"A COMPARATIVE STUDY OF THIOPENTONE AND PROPOFOL AS INDUCTION AGENTS FOR MODIFIED ELECTROCONVULSIVE THERAPY"

Submitted by

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Dissertation submitted to

B.L.D.E. (DEEMED TO BE UNIVERSITY) VIJAYAPUR, KARNATAKA.

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the guidance of

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ACKNOWLEDGEMENT

This piece of work has been accomplished with the grace of **Lord Sai Baba**. It gives me immense pleasure to express my heartfelt gratitude to all. I dedicate this page to each and everyone who has helped me to explore the expanses of knowledge.

With privilege and respect I would like to express my gratitude and indebtedness to my Guide, **DR. Vijaykumar T.K** MD,DA Professor Department of Anaesthesiology and co-guide, **DR. S P Chaukimath** MD Professor and HOD, Department of Psychiatry**,** B.L.D.E (DEEMED TO BE UNIVERSITY) Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapur, for his constant and unfailing support, professional insight, valuable suggestions, motivation and exemplary guidance to carry out and complete this dissertation. I am deeply grateful to him for providing me necessary facilities and excellent supervision to complete this work.

With great respect I express my gratitude to **Dr. D. G. Talikoti,** Professor and Head, Department of Anaesthesiology, who with his vast experience, enthusiasm helped me through my dissertation work.

I am forever grateful to staff, Department of Anaesthesiology, **Dr.Vidya Patil, Dr. R. R. Kusugal, Dr. Sridevi Mulimani, Dr. Vijay katti, Dr. Renuka, Dr. Nirmala, Dr. Shivanand L K, Dr. Basavaraj Patil, Dr. Prathiba, Dr. Ramesh, Dr.Santosh K, Dr. Lalitha, Dr. Geetha, Dr. Sunil, Dr. Mala, Dr. Sharath and Dr.Santosh A** for their guidance and encouragement provided to me, to achieve new heights professionally over my course period.

I am extremely thankful to Professor **Dr. S. P. Guggarigoudar**, Principal, of B.L.D.E. (DEEMED TO BE UNIVERSITY) Shri B. M. Patil Medical College,

Hospital and Research Centre Vijayapur, for permitting me to utilize resources in completion of my work.

I acknowledge my gratitude to**, Dr. Neha, Dr. Rashmi, Dr. Vinuta, Dr.Chandrima, Dr. Muzzammil, Dr. Shreyas, Dr. Raghu, Dr. Adil,** Postgraduate colleagues and seniors,

Dr.Anita, Dr.Ramya Department of Anaesthesiology, B.L.D.E(DEEMED TO BE UNIVERSITY) Shri B. M. Patil Medical College, Hospital and Research Centre Vijayapur, for their support, advice and help in data collection. I also thank all my seniors and my juniors for their co-operation during the preparation of this dissertation.

I am thankful to the members of ethical committee B.L.D.E (DEEMED TO BE UNIVERSITY) Shri B. M. Patil Medical College, Hospital and Research Centre Vijayapur for permitting me to carry out this study.

I thank **Mrs. Vijaya Soraganvi**, Statistician for her masterly guidance and statistical analysis.

My thanks to one and all staff of Library, Anaesthesia Department and Hospital for their co-operation in my study.

My heartfelt thanks to my beloved parents and in-laws, my husband **Dr. Basavaraj Singanal**, and other family members for their blessings, encouragement, support and sacrifices.

Last but not the least, my sincere thanks to all the patients of this study for their co-operation without which this study would not have been possible.

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LIST OF ABBREVIATIONS USED

Ach	→	Acetylcholine
ASA	→	American Society of Anaesthesiologists
BP	→	Blood Pressure
Bpm	→	Beats per minute
CBF	→	Cerebral Blood Flow
CMRO2	→	Cerebral Metabolic Requirement of Oxygen
CPP	→	Cerebral Perfusion Pressure
DBP	→	Diastolic Blood Pressure
EAA	→	Excitatory Amino Acid
ED95	→	Mean Dose producing 95% blockade
EEG	→	Electroencephalogram
GABA	→	Gamma Amino Butyric Acid
HR	→	Heart Rate
ICP	→	Intra Cranial Pressure
IV	→	Intravenous
MH	→	Malignant Hyperthermia
NMS	→	Neuroleptic Malignant Syndrome
Sch	→	Succinylcholine
SBP	→	Systolic Blood Pressure
SPO_2	→	Oxygen Saturation

ABSTRACT

INTRODUCTION

Electroconvulsive therapy (ECT) is a well-established psychiatric treatment in which seizures are electrically induced in anesthetized patients for therapeutic effects.[1]

OBJECTIVES

To compare Thiopentone and Propofol as induction agents in modified electroconvulsive therapy, with respect to induction characteristics, hemodynamic stability, recovery characteristics and interference with seizures.

METHODS

60 patients of ASA grade I and II of either sex, aged 18-60 years undergoing modified ECT were randomly divided into 2 groups using chit method. Both groups were premedicated in usual manner. Patients in Group P were induced with Inj.Propofol 1.5mg/kg , group T with Inj.Thiopentone 3mg/kg . Then, Inj.Succinylcholine 0.5mg/kg given. Patients were ventilated with 100% oxygen with bain circuit and mask. Shock was given after putting bite block. Patients were again ventilated till spontaneous respiration after seizures.Induction characteristics, hemodynamic stability, seizure parameters and recovery characteristics were compared before induction, after induction, 0 min, 5 min, 10 min , 15 min following ECT.

RESULTS AND INTERPRETATION

Mean induction time was significantly shorter in group P 40.83 sec than in group T 47.83 sec with ($p<0.001$*). Seizure threshold was almost same with both groups, showing no statistical significance. Seizure duration was less with Propofol 38.20 sec than Thiopentone 40 sec but was not statistically significant($p=0.123$).

There was no significant difference in heart rate, systolic and diastolic blood pressure between the two groups prior to induction and post induction. Significant rise in heart rate, systolic and diastolic blood pressure was observed following ECT. Significantly faster recovery was seen in Propofol group with (p=0.001*), (p=0.012*), (p=0.001*) for time required for return of spontaneous breathing, Time for eye opening on command and Time for Orientation to time respectively. No significant difference in adverse effects noted between 2 groups.

CONCLUSION

We conclude that, Propofol had advantage of smooth induction, better haemodynamic stability following ECT, with no significant interference with seizures and offered superior recovery profile compared to Thiopentone.

KEYWORDS

Modified ECT, Propofol , Thiopentone.

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INTRODUCTION

INTRODUCTION

Electroconvulsive therapy (ECT) is a well-established psychiatric treatment in which seizures are electrically induced in anesthetized patients for therapeutic effects[1]. The use of electroconvulsive therapy (ECT) to provoke a generalized epileptic seizure was first described in 1938 by Bini and was performed without anesthesia for almost 30 years. It continues to occupy a central place amongst treatment modalities for a large variety of psychiatric disorders like acute depression with suicidal tendency, acute mania, schizophrenia, catatonic psychosis and delirium where pharmacotherapy usually fails.[2,3]

In earlier days for direct ECT, electrical stimulus was given directly without anesthesia in conscious patients. Thus, the complications like tongue bite, bone fracture, joint dislocation and tearing of muscle fibre were frequent.[2,3] Moreover it was very inhuman to look at a convulsing, frothing patient being held by several people to prevent injury .

Use of General anesthesia for ECT led to the reduced incidence of physical and psychological trauma.[4] The induction agent used will leave the patient unaware of potentially frightening sensations, especially muscle paralysis and feeling of suffocation and the image of light flash that may accompany the beginning of the stimulus without obstructing the seizure. Neuro-muscular blocker will prevent injuries to the musculoskeletal system. Successful electroconvulsive therapy treatment requires close collaboration between psychiatrist and anesthesiologist.

