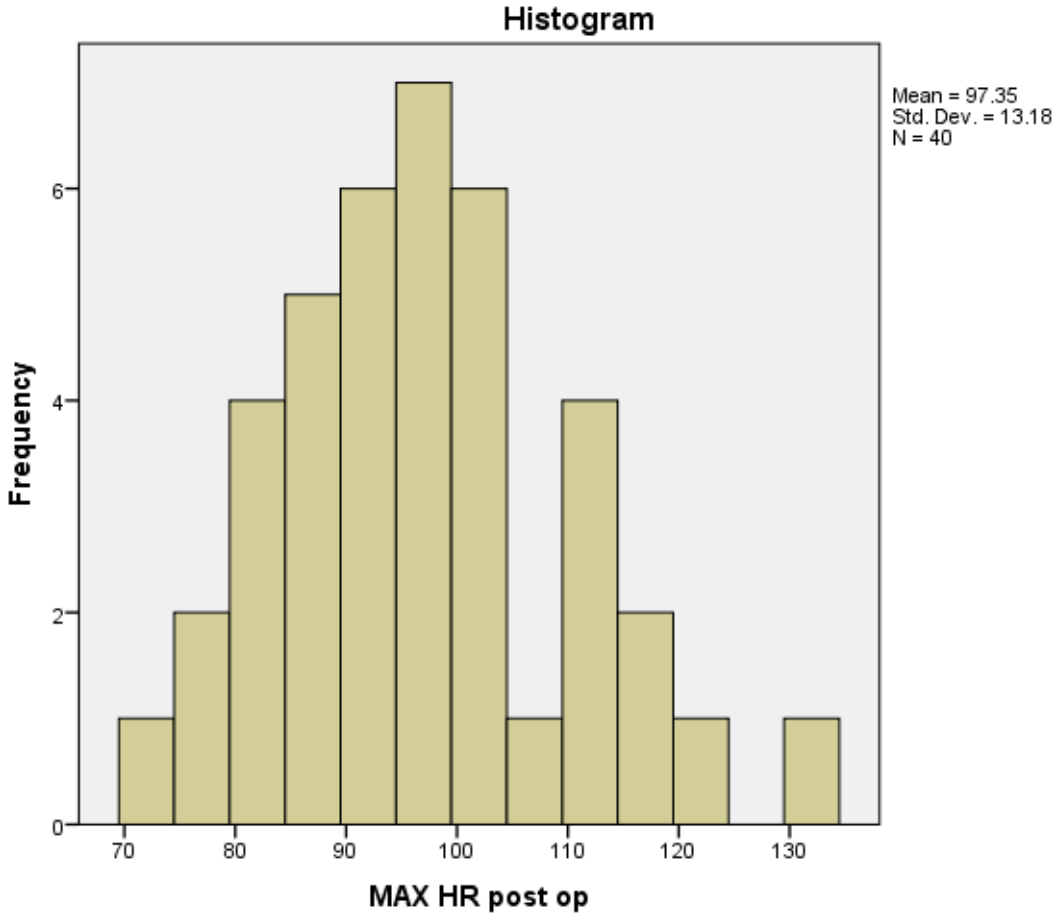
a. Lilliefors Significance Correction

	MEAN		P Value(Student t test)
	P	S	
PRE OP HR	83	78	0.208



Like Pre-operative MAP for pre-operative HR same statistical test applied. Using unpaired student t test p valve obtained is 0.208. Hence both groups comparable.

MAXIMUM HR POST OPERATIVE



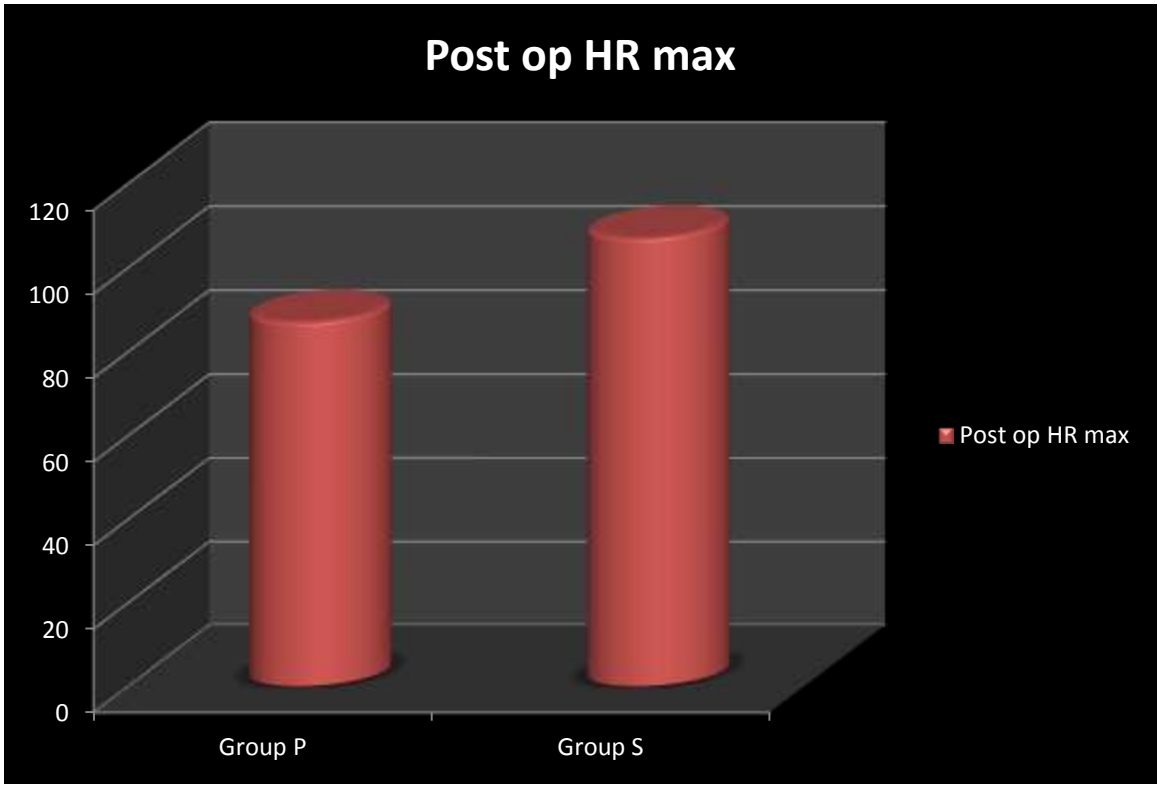
Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
MAX HR post op	.109	40	.200*	.974	40	.474