Despite recent advances in the field of anesthesia and techniques of electroconvulsive therapy administration, practice standards continue to remain unsatisfactory even in developed countries. There is always a need for an ideal

anesthetic agent for ECT which has rapid, smooth induction, short duration of action, rapid recovery, minimal side effects, minimal effect on seizure duration, minimal or no interaction with medicines used in psychiatric disorders.[5]

The introduction of newer anesthetic drugs and techniques in recent years has lead to the situation whereby patients can rapidly be awake and well oriented following cessation of the procedure with minimal anesthetic hangover and can be done as an outpatient procedure successfully. Many intravenous anaesthetics have been used to induce anaesthesia for ECT, including Methohexital, Thiopental, Propofol, and Ketamine.[6]

Thiopentone is a well accepted induction agent for ECT. It has rapid smooth induction, good anticonvulsant activity, less effect on seizure duration but, is associated with side effects like prolonged awakening time, arrhythmias, laryngeal spasm and post ECT nausea and vomiting.

Propofol has properties like smooth induction, good anticonvulsant activity, attenuation of hemodynamic response. Propofol is associated with less nausea and vomiting, faster emergence, better early psychomotor recovery and better early cognitive recovery.[7]

OBJECTIVES

OBJECTIVES

To study and compare Thiopentone and Propofol as induction agents in electroconvulsive therapy, with respect to the following:

- Induction characteristics
- Hemodynamic stability
- Interference with seizure characteristics
- Recovery characteristics

ELECTROCONVULSIVE THERAPY

PRINCIPLE OF ECT

The aim of ECT is to induce generalized cerebral seizure activity of a type that is associated with a tonic—clonic or grand mal convulsion, and to do so with an electrical dose that is sufficiently above the seizure threshold to maximize the clinical efficacy of treatment, but not so high that it needlessly contributes to the cognitive effects of treatment. The precise mechanism of the therapeutic effect of ECT remains unknown despite increasing research in this area.[8]

Although the exact mechanism of ECT is unknown, the induced seizure affects nearly every neurotransmitter system, including β-adrenergic, serotonin, muscarinic, cholinergic, and dopaminergic systems.[9,10] Brain-derived neurotrophic factor may also play a role in the efficacy of ECT. It is known to modulate monoamine systems in the brain such as the serotonergic and noradrenergic pathways. It enhances the activity of dopaminergic systems, which explains some of its effectiveness not only in depressive disorder but also in Parkinson's disease. It has potent anticonvulsant properties, which it shares with the anticonvulsant drugs now used in the treatment and prophylaxis of bipolar disorder. It has powerful effects on excitatory amino acid systems, which are increasingly implicated in psychosis. These wide-ranging actions go some way in explaining the effectiveness of ECT in a range of different conditions, such as depressive disorder, mania and schizophrenia.

Recent studies suggest that ECT has potent effects in bolstering neuronal survival, in sharp contradiction to the commonly held view that ECT may harm neurons. It even promotes the production of new neurons and new neural processes in areas of the brain known to be involved in cognitive and emotional function. In common with chemical antidepressant treatments, ECT enhances the expression of a

neuroprotective protein, brain-derived neurotrophic factor (BDNF), which antagonizes the neurotoxic effects of stress on the brain. These are important findings, because it is increasingly appreciated that chronic depression is associated with atrophy of brain structures in the frontal and temporal lobes, and ECT may act to arrest or even reverse these degenerative effects. Although ECT has effects on many systems in the brain, the individual effects on neurotransmitter systems may be more specific and focused than those induced by chemical antidepressants.

INDICATIONS FOR ECT

- Major depression, single or recurrent episode
- Bipolar major depression, depressed or mixed type
- Mania (bipolar disorder), mania or mixed type
- Schizophrenia
- Catatonia
- Schizophreniform or schizoaffective disorder
- Atypical psychosis
- Other conditions
  - Organic delusional disorder
  - Organic mood disorder
  - Acute psychotic disorder
  - Obsessive-compulsive disorder
  - Dysthymia
  - Parkinson's disease
  - Neuroleptic malignant syndrome
  - Secondary catatonia
  - Lethal catatonia

Relative contraindications include increased intracranial pressure, recent cerebrovascular accident, cardiovascular conduction defects, high-risk pregnancy, and aortic and cerebral aneurysms.[11,12]

To optimize the anesthetic management of patients undergoing ECT, it is important to understand the physiologic responses to the electrical stimulus, the effect

of anesthetic drugs on the ECT response, and the pharmacologic effects of the drugs used to attenuate the side effects related to ECT.

Typically, the acute phase of ECT is performed three times a week for 6 to 12 treatments. In successful cases, initial clinical improvement is usually evident after three to five treatments. Maintenance therapy can be performed at progressively increasing intervals from once a week to once a month to prevent relapses.

PHYSIOLOGIC RESPONSE TO ELECTROCONVULSIVE THERAPY

CENTRAL NERVOUS SYSTEM

The exact mode of action in the treatment of psychiatric illness is poorly understood. The ECT device delivers a brief pulse of current (0.5-0.8amps) through electrodes placed at specific locations on the head to induce a seizure or grandmal convulsion. Direct brain effects of the stimulus and seizure include large increases in cerebral blood flow and intracranial pressure.[13] There may be a post-ictal phase with confusion, agitation or amnesia. The patient may complain of headache after the procedure.

When an electrical current is applied to the brain via transcutaneous electrodes, the resultant electroencephalographic (EEG) spike and wave activity is accompanied by a generalized motor seizure and an acute cardiovascular response, which results in a marked increase in cerebral blood flow and intracranial pressure. The maximal blood flow velocity increases approximately 133% above the baseline value. However, the magnitude of the acute hyper dynamic response to ECT appears to be independent of the duration of the motor and EEG seizure activity. The hemodynamic response to ECT can produce myocardial ischemia and even infarction, as well as transient neurologic ischemic deficits, intracerebral hemorrhages, and cortical blindness. Short-term memory loss is common after ECT and more serious cognitive dysfunction has been described in the ECT literature, even though there is no scientific evidence of direct neuronal damage. However, use of brief pulse stimulation, unilateral nondominant electrode placement, and individual stimulus titration have all been alleged to minimize cognitive dysfunction after ECT.

CARDIOVASCULAR AND RESPIRATORY SYSTEM

Seizure activity causes an initial parasympathetic discharge manifested by bradycardia, occasional asystole, premature atrial and ventricular contractions, or a combination of these abnormalities. Hypotension and salivation may be noted. The parasympathetic discharge is followed immediately by sympathetic discharge associated with tachycardia, hypertension, premature ventricular contractions, and rarely, ventricular tachycardia. The tachycardia peaks at 2 minutes after the stimulus and is normally selflimited.[14] ECG changes, including ST-segment depression and T-wave inversion, may also be seen after ECT without any of the myocardial enzyme changes consistent with myocardial infarction. These ECG changes are presumed to be secondary to the sympathetic discharge.[15,16]ECT has been found to be relatively safe even in high-risk cardiac patients, if careful management is provided.[17,18]

Hyperventilation-induced hypocapnia appears to augment the heart rate and RPP(Rate Pressure Product) responses compared with normocapnic conditions. In patients with compromised cardiac function, ECT can result in myocardial ischemia and infarction. As a result of the acute hemodynamic responses, ECT can result in ventricular tachycardia and even cardiac rupture. Patients with preexisting cardiac diseases are at an increased risk of developing cardiac complications during and after ECT. Left ventricular systolic and diastolic function was decreased after ECT treatments even in patients without cardiac diseases.

GASTROINTESTINAL SYSTEM

There is an increase in intragastric pressure and there may be increased salivation and nausea and vomiting.

MUSCULOSKELETAL SYSTEM

Uncontrolled myoclonic-tonic contractions may cause bony [fracture-dislocations] or musculoskeletal injury to the patient . The passage of current directly stimulates the jaw muscles and causes the teeth to clench which may lead to dental or oral injury. Because of increased muscular activity oxygen extraction is greatly increased and the patient may desaturate or become cyanosed.

Other complications related to ECT include nausea, headache, emergence agitation, and sudden death.

Table 1: Common Physiologic responses and side effects associated with Electroconvulsive Therapy

Variable	Response
Central nervous system	Increased blood flow velocity, intracranial pressure, and cerebral metabolism; dizziness, amnesia, confusion, agitation, and headaches
Cardiovascular system	Increased blood pressure, heart rate, and cardiac output; cardiac arrhythmias
Musculoskeletal system	Myoclonic-toxic contractions,bone fractures/dislocations,muscle and joint pain
Miscellaneous responses	Increased salivation, nausea and vomiting, dental damage, and oral cavity lacerations

Table 2: Effects of anesthetic and cardiovascular drugs on the duration of ECT-Induced Seizure Activity (relative to Methohexital or saline, respectively)

Drug	Increased	No change	Decreased
Anesthetic drugs	Etomidate Alfentanil Remifentanil	Methohexital	Thiopental, Thiamylal, Lorazepam, Midazolam, Ketamine , Fentanyl , Propofol
Cardiovascular drugs	Aminophylline Caffeine	Clonidine, Esmolol, Labetalol, Dexmedetomidine, Nifedipine, Nicardipine, Nitroglycerin, Trimethaphan, Nitroprusside.	Diltiazem, Lidocaine, Labetalol, Esmolol

ANAESTHETIC DRUGS USED FOR ECT

The efficacy of ECT in alleviating acute depression is dependent on the duration of the induced seizure. EEG seizure activity lasting from 25 to 50 s is said to produce the optimal antidepressant response.

Patients experiencing an initial seizure duration of < 15 s or >120 s achieve a less favorable response to ECT[7]. Because many of the anesthetic drugs used for ECT have anticonvulsant properties, they would be expected to decrease the duration of ECT-induced seizure activity in a dose-dependent manner. Use of larger than necessary dosages of general anesthetics will shorten the duration of ECT induced seizure activity and could adversely affect the efficacy of the ECT treatments. Therefore, there is a delicate balance between achieving an adequate anesthetic state and an optimal duration of EEG seizure activity. In the current health care environment, use of general anesthetic techniques with a rapid onset and recovery is essential to facilitate fast tracking and permits the discharge of these patients within 1-2 h after the ECT treatment.

INDUCTION AGENTS

They prevent the patient from being aware of potentially frightening sensations, particularly muscle paralysis and feelings of suffocation and the image of a light flash that may accompany the beginning of the stimulus, without obstructing the seizure.

The aim is to promote ultra-brief, light general anesthesia. Excessive anesthetic dosage may prolong unconsciousness and apnea, have more anticonvulsant effect, increase the risk of cardiovascular complications, and intensify amnesia

An ideal induction agent should have a short half-life with rapid onset and recovery, maintain haemodynamic stability and have no interference with seizure duration or seizure threshold.[19] No drug has all these characteristics.

Since most short-acting anesthetics possess anticonvulsant properties, they can increase the threshold and inhibit the spread of seizure, thus modifying the seizure activity and shortening its duration. Large doses of these anesthetics can abort the ECT-induced seizure. To the extent that the seizure duration is related to the therapeutic outcome (3-5), hypnotic doses of anesthetic drugs can presumably counteract the therapeutic effects of ECT.

Many intravenous anesthetics have been used to induce anesthesia for ECT, including Methohexital, Thiopental, Propofol and Ketamine. Methohexital (0.75 to 1.0 mg/kg) is the most commonly used drug for ECT anesthesia and is considered the "gold standard."[20] Propofol (0.75 mg/kg) was found to reduce seizure duration, which was believed to decrease the efficacy of ECT.

However, more recent studies have demonstrated no difference in outcome with Propofol versus Methohexital. The use of Thiopental (1.5 to 2.5 mg/kg) associated with more hypertension and tachycardia than Propofol.

Ketamine (1.5–2 mg/kg) and Etomidate (0.15–0.6 mg/kg) might seem preferable to other agents in the light of their lack of anticonvulsant properties, however, other aspects such as drug's safety require consideration. Ketamine-Propofol mixture ("Ketofol") and Ketofol-Dexmedetomidine combination (Ketofol-Dex mixture) can be used as alternative induction agents, which overcome disadvantages of individual agents.[21,22]

Sevoflurane (5%–8% for induction, followed by 1–2 minimal alveolar concentration [MAC] is the only inhalational agent in widespread use for induction in ECT, with comparable effects to intravenous (IV) agents. It is preferred in patients not cooperative for IV access. It has the advantage of attenuating uterine contractions following ECT and is used in the third trimester of pregnancy.[23,24]

Opioids, such as Remifentanil in higher doses, can be used as a sole agent in patients refractory to seizure induction. However, they are not usually recommended as sole agents and are combined with other anaesthetic agents. They offer an advantage of attenuating haemodynamic responses to ECT and also increase the seizure duration by an induction agent dose-sparing effect.[25,26]

In the current health-care environment, use of general anaesthetic techniques with a rapid onset and recovery is essential to facilitate the discharge of the patients within 1–2 hours after the ECT. Since the half-life of Propofol is shorter than that of anaesthetic barbiturates and, with the advantage of minor hemodynamic effects, it is universally becoming the induction agent of choice, in spite of higher cost. It is also considered as reference agent due to its wider use and advantages over others.[21,27,28]

NEUROMUSCULAR BLOCKERS

They prevent injuries to the musculoskeletal system and improve airway management. The aim is to provide a moderate degree of muscular relaxation. Complete paralysis is neither necessary nor desirable since it may be associated with prolonged apnea. In addition, the intensity and the duration of ictal motor movements should be observed and monitored.

Muscle paralysis not only facilitates oxygenation, but also decreases oxygen utilization by muscles during the seizure. Consideration should be given to higher dosage of muscle relaxants for patients with Harrington rods, or at risk for developing pathologic bone fracture.

The adequacy of muscular relaxation can be ascertained before applying the ECT stimulus. This process is done by testing for a reduction in deep tendon reflex muscle tone. In patients receiving high dose of Succinylcholine, peripheral nerve stimulator should be used. Complete neuromuscular blockade is not necessary for ECT and may not be desirable because monitoring of peripheral seizure duration would be impeded. Partial neuromuscular blockade is necessary to reduce the peripheral manifestations of the seizure and to prevent trauma to the patient.

Succinylcholine has been used most frequently for neuromuscular blockade during ECT because of its short duration of action and low frequency of side effects.

Succinylcholine is metabolized by plasma cholinesterase, and alternative nondepolarizing muscle relaxants such as Vecuronium or Atracurium may need to be used in patients with plasma cholinesterase deficiency.

GUIDELINES FOR GENERAL ANESTHETIC TECHNIQUE IN ECT

The essential elements of anesthesia for ECT include:

- Rapid loss of consciousness,
- Effective attenuation of the hyper dynamic response to the electrical stimulus,
- Avoidance of gross movements,
- Minimal interference with seizure activity,
- Prompt recovery of spontaneous ventilation and consciousness.

Therefore, the use of rapid and short-acting anesthetic drugs (e.g Methohexital, Propofol, Succinylcholine, Esmolol, and Labetalol) facilitates the ECT procedure.

Patients are required to fast overnight for solid food, clear liquids are allowed for taking oral medication up to 2 h before the procedure. Patients with cardiovascular disease should be encouraged to take all chronic antihypertensive medications before ECT. To minimize the pain on injection of Propofol, Lidocaine 0.5-1 ml can be injected into the IV catheter immediately before • administering the induction drug or premixed with the induction agent.

Because ECT is typically performed three times a week for 3-4 weeks and each procedure lasts only a few minutes, tracheal intubation is not recommended except in very specific situations (e.g. late pregnancy or emergency treatments with full-stomach precautions).

Ventilation is assisted with a face mask with a standard circle or a simple bag valve-mask system. A Guedel oral airway can be used to facilitate assisted ventilation during the procedure. Appropriate resuscitative equipment must be available, as must a laryngoscope, tracheal tube, and laryngeal mask airway for management of an airway emergency. Noninvasive hemodynamic monitoring is recommended except in rare cases in which arterial cannulation is required to control blood pressure in patients with cerebral aneurysms. Standard EEG and tourniquet technique to isolate the circulation to an extremity before the muscle relaxant is administered (or electromyographic monitoring) are used to quantify the durations of the motor and EEG seizure activity. A bite-block should be carefully placed before application of the electrical stimulus to protect the patient`s teeth and to minimize the risk of lacerating the tongue.