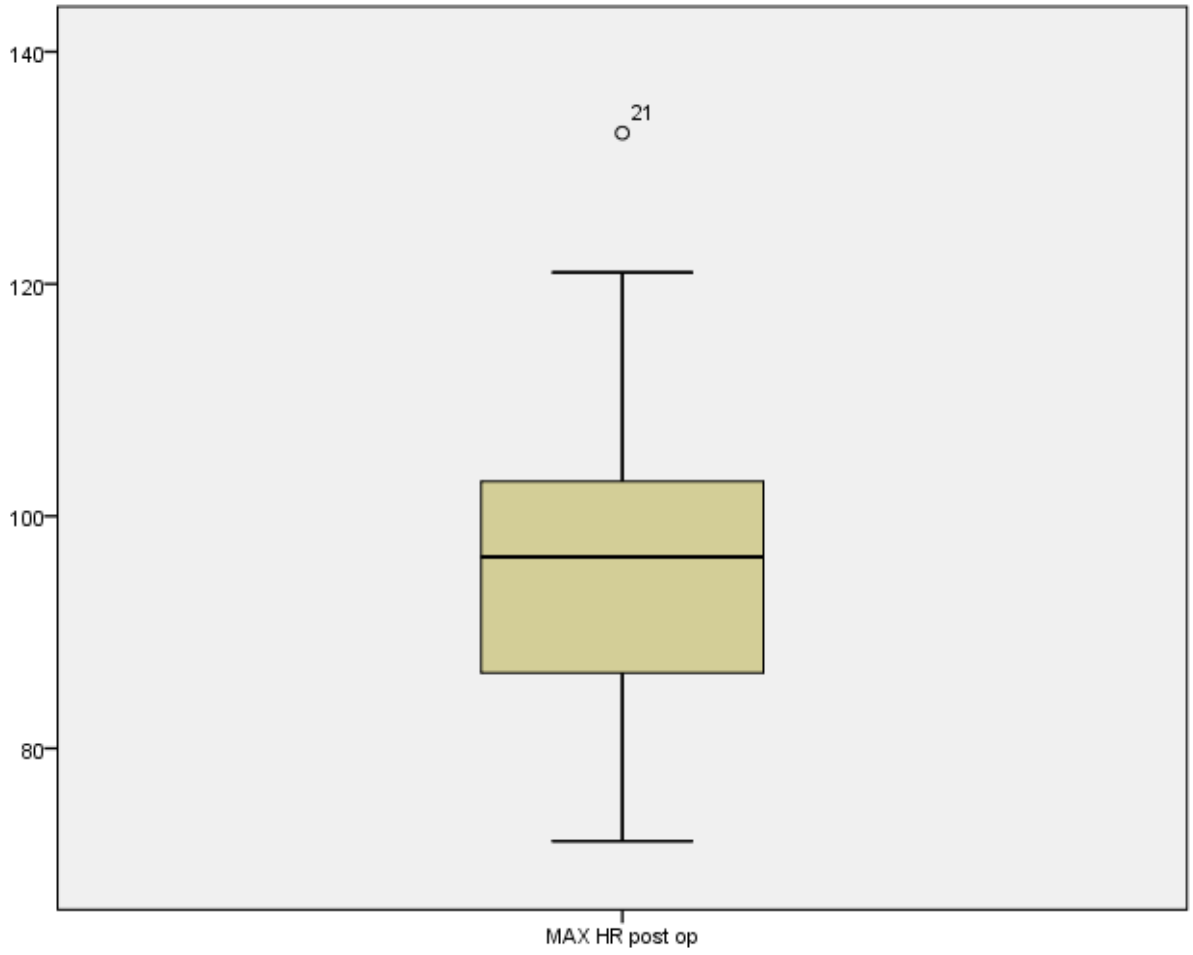
*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

	Distribution	Mean		P value(student t}
		P	S	
MAX HR	Normal	**87**	**107**	**0.00**

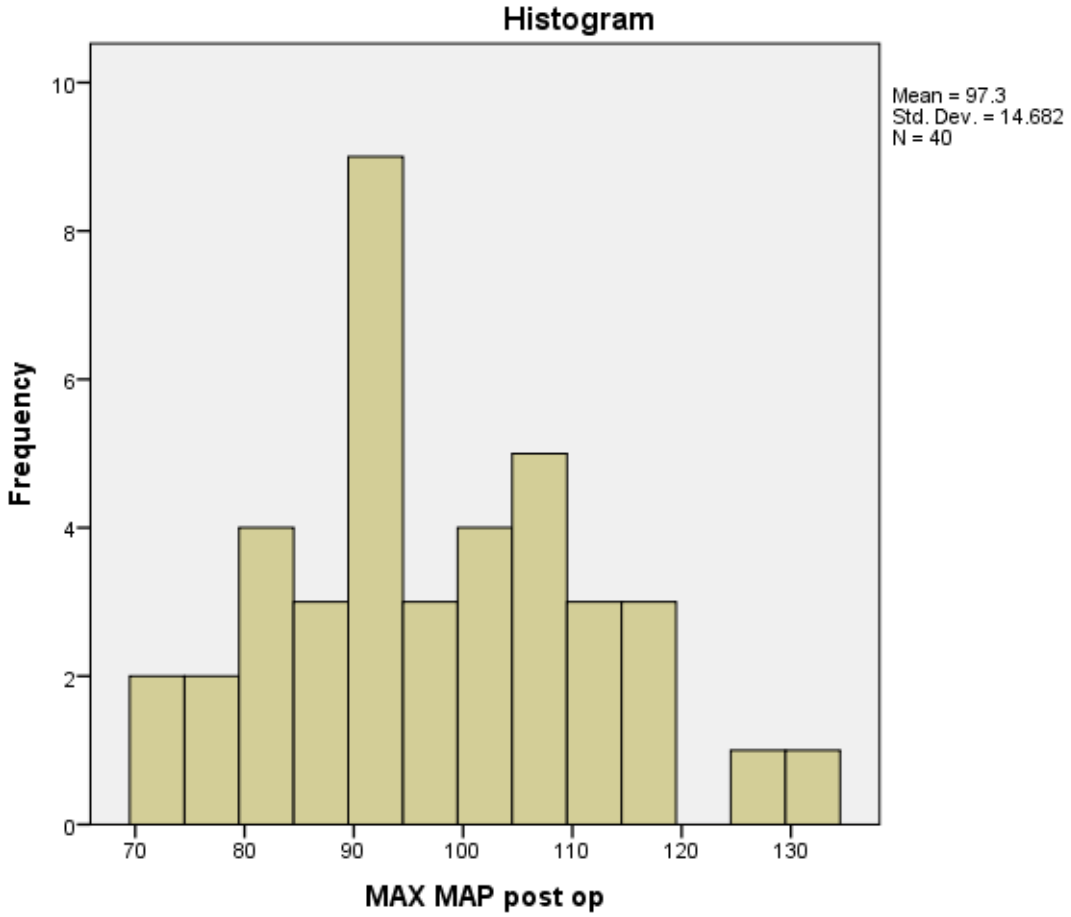


This is one of primary objectives. Using the same statistical test above for normality this variable concluded as normally distributed. Mean for Group P is 87 and Group S is 107. Unpaired student t applied. p value is 0.00 (significant). Hence Propofol maintenance reduces the post extubation HR shoot up.