During the recovery period, the most common side effects are confusion, agitation, amnesia, and headache. Nausea and vomiting as well as dizziness are infrequent complications after ECT. Rare complications after ECT include acute cardiovascular and neurologic events, splenic rupture, and pulmonary edema.

Standard noninvasive hemodynamic variables and oxygen saturation should be monitored for 15-30 min after ECT. Emergence agitation after ECT is usually treated by administering a small dose of midazolam (0.5-1 mg IV).

MECHANISM OF ACTION OF INDUCTION AGENTS

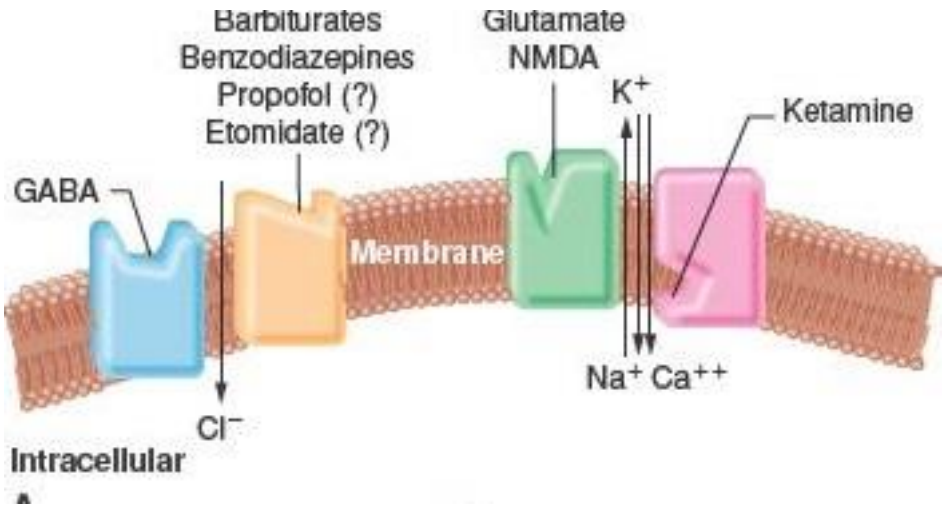


Fig 1: Model depicting the postsynaptic site of GABA and glutamate within the CNS.

GABA decreases the excitability of neurons by its action at the $GABA_A$-receptor complex.

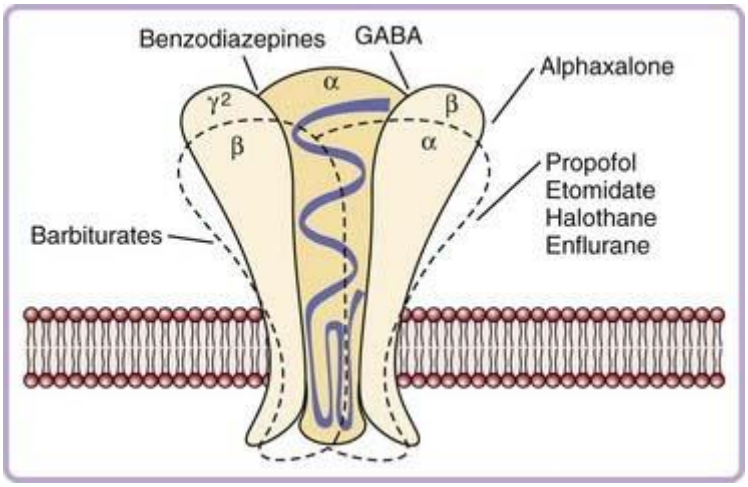


Fig 2: Schematic model of the GABAA-receptor complex illustrating recognition sites for many of the substances that bind to the receptor.

PHARMACOLOGY

PHARMACOLOGY

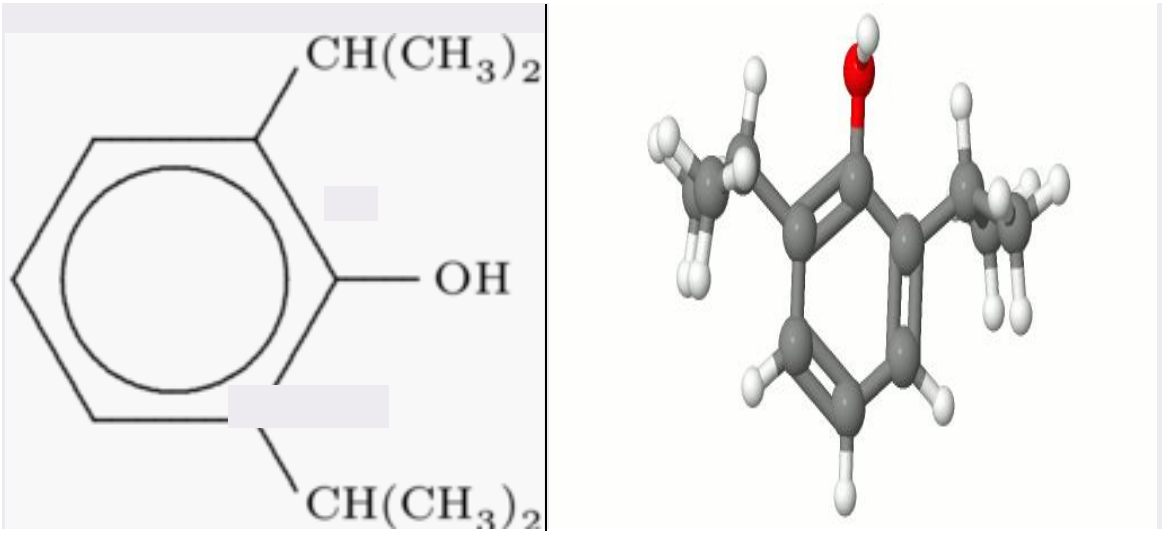
PROPOFOL

HISTORY

Researches in 1970s on substituted derivatives of phenol with hypnotic properties resulted in the development of 2, 6-diisopropofol.

Kay and Rolly in 1977, confirmed the potential of Propofol as an anesthetic induction agent.

Propofol is insoluble in water and was therefore initially prepared with Cremophor. Because of anaphylactoid reactions associated with Cremophor in this early formulation of propofol, the drug was reformulated as an emulsion.



PHYSIOCHEMICAL CHARACTERISTICS

Fig 3: Structure of Propofol

Propofol (2, 6-diisopropylphenol) consists of a phenol ring with two isopropyl groups attached. Propofol is not water soluble, but a 1% aqueous solution (10 mg/mL) available for intravenous administration as an oil-in-water emulsion. The formulation that followed the removal of Cremophor consists of 1% (wt/vol) Propofol, 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide. This formulation has a pH of 7 and appears as a slightly viscous, milky white substance.[29] This formulation can cause pain during injection that can be decreased by prior injection of Lidocaine or by mixing Lidocaine with Propofol prior to injection.

A wide variety of drugs have been used for reducing pain on injection of Propofol (e.g., Metoprolol, Granisetron, Dolasetron, and even Thiopental). Diluting the formulation with additional solvent (Intralipid) or changing the lipid carrier (Lipofundin) also reduced Propofol induced injection pain, probably because of a decrease in the concentration of free Propofol in the aqueous phase of the emulsion.

Propofol formulations can support the growth of bacteria, so good sterile technique must be observed in preparation and handling. Administration should be completed within 6 h of opening the ampoule. Current formulations of Propofol contain 0.005% Disodium edetate or 0.025% Sodium metabisulfite to help retard the rate of growth of microorganisms.

MECHANISMS OF ACTION

Propofol is a relatively selective modulator of g-aminobutyric acid ($GABA_A$) receptors although it also has activity at glycine receptors. Propofol is presumed to exert its sedative-hypnotic effects through a $GABA_A$ receptor interaction[30].