BOX – PLOT DIAGRAM FOR MAX HR POST OP

POST OPERATIVE MAXIMUM MAP

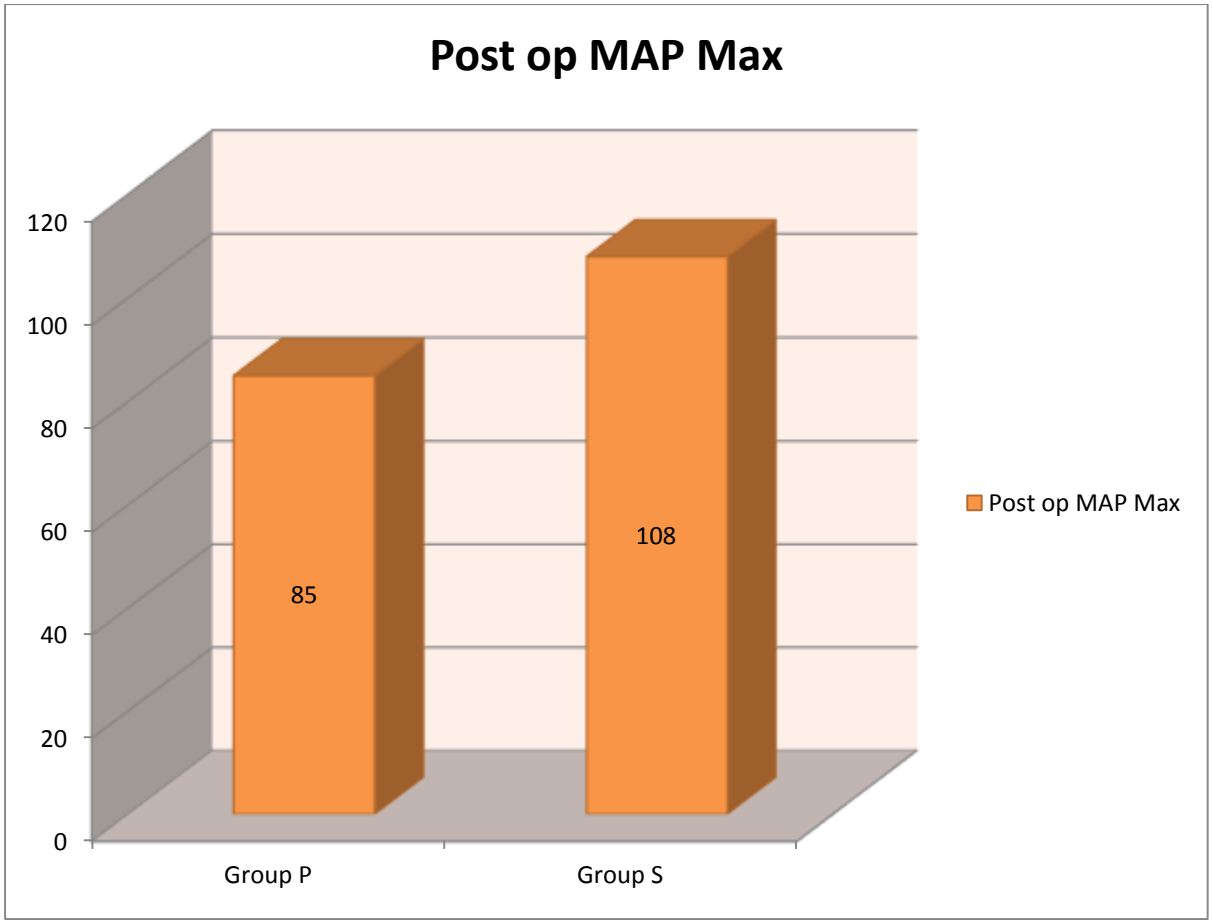


Tests of Normality

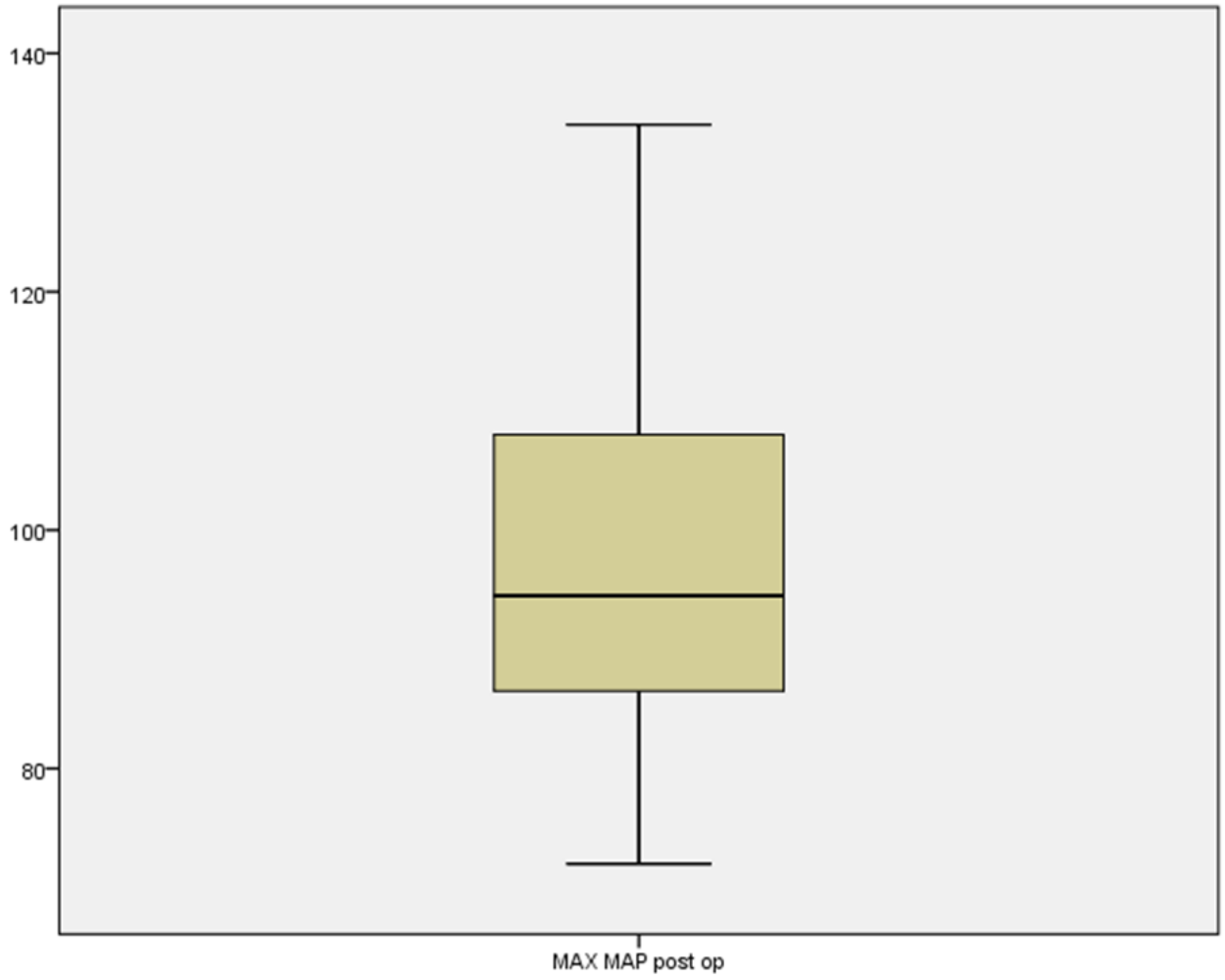
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
MAX MAP post op	.116	40	.191	.976	40	.546

a. Lilliefors Significance Correction

	DISTRIBUTION	MEAN		P Value(Student t test)
		P	S	
POST OP MAP	Normal	85	108	**0.00**

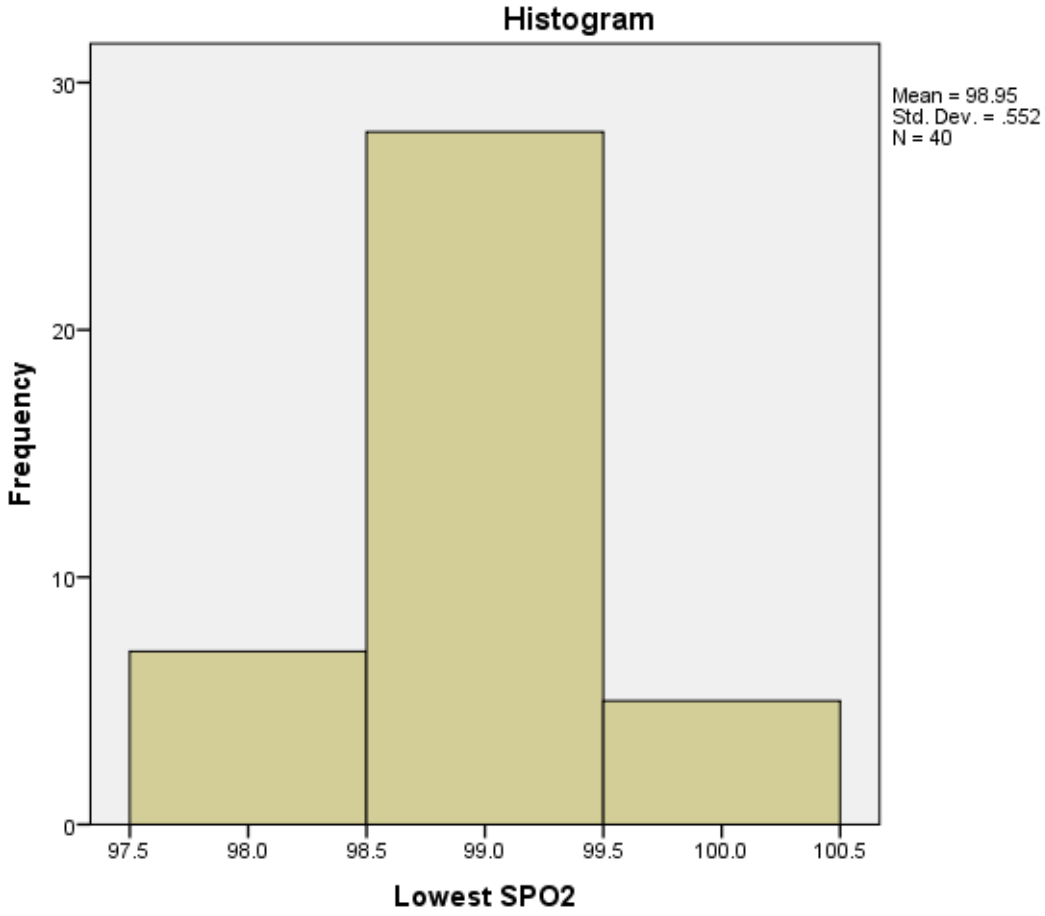


This is also one of our primary objectives. With the same normality test for above continuous data used and concluded as normally distributed. Unpaired student t test applied and concluded as significant (p value 0.00). Hence the propofol maintenance reduces the post op MAP shoot up.



BOX-PLOT DIAGRAM FOR MAX MAP POST OP

LOWEST SPO2



Tests of Normality

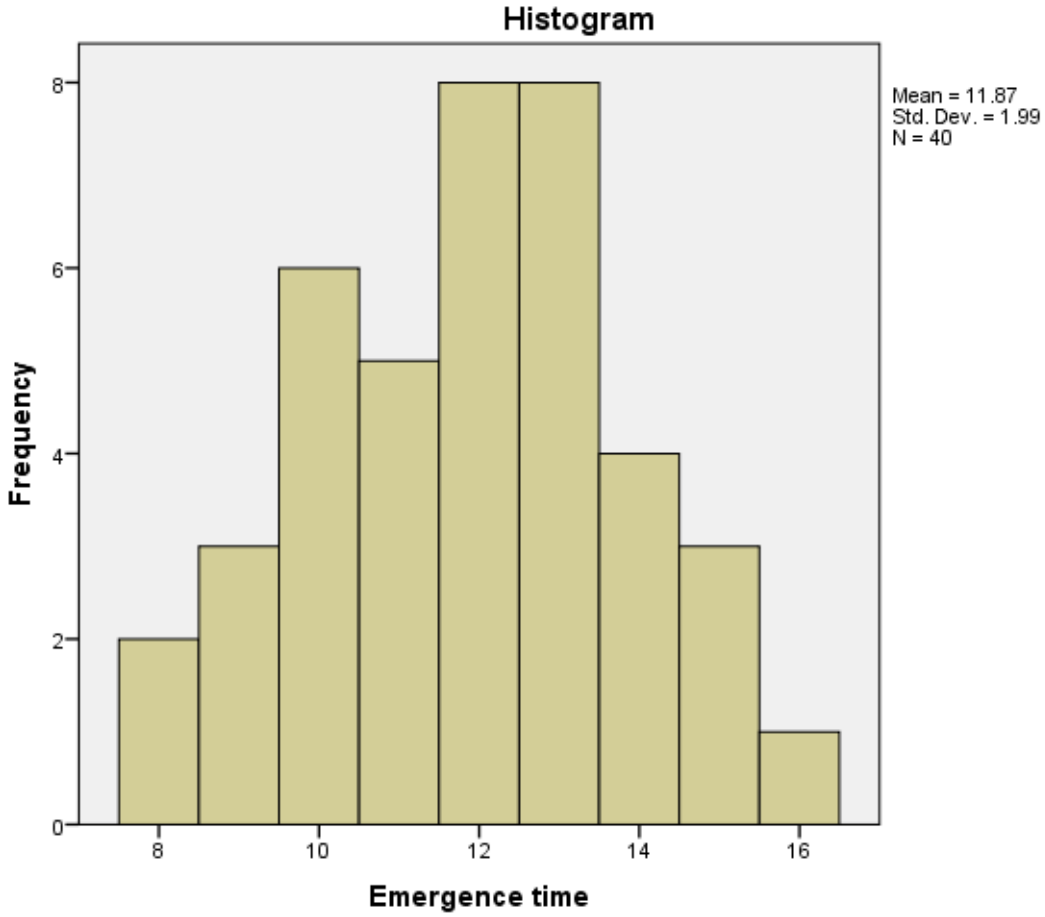
	GRoup	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Lowest SPO2	Group P	.372	20	.000	.728	20	.000
	Group S	.350	20	.000	.736	20	.000

Test Statistics[a]

	Lowest SPO2
Mann-Whitney U	183.000
Wilcoxon W	393.000
Z	-.570
Asymp. Sig. (2-tailed)	.568
Exact Sig. [2*(1-tailed Sig.)]	.659[b]

We compared lowest Spo_2 to see which group is desaturating. This variable is not normally distributed so Mann-Whitney used as diagnostic test. And p value is 0.568. Hence this is insignificant.