METABOLISM AND EXCRETION

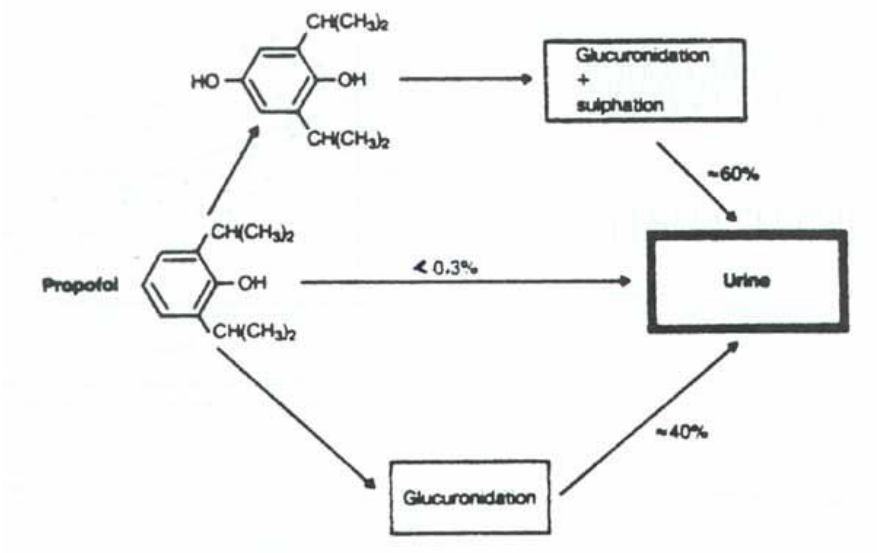


Fig 4 :Metabolism of Propofol

Propofol is rapidly metabolized in the liver by conjugation to glucuronide and sulfate to produce water-soluble compounds, which are excreted by the kidneys[31]. Less than 1% of Propofol is excreted unchanged in urine, and only 2% is excreted in feces. The metabolites of Propofol are not active. Because clearance of Propofol exceeds hepatic blood flow, extra hepatic metabolism or extra renal elimination has been suggested. The lungs seem to play an important role in this extra hepatic metabolism. They are responsible for approximately 30% of the uptake and first-pass elimination after a bolus dose. Other sites of Propofol metabolism are human kidney and

small intestine, microsomes in these tissues demonstrated an ability to form Propofol glucuronide. Propofol itself results in a concentration-dependent inhibition of cytochrome P450 and thus may alter the metabolism of drugs dependent on this enzyme system (e.g., opiates).

PHARMACOKINETICS

Propofol's pharmacokinetics has been studied using single bolus dosing and continuous infusions. The initial distribution half-life of Propofol is 2 to 8 minutes.[31,32]

Studies in which the disposition of Propofol is described by a three-compartment model give initial and slow distribution half lives of 1 to 8 minutes and 30 to 70 minutes and an elimination half-life of 4 to 23.5 hour[33,34]. This long elimination half-life is indicative of the existence of a poorly perfused compartment from which Propofol slowly diffuses back into the central compartment. Propofol is rapidly cleared from the central compartment by hepatic metabolism and the context-sensitive half-life for Propofol infusions up to 8 hours is less than 40 minutes.

The high lipid solubility of Propofol results in an onset of action that is almost as rapid as that of Thiopental (one-arm-to-brain circulation time). Awakening from a single bolus dose is also rapid due to a very short initial distribution half-life (2-8 min). This makes it a good agent for outpatient anesthesia. A lower induction dose is recommended in elderly patients because of their smaller Vd.

The clearance of Propofol exceeds hepatic blood flow, implying the existence of extra hepatic metabolism. This exceptionally high clearance rate (10

times that of Thiopental) probably contributes to relatively rapid recovery after a continuous infusion. Conjugation in the liver results in inactive metabolites that are eliminated by renal clearance. The pharmacokinetics of Propofol does not appear to be affected by moderate cirrhosis.

Table 3: Uses and doses of Propofol

Induction of general anesthesia	1-2.5 mg/kg IV; dose reduced with increasing age
Maintenance of general anesthesia	50-150 µg/kg/min IV combined with N2 **O** or an opiate
Sedation	25-75 µg/kg/min IV
Antiemetic	10-20 mg IV; can repeat q5-10min or start infusion of 10 µg/kg/min

PHARMACODYNAMICS

CARDIOVASCULAR SYSTEM

The most prominent effect of Propofol is a decrease in arterial blood pressure during induction of anesthesia. This decrease in arterial blood pressure associated with decrease in cardiac output/ cardiac index, stroke volume index and systemic vascular resistance. The above effect is both due to vasodilation and myocardial depression. The decrease in arterial pressure is associated with a decrease in cardiac output/cardiac index (±15%)[35,36] stroke volume index (±20%)[36], and systemic vascular resistance (15% to 25%)[35]

Heart rate does not change significantly. No direct effect on sinoatrial node function or on normal atrio-ventricular and accessory pathway of conduction.

Infusion results in significant reduction in both myocardial blood flow and myocardial oxygen consumption.

Clinically, the myocardial depressant effect and the vasodilation seem to be dose-dependent and plasma concentration–dependent[37]. In addition to arterial vasodilation, Propofol produces venodilation (due both to a reduction in sympathetic activity and to a direct effect on the vascular smooth muscle), which further contributes to its hypotensive effect.

Factors exacerbating the hypotension include large doses, rapid injection, and old age. Propofol markedly impairs the normal arterial baroreflex response to hypotension, particularly in conditions of normocarbia or hypocarbia.

RESPIRATORY SYSTEM

Propofol produces dose-dependent depression of ventilation,

with apnea occurring in 25% to 35% of patients after induction of anesthesia with Propofol[38]. Prolonged apnoea, ie. for than 30 second; increased incidence seen with addition of an Opiate. More pronounced effect on tidal volume than on respiratory rate. The ventilatory response to arterial hypoxemia are also decreased by Propofol due to an effect at the central chemoreceptors.[39]

Conscious sedation in sub anesthetic doses, Propofol infusion inhibits hypoxic ventilatory drive and depresses the normal response to hypercarbia. Propofol-induced depression of upper airway reflexes exceeds that of thiopental and can prove helpful

during intubation or laryngeal mask placement in the absence of paralysis. Propofol can produce bronchodilation in patients with chronic obstructive pulmonary disease and does not inhibit hypoxic pulmonary vasoconstriction.

CENTRAL NERVOUS SYSTEM

Propofol potentiates the function of GABA through activation of chloride channel, thereby enhancing inhibitory synaptic transmission. The duration of hypnosis is dose-dependent, being 5 to 10 minutes after 2 to 2.5 mg/kg.[40]Cerebral protective effect following an acute ischemic insult is of same degree as either Halothane or Thiopentone. Propofol reduces intraocular pressure by 30-40%. There is no anti-analgesic effect like Thiopentone. Propofol has been used successfully to terminate status epilepticus, and may be safely administered to epileptic patients. The duration of motor and EEG seizure activity following electroconvulsive therapy is significantly shorter with Propofol than with other IV anesthetics.

OTHER EFFECTS

Good intubating conditions after Propofol alone have been reported. It has been used successfully to treat postoperative nausea in a bolus dose of 10 mg[41.]The median concentration of Propofol that was associated with an antiemetic effect was 343 ng/mL.[42] The maintenance Propofol infusion also was superior to adding Propofol only at the end of the procedure (sandwich technique)[43]**.** Does not potentiate neuromuscular block produced by both non depolarizing and depolarizing agents.

Induction is occasionally accompanied by excitatory phenomena such as muscle twitching, spontaneous movement, opisthotonus, or hiccupping possibly due to subcortical glycine antagonism.