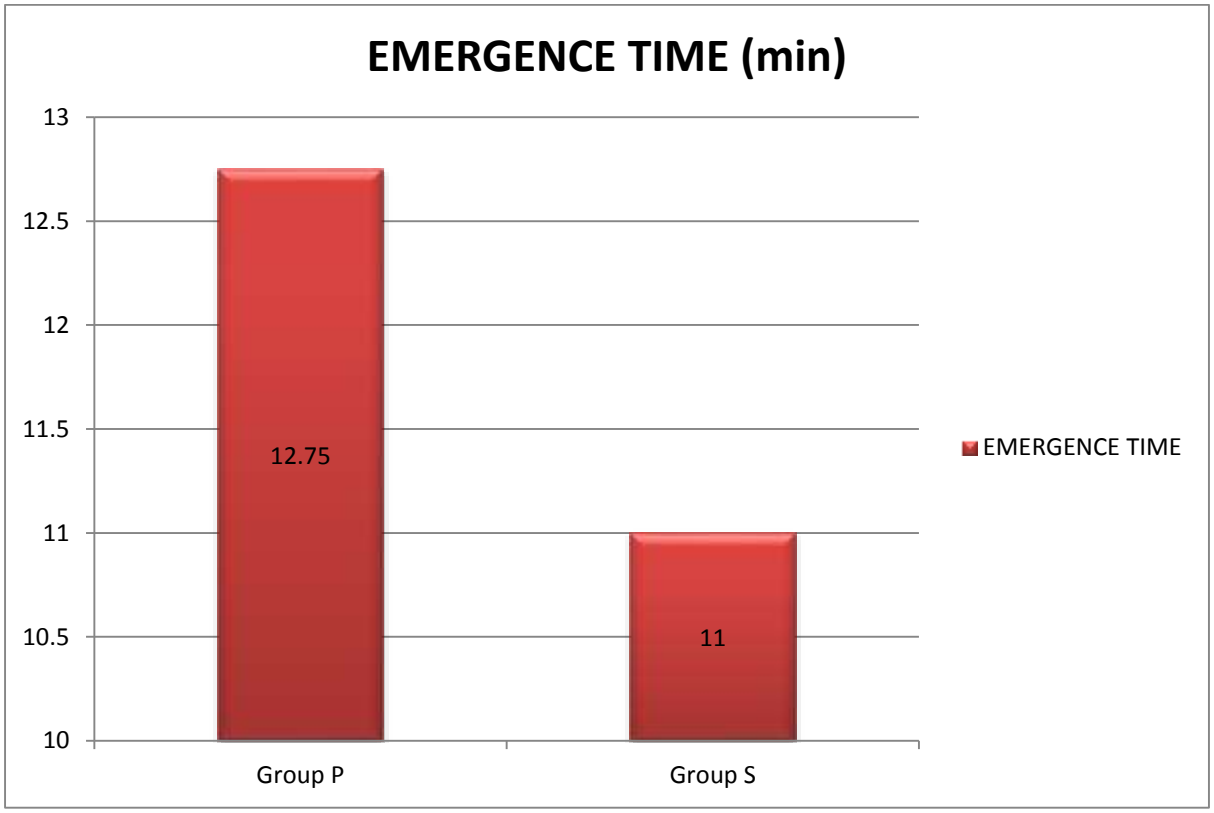
EMERGENCE TIME



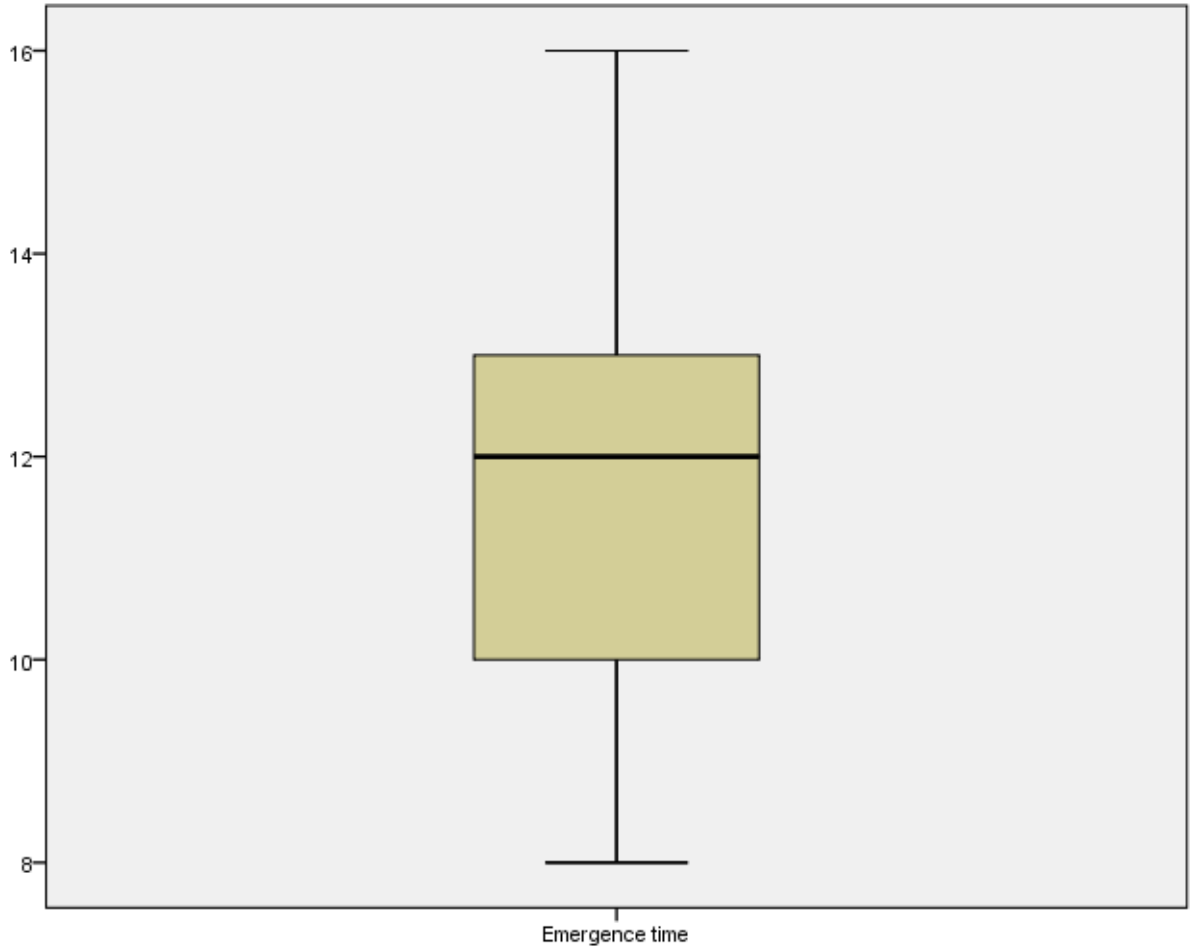
Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Emergence time	.125	40	.116	.969	40	.340

	DISTRIBUTION	MEAN		P Value(student t)
		P	S	
EMERGENCE TIME	Normal	12.75	11	0.04

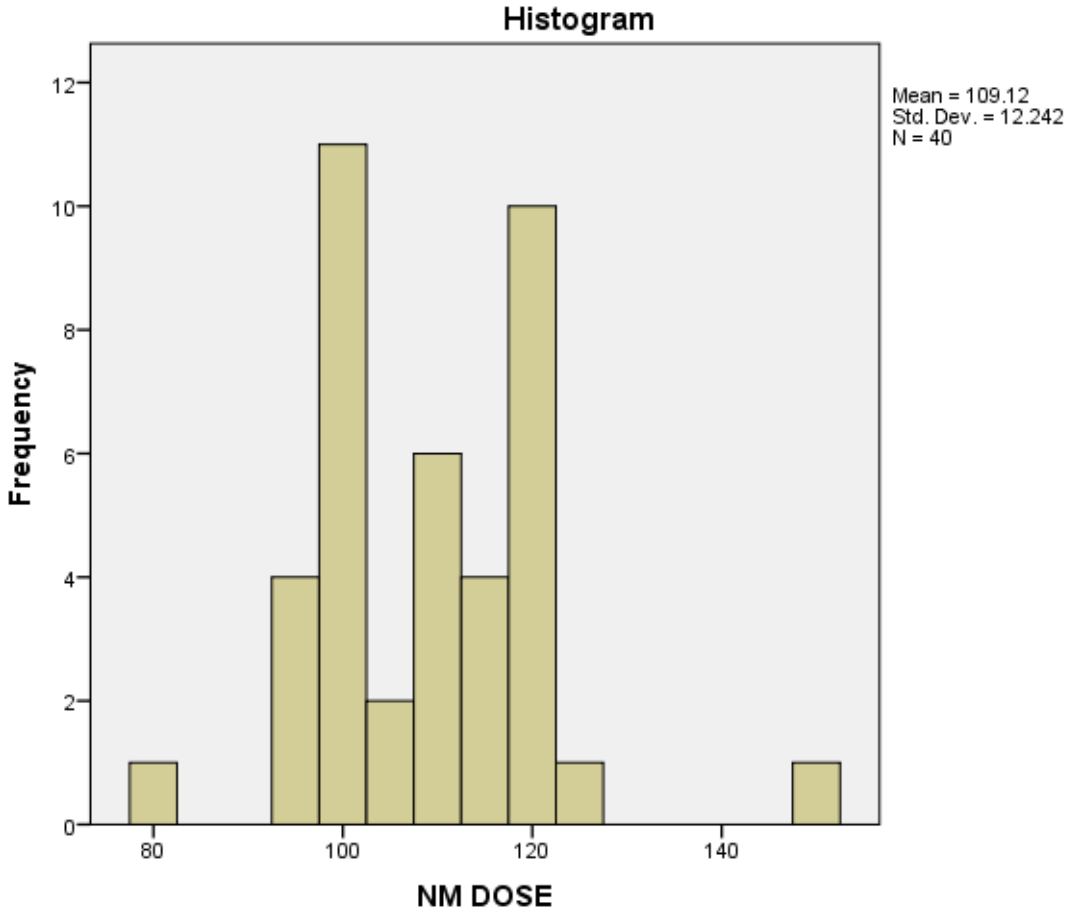


The emergence time is a continuous data. And as above its concluded as normally distributed. Mean time for Group P is 12.75 min and Group S is 11 min. Unpaired t test applied. p value is 0.04 (significant)