Unique to Propofol are its antipruritic properties. A potential advantage of Propofol for sedation of ICU patients is that it seems to possess antioxidant properties.[44] Its antiemetic effects (requiring a blood Propofol concentration of 200 ng/mL) make it a preferred drug for outpatient anesthesia The postulated mechanisms include antidopaminergic activity, depressant effect on the chemoreceptor trigger zone and vagal nuclei, decreased release of glutamate and aspartate in the olfactory cortex, and reduction of serotonin concentrations in the area postrema.

Propofol does not trigger malignant hyperthermia (MH) and may be considered the induction agent of choice in MH-susceptible patients.

SIDE EFFECTS

Induction of anesthesia using Propofol has several side effects, including pain on injection, hypotension , apnea, myoclonus, and, rarely, thrombophlebitis of the vein into which Propofol is administred.

Propofol infusion syndrome is lethal syndrome which is associated with infusion of Propofol at 4 mg/kg/hr or more for 48 hours or longer.

Lactic acidosis ("Propofol infusion syndrome") has been described in pediatric and adult patients receiving prolonged high-dose infusions of Propofol (0.75 mg/kg/ minute) for longer than 24 hours.[45,46]

PROPOFOL IN ECT

Propofol appears to have more potent anticonvulsant effects during ECT than other IV anesthetics. The use of a minimally hypnotic dose of Propofol (0.75 mg/kg) was associated with a seizure duration that was comparable to standard hypnotic doses of Methohexital. The ECT seizure duration after larger dosages of Propofol (1.0-1.5 mg/kg) was significantly shorter than after Methohexital, Etomidate and Thiopental. Even the largest dose of Propofol (1.5 mg/kg) may result in duration of EEG seizure activity that is considered clinically acceptable.

Because use of Propofol can significantly shorten the duration of seizure activity, its effect on the antidepressant action of ECT has been a concern. Seizure duration in any case may be only marginally related to the clinical efficacy of ECT [47]. The magnitude of improvement in the patients depression symptoms was apparently unrelated to either the total duration of seizure activity during the series of ECT treatments or the concurrent use of Tricyclic antidepressant (TCA) drugs. The addition of a small amount of Lidocaine or the use of Propofol emulsion to reduce pain on injection does not seem to have any adverse effect on seizure activity. Because of the well known cardiovascular depressant effects of Propofol, the acute hemodynamic response during the ECT procedure is reduced with Propofol compared with Etomidate, Methohexital, and Thiopental.

THIOPENTONE

HISTORY

Thiopental, the flagship of the barbiturate anesthetic group, has been for more than 65 years as a standard anesthetic induction agent to which all others are compared.

Tabern and Volwiler in 1935 synthesized a series of sulfur-containing barbiturates including Thiopentone. It was introduced clinically by Ralph Waters and John Lundy and became preferred clinically because of its rapid onset of action and short duration.

Although criticized after many casualties during the attack on Pearl Harbour as "the ideal form of euthanasia in war surgery," the barbiturates continued to be widely used in clinical practice.[48]

STRUCTURE OF THIOPENTONE

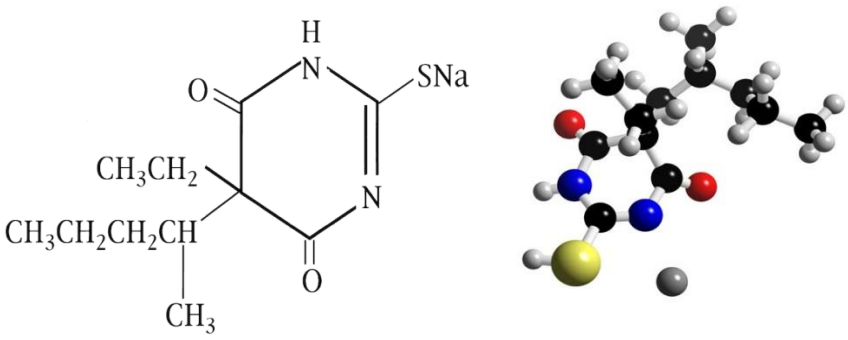


Fig 5: Structure of Thiopentone

PHYSIOCHEMICAL CHARACTERISTICS

Thiopental(Pentothal) is a Thiobarbiturate-(5-ethyl-5methylbuty1]-2-thiobarbituric acid).

Barbiturates are hypnotically active drugs that are derivatives of barbituric acid (2,4,6---trioxohexahydropyrimidine), formed by the condensation of malonic acid and urea.

Thiopentone is available as sodium salts and must be dissolved in isotonic sodium chloride (0.9%) or water to prepare solutions of 2.5% Thiopental. If refrigerated, solutions of the Thiobarbiturates are stable for up to 2 weeks. When Thiopentone is added to Ringer's lactate or an acidic solution containing other water-soluble drugs, precipitation will occur and can occlude the IV catheter. Although solution of Thiopental (2.5%) is highly alkaline (pH 9) and can be irritating to the tissues if injected extravenously, it does not cause pain on injection and venoirritation is rare. Intra-arterial injection of Thiopentone is a serious complication as crystals can form in the arterioles and capillaries, causing intense vasoconstriction, thrombosis, and even tissue necrosis. Accidental intra-arterial injections should be treated promptly with intra-arterial administration of Papaverine and Pidocaine (or Procaine), as well as a regional anesthesia-induced sympathectomy (stellate ganglion block, brachial plexus block) and heparinization.

MECHANISM OF ACTION Acts on CNS neurophysiologic systems by enhancement of the synaptic actions of inhibitory neurotransmitters like GABA and blockade of the synaptic actions of excitatory neurotransmitters.[49]

METABOLISM AND EXCRETION

Thiopentone is metabolized in the liver to hydroxythiopental and the carboxylic acid derivative by four processes: (1) Oxidation of the aryl, alkyl, or phenyl moiety at C5; (2) N- dealkylation; (3) Desulfuration at C2; and (4) destruction of the barbituric acid ring[50]. These metabolites are almost all inactive, water soluble and readily excreted in urine or as glucuronic acid conjugates in bile. Chronic administration of Thiopentone will induce the hepatic enzymes. Because of the induction of hepatic enzymes, Thiopentone should not be administered to patients with acute intermittent porphyria.It may precipitate an attack by stimulating y-aminolevulinic acid synthetase, the enzyme responsible for the production of porphyrins.

PHARMACOKINETICS AND DOSAGE

The duration of action of highly lipid-soluble Thiopentone is determined by redistribution, not metabolism or elimination. The pharmacokinetics of Thiopentone is described in both physiologic and compartmental models. Physiologic models of barbiturates describe rapid mixing of the drug with the central blood volume followed by quick distribution of the drug to the highly perfused, low-volume tissues (i.e., brain) and slower redistribution of the drug to lean tissue (muscle), which terminates the effect of the induction dose. Uptake by adipose tissue and metabolic clearance (elimination) play only a minor role in termination of the

effects of the induction dose because of the minimal perfusion ratio in comparison to other tissues and the slow rate of removal, respectively.

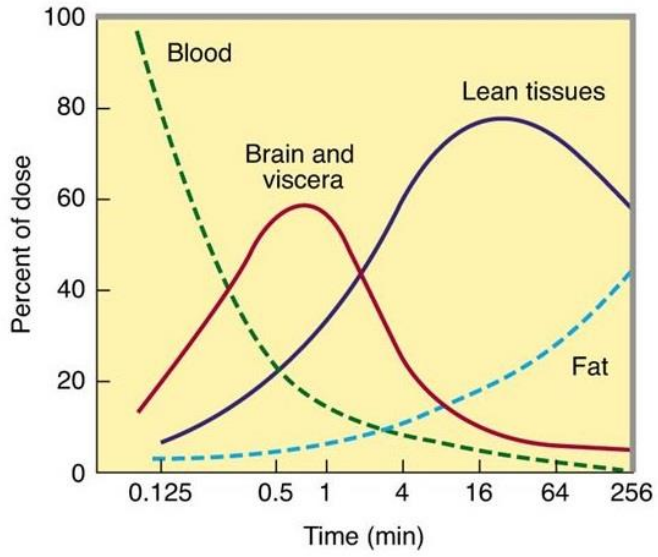


Fig 6: Redistribution of Thiopental after an intravenous bolus administration

These models describe rapid redistribution as the primary mechanism that terminates the action of a single induction dose. The compartmental model explains the delay in recovery when a continuous infusion of a barbiturate is used. This model describes the phenomena whereby the termination of effect becomes increasingly dependent on the slower process of uptake into adipose tissue and elimination or clearance through hepatic metabolism. Repetitive administration of barbiturates saturates the peripheral compartments, so that redistribution cannot occur and the duration of action becomes more dependent on elimination. After prolonged infusions, the pharmacokinetics of barbiturate metabolism is best approximated by nonlinear Michaelis Menten metabolism.