BOX PLOT DIAGRAM FOR EMERGENCE TIME

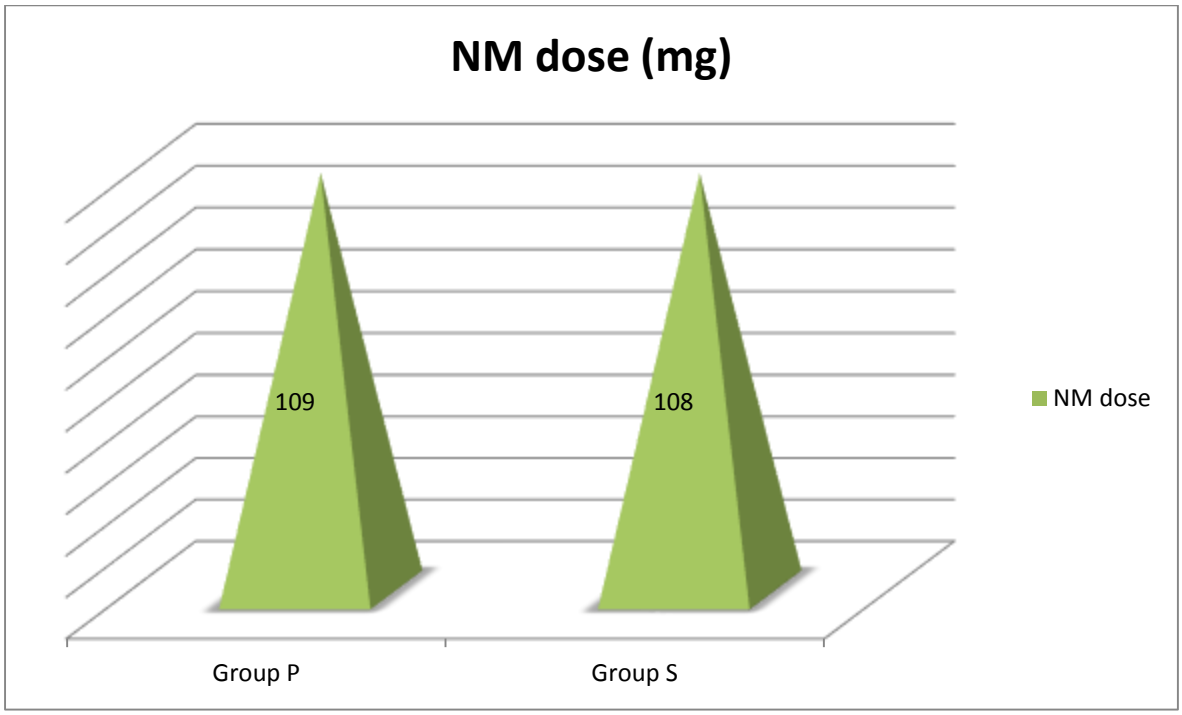
NEUROMUSCULAR DOSE



Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
NM DOSE	.172	40	.004	.910	40	.004

	Distribution	Mean P	Mean S	P value(Mean rank)
NM dose	Not normal	109	108	0.565



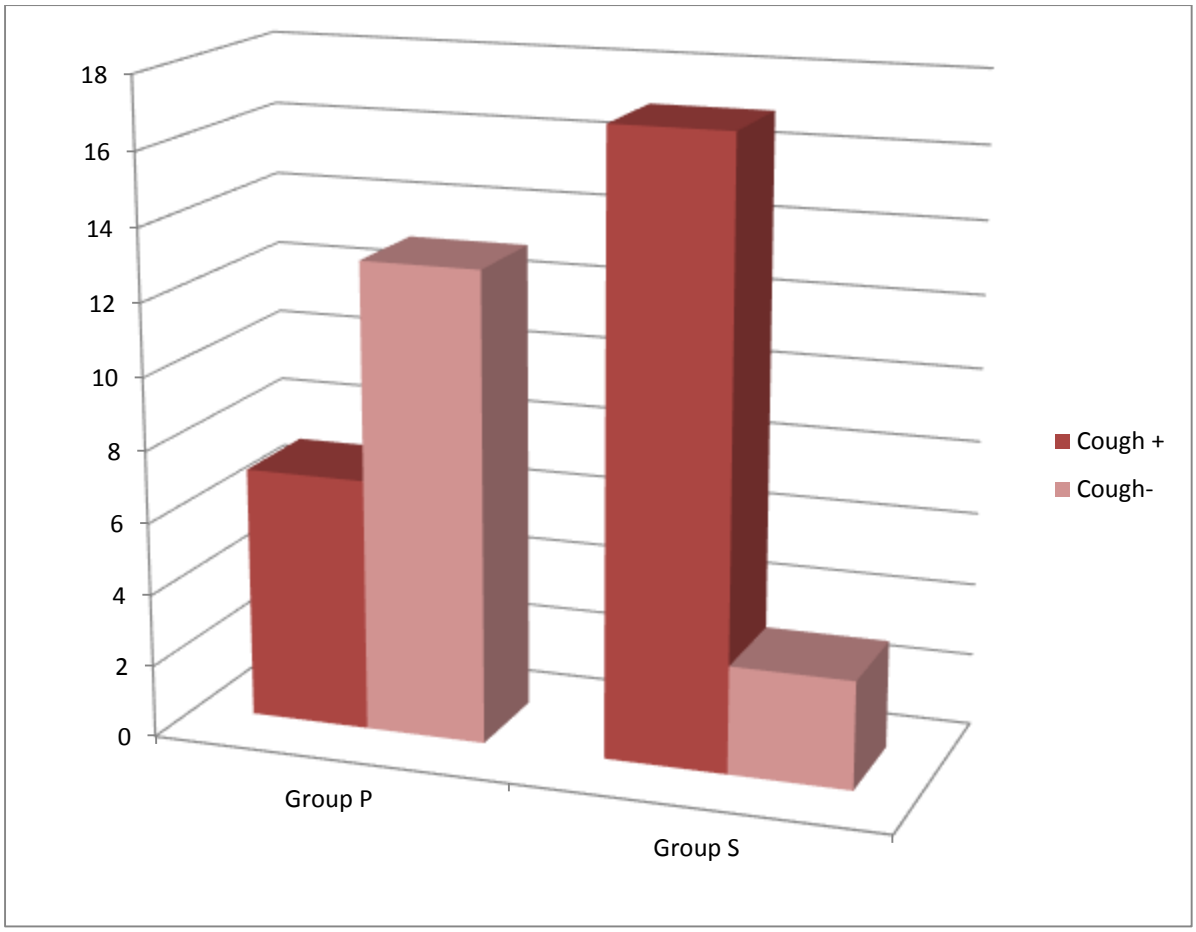
This is a continuous data. And also normally distributed. Mean of Group P is 109 and Group S is 108. Unpaired student t test is applied. p value is 0.565. Hence it is statistically insignificant.

COUGH AT EMERGENCE

	Emergence Cough			Total
	-	+	Plus	
Group P	13	1	6	20
Group S	3	17	0	20
Total	16	18	6	40

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	26.472[a]	2	.000	.000
Likelihood Ratio	32.285	2	.000	.000
Fisher's Exact Test	28.193			.000
N of Valid Cases	40			



Emergence cough is a primary objective and it is a non-continuous data so Fisher's exact test used. The p value of this test is 0.00 which is a significant value. Hence maintenance with Propfol reduce the emergence coughing.