In usual doses (4 to 5 mg/kg), Thiopental exhibits first-order kinetics. At very high doses of Thiopental (300 to 600 mg/kg) with receptor saturation, zero-order kinetics occurs. Pregnancy increases the volume of distribution of Thiopental, thereby prolonging the elimination half-life.[51]

The low elimination clearance of Thiopental (3.4 mL/kg/min) contributes to a long elimination half-life (t1/2 10-12 h).

The usual induction dose of Thiopental is 3 to 5 mg/kg in adults, 5 to 6 mg/kg in children, and 6 to 8 mg/kg in infants. Geriatric patients require a 30 to 40% reduction in the usual adult dose because of a decrease of the volume of the central compartment and slowed redistribution of Thiopental from the vessel-rich tissues to lean muscle. Thiopental infusion is not used to maintain anesthesia because of the long context-sensitive half-time and prolonged recovery period. Plasma Thiopental levels necessary to maintain a hypnotic state range between 10 and 20 mg/ml.

PHARMACOKINETIC VARIABLES OF THIOPENTONE

Elimination Half-Life (hr)	**Clearance (mL/kg/min)**	**Vd$_s$, (L/kg)**
7-17	**3-4**	**1.5-3**

PHARMACODYNAMICS

CENTRAL NERVOUS SYSTEM

Thiopentone produce a proportional decrease in CMRO2 and CBF, thereby lowering ICP. The maximal decrease in CMRO2 (55%) occurs when the EEG becomes isoelectric. An isoelectric EEG can be maintained with a thiopental

infusion rate of 4 to 6 mg/kg/h. Because the decrease in systemic arterial pressure is usually less than the reduction in ICP, Thiopental improves cerebral perfusion and compliance. Thiopental is widely used to improve brain relaxation during neurosurgery and to improve cerebral perfusion pressure (CPP) after acute brain injury.

Barbiturates also possess "neuroprotective" properties secondary to their ability to decrease oxygen demand. It can also be explained by ,a reverse steal ("Robin Hood effect") on CBF, free-radical scavenging, stabilization of liposomal membranes, as well as excitatory amino acid (EAA) receptor blockade. Barbiturates are frequently used for cerebroprotection during incomplete brain ischemia (e.g., carotid endarterectomy, temporary occlusion of cerebral arteries, profound hypotension, and cardiopulmonary bypass).

Thiopentone causes predictable, dose-dependent EEG changes and possess potent anticonvulsant activity. Continuous infusions of Thiopental have been used to refractory status epilepticus. Relatively small doses of Thiopental (50-100 mg intravenously) rapidly control most grand mal seizures.

RESPIRATORY SYSTEM

Thiopentone cause dose-dependent respiratory depression. Bronchospasm or laryngospasm following induction with Thiopental is usually the result of airway manipulation in "lightly" anesthetized patients. Laryngeal reflexes appear to be more active after induction with Thiopental than with Propofol.

CARDIOVASCULAR SYSTEM

The cardiovascular effects of thiopental include decreases in cardiac output, systemic arterial pressure, and peripheral vascular resistance. The depressant effects of Thiopental on cardiac output are primarily a result of a decrease in venous return caused by peripheral pooling, as well as a result of a direct myocardial depressant effect, which assumes increasing importance in the presence of hypovolemia and myocardial disease. Use of appropriate doses can minimize the cardio depressant effects of Thiopental, even in infants.

THIOPENTONE IN ECT

Thiopental has greater anticonvulsant effects and longer duration of action than Methohexital. Its recovery characteristics do not appear to be particularly disadvantages, but it has been suggested that postictal dysrhythmias may be more common with Thiopental than with Propofol. The advantage of thiopental is its low cost compared to Propofol hence widely used in developing countries. Thiopental (2-5 mg/kg) has the disadvantage of having to be reconstituted into solution and haemodynamic parameters appear less well attenuated when compared with Propofol. Compared with Propofol, the middle cerebral artery flow velocities immediately after ECT were significantly higher with Thiopental.

SUCCINYLCHOLINE

HISTORY

Reid Hunt and Taveau of Boston are credited with first synthesis of the drug in 1906. Forty years later it was left to Bovet et al, to elucidate its curariform action.

It was introduced into clinical practice by Thesleff and by Foldes and colleagues in 1952. Its rapid onset of effect and ultra short duration of action allowed for rapid tracheal intubation.

PHYSIOCHEMICAL PROPERTIES

- White solid, crystallizing with two molecules of water. Readily soluble in water, giving a slightly acidic solution. Hydrolysis occurs at room temperature and so it should be stored at 4°c.

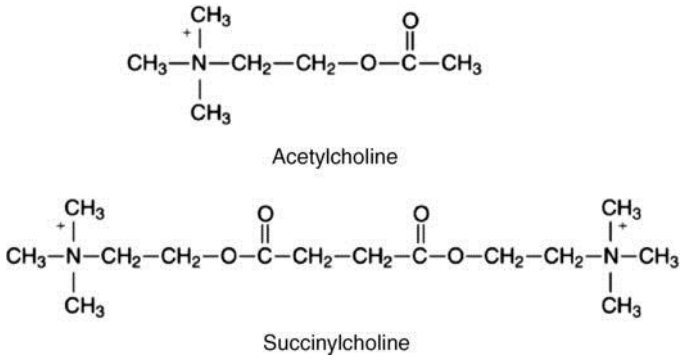


Fig 7: Chemical Structure of Succinylcholine

Succinylcholine is a long, thin, flexible molecule composed of two molecules of acetylcholine linked through the acetate methyl groups. The active part of the

molecule is the cation formed by succinic radical with a quaternary ammonium group at each molecular chain.

MECHANISM OF ACTION

Depolarizes the muscular membrane by opening channels similar to Acetylcholine. Unlike Ach it is not hydrolyzed by Acetylcholine esterase at the neuromuscular junction, but by plasma choline esterase (also called pseudocholinesterase). Hence, it persists at the neuromuscular junction and depolarization will last long. So there will be a brief period of excitation initially, which may be manifested as transient muscle fasciculations, followed by block of neuromuscular transmission and flaccid paralysis.

METABOLISM KINETICS AND EXCRETION

Succinylcholine is metabolized by first order pharmacokinetics. Succinylcholine undergoes rapid hydrolysis to Succinylmonocholine, then to choline and succinic acid by plasma cholinesterase (also called pseudo cholinesterase) with an elimination half-life of <1 minute. Plasma cholinesterase is a lipoprotein synthesized in the liver. Failure of its action due to deficiency or abnormality prolongs the action of Succinylcholine.

The rapid onset of action is largely due to its low lipid solubility. As Succinylcholine enters the circulation, most of it is rapidly metabolized by pseudo cholinesterase into Succinylmonocholine.

Because of the rapid disappearance of Succinylcholine from plasma, the maximum effect is reached quickly. Sub paralyzing doses (up to 0.3 to 0.5 mg/kg) reach their maximal effect within —1.5 to 2 minutes at the adductor pollicis, and within 1 minute at more central muscles, such as the masseter and the larynx. With larger doses (1 to 2 mg/kg), abolition of twitch response can be reached even more rapidly.

The mean dose producing 95% blockade (ED95) at the adductor pollicis is 0.30 to 0.35 mg/kg with Opioid nitrous oxide anesthesia. In the absence of nitrous oxide, the ED95 is increased to 0.5 mg/kg. The time until full recovery is dose dependent and reaches 10 to 12 minutes after a dose of 1 mg/kg.