SUMMARY OF RESULTS

Age	41. 46	Normal	0.166	No
	P. S (mean)	Distribution	P value (unpaired t test)	Significance
Sx Duration	164. 173	Normal	0.407	No
Emergence	12.75. 11	Normal	**0.04**	**Yes**
Preop MAP	95.75. 96.10	Normal	0.929	No
Preop HR	83. 78	Normal	0.208	No
Postop max HR	87. 107	Normal	**0.00**	**Yes**
Postop max MAP	85. 108	Normal	**0.00**	**Yes**

40 Patients posted for Spine surgery randomly allotted to two groups, Group P and Group S. Propofol infusion kept as maintenance for Group P and Sevoflurane for Group S. Extubation hemodynamics like MAP, HP,SPO_2, emergence cough are compared as primarily objective and neuro muscular dose , intra op hemodynamics changes as secondary objectives. All results obtained were analyzed by SPSS statical package version 16 and Microsoft Excel. All continuous data with normal distribution analyzed with independent student t test. And not normal distribution data had done with mean rank sum test and non-parametric test by Mann Whitney U test. All nominal data analyses with fisher exact and chi square test.

Age, sex, preoperative MAP, HR, Surgical duration, Intra operative Hemodynamics , Neuro muscular dose were comparable to both groups. Post-operative Maximum MAP (p value 0.00), Maximum HR (0.00) are decreased with Propofol group and so incidence of cough at emergence (p value 0.00).

And emergence time was longer with Propofol group compared to sevoflurane group (p valve 0.04).

DISCUSSION

Extubation is a vital event and need to manage carefully because of hemodynamic changes, bucking, coughing and vomiting. MAP, heart rate might get increased and if there is incomplete recovery Spo_2 might be decreased. And due tracheal irritation from endotracheal tube patients may experience coughing. Even though it's a protective reflex might cause distress to the patients and raise intra cranial, intra thoracic and intra-abdominal pressure. There are many methods to bring smooth emergence. In our study we observed with TIVA with Propofol for maintenance of general anaesthesia in spine surgery patients.

. A close study from M. Hohlrieder1, W et al. Who compared TIVA with balanced anaesthesia group and concluded TIVA group has less cough emergence and hemodynamic changes than volatile. This author also taken sevoflurane since it is a less airway irritant than other volatile so it will be less biased when to compare cough emergence. And effects of smoking also taken to accounts.

Another study by Liang C and Ding M et al compared sevoflurane with Propofol to only sevoflurane in combined epidural with general anaesthesia posted for gastrointestinal surgeries. On contrary to previous study awakening time shorter with sevoflurane and Propofol group than sevoflurane only group. He also concluded that lower cough and agitation and lower emergence Spo_2 in combined sevoflurane and Propofol group.

LD Mishra and SK Pradan et al did a study in spine surgery patients with Propofol alone for maintenance with conventional inhalational anesthesia with isoflurane. He

concluded that post-operative nausea vomiting is reduced with Propofol group also this group associated with clear awakening than isoflurane group.

Application of TIVA as maintenance for general anaesthesia, in smooth emergence and intra operative hemodynamic. And to avoid interruption by shifting from TIVA induction to volatile anaesthesia maintenance during intubation. As we observed in our study TIVA group had subtle hemodynamic changes during emergence than sevoflurane group and also emergence cough response is suppressed. This might be very helpful in surgeries which might get affected by coughing like neuro surgery where the intra cranial pressure will rise. Although there is chance that this might lead to inadequate recovery so careful post-operative monitoring is essential in these cases. Also anaesthesia with Propofol will reduce postoperative nausea and vomiting compared to volatile agent maintenance because of antiemetic action of this drug even in sub anaesthetic dose.

CONCLUSION

In our prospective randomized comparative study to evaluate the effect of Sevoflurane vs Propofol as total intravenous anaesthesia on extubation response and hemodynamic changes during emergence from anaesthesia in spine surgery patients. We conclude that maintenance of anaesthesia with Propofol is associated with reduced MAP and HR shoot up during emergence and prolonged emergence time than sevoflurane, with comparable intraoperative hemodynamics, neuromuscular agent dose requirements and lowest Spo_2 in both groups.

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ANNEXURE

ABBREVIATIONS

TIVA- Total intravenous anaesthesia

LMA- Laryngeal Mask Airway

TCI- Target Controlled Infusion

CSHT- Context Sensitive Half Life

BP- Blood Pressure

MAC- Minimum Alveolar Concentration

NMDA- N Methyl D Aspartate

ICP- Intra cranial pressure

PONV- Post Operative Nausea and Vomiting

COPD- Chronic Obstructive Pulmonary Disease

ECG- Electro Cardiogram

NIBP- Non Invasive Blood Pressure

EtCO2- End Tidal Carbon di oxide

IV- Intra venous

Vd-Volume of distribution

PROFORMA

DATE: ROLL NO: AIRWAY DEVICE:

NAME:

AGE: SEX: IP NO:

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

Ht: CVS: HB:

Wt: RS:

AIRWAY: MMS - IID - DENTITION -

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

MEASURES OF STUDY OUTCOME:

INTUBATION RESPONSE:

Premedication:

Induction:

Intubation:

Maintenance:

Positioning;

Drugs

COMPLICATIONS IN INTRA OPERATIVE PERIOD:

COMPLICATIONS POST EXTUBATION:

Events	Time	Systolic BP (mmHg)	Diastolic BP (mmHg)	MAP	Heart rate Beats/min	SPO2
Baseline						
Induction						
Incision						
Intra op range						
End of procedure						
Extubation						

TIME(MIN)	0	5	10	15	20	25	30	45	60	75	90	105	120	135	150	165	180
HR																	
SBP																	
DBP																	
MAP																	
SPO2																	
ETCO2																	
ATRACURIUM																	

POST OPERATIVE

Time(min)	0	5	10	15	20	25	30
Emergence time							
Coughing							
PR							
BP							
MAP							
Spo2							

INFORMATION TO PARTICIPANTS

Investigator: Name of the Participant:

Title: "To Compare Effect of Sevoflurane vs Total intravenous anaesthesia on Extubation response and hemodynamic changes during General Anaesthesia IN SPINE SURGERY PATIENTS"

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria. We want to compare and study the extubation response and hemodynamic changes for Spinal Surgeries under General Anaesthesia.

What is the Purpose of the Research?

For Spine surgeries, Sevoflurane or Propofol used for maintenance

1. To evaluate coughing during emergence
2. To evaluate the extubation response.
3. To assess Intraoperative and post-operative haemodynamics.
4. To evaluate intra operative Neuro Muscular Agents dosage.

The Study Design:

All the patients in the study will be divided into two groups.

GroupP- Propofol dose of 100 to 300 mcg/kg/min as TIVA for maintenance.

Group S-Sevoflurane 0.5 to 2% for maintenance

Benefits

Reduce fluctuations of Hemodynamic changes and dose of Neuro Muscular blockade agents.

Discomforts and risks

Increased post-operative sedative effect

Adverse effects of drugs used in this study

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative of setting the standard treatment and your safety is our prime concern.

Time:

Date: Signature of the Investigator:

Name of the Investigator:

Place:

Signature / Thumb Impression of Patient

Patient Name:

PATIENT CONSENT FORM

Study title: “To Compare Effect of Sevoflurane vs Total intravenous anaesthesia on Extubation response and hemodynamic changes during General Anaesthesia IN SPINE SURGERY PATIENTS”

Study centre: INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE,

RAJIV GANDHI GOVT. GENERAL HOSPITAL,

MADRAS MEDICAL COLLEGE,

CHENNAI-03.

Participant name: Age: Sex:
I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction. I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time:

Date: Signature / thumb impression of patient

Place: Patient name:

Signature of the investigator:

Name of the investigator:

சுய ஒப்புதல் படிவம்

முதுகு தண்டு அறுவை சிகிச்சையின் போது முழுமயக்கத்தில் புரபஃபால் மற்றும் சீவோபுளுரேனின் மயக்கத்திற்கு பின் ஏற்படும்
மாற்றங்கள் மீதான செயல் திறன் ஒப்பீடு

ஆய்வு நடத்தபடும் இடம் : மயக்கவியல் மற்றும் தீவிர சிகிச்சை பிரிவு
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை
சென்னை மருத்துவக் கல்லூரி,சென்னை

பங்கு பெறுபவரின் பெயர்: பங்குபெறுபவரின் வயது

இந்த ஆய்வில் குறிப்பிடப் பட்ட மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப் பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன்.எந்த காரணத்தினாலும் எந்த சட்ட சிக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாக அதை தொடர்பான முழு அய்வு மேற்கொள்ளும் பொழுது இந்த ஆய்வில் பங்கு கொள்ளும் மருத்துவர் என் மருத்துவ அறிக்கை பார்பதற்கு என் அனுமதி தேவை இல்லை என்பதையும் அறிந்து கொண்டேன். இந்த ஆய்வின் மூலம் கிடைக்கும் முடிவை பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.

இவ்வாய்வில் பங்கு கொள்ள ஒப்பு கொள்கிறேன்.ஆய்வில் பங்கேற்கும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேனென உறுதியளிக்கிறேன்.

பங்கு பெறுபவரின் கையொப்பம் சாட்சிகளின் கையொப்பம்

இடம்: இடம்:
தேதி: தேதி:

பங்கு பெறுபவரின் பெயர் மற்றும் விலாசம்:

ஆய்வாளரின் கையொப்பம்:

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36

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"TO COMPARE EFFECT OF SEVOFLURANE vs TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS"** of the candidate DR.S.VISHNUPRIYA with registration number **201720022** for the award of **M.D** in the branch of **ANAESTHESIOLOGY** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 12**%**percentage of plagiarism in the dissertation.

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CERTIFICATE OF APPROVAL

To
Dr.Vishnupriya.S.
I Year Post Graduate in MD Anaesthesiology
Institute of Anaesthesiology & Critical Care
MMC, Chennai

Dear Dr.Vishnupriya.S.

The Institutional Ethics Committee has considered your request and approved your study titled **"TO COMPARE EFFECT OF SEVOFLURANE VS TOTAL INTRAVENOUS ANAESTHESIA ON EXTUBATION RESPONSE AND HEMODYNAMIC CHANGES DURING GENERAL ANAESTHESIA IN SPINE SURGERY PATIENTS" - NO.10052018**

The following members of Ethics Committee were present in the meeting hold on **15.05.2018** conducted at Madras Medical College, Chennai 3

1. Prof.P.V.Jayashankar :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 : Member Secretary
4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch : Member
5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
6. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC : Member
7. Prof.Shanthy Gunasingh, Director, Inst.of Social Obstetrics,KGH : Member
8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
9. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 : Member
10. Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 : Member
11. Prof.Bharathi Vidya Jayanthi,Director, Inst. of Pathology,MMC,Ch-3: Member
12. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
13. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
14. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

GROUP P

S.No	Age	Sex	Duration	HR(preop)	MAP(preop	spo2	HR(I)min	HR(I)max	MAP(I)min	MAP(I)max	spo2(I)	NM Dose	emerg time	MAX MAP	MAX HR	lowestSpo2	cough
1	53	F	240	92	124	100	85	105	61	86	100	120	12	90	101	99	Plus
2	65	M	115	79	105	99	68	85	104	114	100	100	15	102	85	98	minus
3	41	F	135	104	103	99	86	104	98	105	100	100	12	86	93	100	minus
4	27	M	110	72	90	99	69	82	68	97	100	95	16	91	79	99	plus
5	37	M	150	88	93	100	69	98	62	115	100	100	13	82	84	98	minus
6	28	M	135	60	84	99	62	75	62	86	100	120	14	72	72	99	minus
7	56	M	240	104	129	100	79	85	62	107	100	100	15	91	82	99	Plus
8	33	M	195	110	91	100	67	98	65	86	100	120	13	72	86	99	minus
9	27	M	165	82	89	99	66	97	92	61	100	100	14	86	96	100	minus
10	35	F	180	83	91	99	61	87	62	87	100	120	13	81	82	99	minus
11	36	M	120	83	92	100	67	86	71	92	100	115	14	84	86	99	Plus
12	24	M	135	91	95	100	61	94	70	100	100	120	13	91	83	99	minus
13	37	F	180	72	94	99	69	82	69	98	100	110	12	92	94	99	minus
14	42	F	165	92	93	99	76	98	72	97	100	120	11	87	87	98	Plus
15	47	M	135	89	100	100	79	101	82	108	100	95	12	92	90	99	minus
16	39	F	150	84	91	99	74	106	87	104	100	100	13	82	89	98	minus
17	52	F	195	86	88	100	69	98	67	98	100	110	10	76	94	99	Plus
18	57	M	190	67	72	100	64	97	61	94	100	120	12	77	79	99	minus
19	47	F	180	69	97	99	71	101	72	104	100	110	11	90	96	99	Plus
20	39	F	165	72	94	100	67	92	79	108	100	120	10	91	94	99	minus
			164	83.95	95.75		70.45	93.55	73.3	97.35		109.75	12.75	85.75	87.6		

GROUP S

S.No	Age	Sex	Duration	HR(preop)	MAP(preop)	SPO2(PREOP)	NM dose	HR(I)min	HR(I)max	MAP(I)min	MAP(I)max	spo2	Emertime	MAX HR	MAX MAP	spo2 low	cough
1	60	M	210	108	85	100	80	101	141	58	113	100	11	133	94	99	plus
2	58	M	165	108	80	99	150	90	96	65	84	99	12	113	127	98	plus
3	63	M	255	98	86	100	100	90	108	71	124	99	13	119	134	99	minus
4	44	M	205	74	88	100	120	74	94	86	98	100	10	109	118	99	plus
5	23	F	180	67	109	100	110	90	125	78	106	100	12	118	117	99	plus
6	30	M	205	82	104	100	125	90	120	62	97	100	13	112	108	99	plus
7	51	M	165	87	108	99	100	60	100	86	101	100	14	112	111	98	plus
8	60	M	120	62	127	100	115	65	89	69	109	100	15	98	112	98	minus
9	37	M	135	72	96	100	100	79	98	96	105	100	9	102	116	99	plus
10	45	M	165	77	97	99	95	94	101	72	99	100	10	103	110	100	minus
11	32	F	135	69	107	100	105	77	109	64	107	100	11	97	104	100	plus
12	47	F	205	72	86	99	115	76	102	62	91	100	8	102	108	100	plus
13	45	F	180	87	107	99	105	62	99	65	98	100	9	112	107	99	plus
14	47	F	165	92	95	100	95	65	108	68	97	100	10	121	98	99	plus
15	51	F	180	86	93	100	115	61	99	69	94	100	11	103	96	99	plus
16	37	F	180	72	98	100	120	69	117	52	102	100	10	98	107	99	plus
17	32	F	165	64	102	100	100	74	110	64	107	100	8	99	109	99	plus
18	47	F	135	69	91	100	110	79	106	59	89	100	9	97	104	99	plus
19	48	F	180	61	79	100	110	68	92	54	84	100	12	101	102	99	plus
20	69	F	135	59	84	99	100	58	89	67	90	100	13	93	95	99	plus
			173.25	78.3	96.1		108.5	76.1	105.15	68.35	99.75		11	107.1	108.85		