The duration of action is prolonged by high doses or by abnormal metabolism. The latter may result from hypothermia, low pseudo cholinesterase levels, or a genetically aberrant enzyme. Hypothermia decreases the rate of hydrolysis. Low pseudo cholinesterase levels generally produce only modest prolongation of Succinylcholine actions (2-20 min).

Causes for the decreased concentration of the enzyme

- Pregnancy
- Liver disease
- Burns
- Drugs-anticholineesterases, Metoclopramide, oral contraceptives.
- Genetically aberrant pseudocholinesterase gene.

CHARACTERISTICS OF DEPOLARIZING BLOCKADE BY SCh

After injection of Succinylcholine, single-twitch height is decreased. The response to high-frequency stimulation is sustained: minimal train-of-four and tetanic fade is observed. The block is antagonized by nondepolarizing agents so that the ED95 is increased by a factor two if a small dose of nondepolarizing drug is given before.

Succinylcholine blockade is potentiated by inhibitors of acetyl cholinesterase, such as Neostigmine and Edrophonium.

PHASE II BLOCK [DESENSITISATION BLOCK]

Its occurrence is related to both dose and duration of administration of Succinylcholine. It results in an abnormally prolonged duration of neuromuscular block. The train of four and tetanic fade become apparent. Neostigmine or Edrophonium can antagonize this block, which has been termed "nondepolarizing," "dual," or "Phase II block." The onset of Phase II block coincides with tachyphylaxis, as more Succinylcholine is required for the same effect.

DOSAGE OF SUCCINYL CHOLINE

Routes of administration are IM, IV and S/C

The adult dose of Succinylcholine needed for intubation is 1-1.5 mg/kg intravenously with an onset of action in 10-30 seconds and clinical duration of action of 1-10 minutes. Repeated small boluses (10 mg) can be used during surgical procedures that require brief but intense paralysis (eg, otolaryngological endoscopies). Neuromuscular function should be

constantly monitored with a nerve stimulator to prevent overdosing and the development of phase II block.

ADVERSE EFFECTS

1. CARDIOVASCULAR

Succinylcholine not only stimulates nicotinic cholinergic receptors at the neuromuscular junction, it stimulates all ACh receptors. Succinylcholine's cardiovascular actions are due this property. Stimulation of nicotinic receptors in parasympathetic and sympathetic ganglia and muscarinic receptors in the sinoatrial node of the heart can increase or decrease blood pressure and heart rate. Low doses of succinylcholine can produce negative chronotropic and inotropic effects, but higher doses usually increase heart rate and contractility and elevate circulating catecholamine levels.

Children are susceptible to profound bradycardia following administration of Succinylcholine. Bradycardia typically occurs in adults only if a second bolus of Succinylcholine is administered approximately 3-8 min after the first dose. Succinylcholine metabolite, Succinylmonocholine, sensitizes muscarinic cholinergic receptors in the sinoatrial node to the second dose of Succinylcholine, resulting in bradycardia. This bradycardia can be blocked by Thiopentone, Atropine, ganglion blocking drugs and nondepolarizing muscle relaxants. Other arrhythmias seen are nodal/junctional rhythms and ventricular arrhythmias ranging from unifocal premature ventricular contractions to fibrillation.

2. FASCICULATIONS

The onset of paralysis by Succinylcholine is usually signaled by visible motor unit contractions called fasciculations. These can be prevented by pretreatment with a small dose of nondepolarizing relaxant. Because this pretreatment usually antagonizes a depolarizing block, a higher dose of Succinylcholine is subsequently required (1.5 mg/kg). Fasciculations are typically not observed in young children and elderly patients.

3. HYPERKALEMIA

Normal muscle releases enough potassium during Succinylcholine-induced depolarization to raise serum potassium by 0.5 mEq/L. Although this is usually insignificant in patients with normal baseline potassium levels, it can be life-threatening in patients with preexisting hyperkalemia or those with burn injury, massive trauma, neurological disorders, and several other conditions. Subsequent cardiac arrest can prove to be quite refractory to routine cardiopulmonary resuscitation, requiring Calcium, Insulin, Glucose, Bicarbonate, Epinephrine, cation-exchange resin, Dantrolene, and even cardiopulmonary bypass to reduce metabolic acidosis and serum potassium levels.

Following denervation injuries, the immature isoform of the ACh receptor may be expressed inside and outside the neuromuscular junction (up-regulation). These extrajunctional receptors allow Succinylcholine to effect widespread depolarization and extensive potassium release. Life-threatening potassium release is not prevented by pretreatment with a nondepolarizer.

4 MUSCLE PAINS

Patients who have received Succinylcholine have an increased incidence of postoperative myalgia. It is more frequent in females and outpatients. The myalgias are due to damage produced by the unsynchronized contractions, fasiculations of muscle groups just before onset of paralysis. Though precurarisation prevents fasciculations from Succinylcholine, its efficacy in preventing muscle pain is controversial. The relationship between fasciculations and postoperative myalgias is also inconsistent. Perioperative use of nonsteroidal anti-inflammatory drugs may reduce the incidence and severity of myalgias.

5. INTRAGASTRIC PRESSURE ELEVATION

The increase in intragastric pressure appears to be related to (a) the intensity of fasciculations of the abdominal skeletal muscles,[52] which could be prevented by prior administration of a nondepolarizing neuromuscular blocker; and (b) a direct increase in vagal tone. Administration of Succinylcholine does not predispose to regurgitation in patients with an intact lower oesophageal sphincter because the increase in intragastric pressure does not exceed the "barrier pressure."[53]

6. INTRAOCULAR PRESSURE ELEVATION

Prolonged membrane depolarization and contraction of extra ocular muscles following administration of Succinylcholine transiently raise intraocular pressure and could compromise an injured eye. The increased IOP is manifested within 1 minute after injection, peaks at 2 to 4 minutes, and subsides by 6 minutes.[54] The use is not contraindicated unless anterior chamber is open.

7. MASSETER MUSCLE RIGIDITY

Succinylcholine transiently increases muscle tone in the masseter muscles. Some difficulty may initially be encountered in opening the mouth because of incomplete relaxation of the jaw. This is not a prodorme of malignant hyperthermia as was once believed.

8. MALIGNANT HYPERTHERMIA

Succinylcholine is a potent triggering agent in patients susceptible to malignant hyperthermia, a hyper metabolic disorder of skeletal muscle. The signs and symptoms of neuroleptic malignant syndrome (NMS) resemble those of malignant hyperthermia, the pathogenesis is completely different and there is no need to avoid use of Succinylcholine in patients with NMS.

9. INTRACRANIAL PRESSURE

Succinylcholine leads to an activation of the electroencephalogram and transient increases in cerebral blood flow and intracranial pressure. Muscle fasciculations stimulate muscle stretch receptors, which subsequently increase cerebral activity. The transient increase in intracranial pressure can be attenuated by maintaining good airway control and instituting hyperventilation. It can be prevented by pretreating with a nondepolarizing muscle relaxant and administering intravenous Lidocaine (1.5-2.0mg/kg) 2-3 min prior to intubation.

SUCCUNYLCHOLINE IN CHILDREN

There have been incidences of intractable cardiac arrests in hitherto apparently healthy children following Succinylcholine administration. In many of these cases there were associated hyperkalemia , rhabdomyolysis and acidosis. United States Food and Drug Administratin recommends that the use of Succinylcholine in children should be reserved for emergency.

SUCCINYL CHOLINE IN BURNS PATIENT

Hyperkalemia is markedly exaggerated in these patients (6-13 mEq/L). This is due to apparent proliferation of extrajunctional receptors, stimulation of which causes massive potassium release sufficient to cause ventricular tachycardia, fibrillation and even cardiac arrest. Magnitude of this response does not correlate with magnitude of burn injury.

SUCCINYLCHOLINE IN ECT

Succinylcholine remains the most commonly used muscle relaxant to reduce the intense muscle contractions associated with ECT-induced seizure activity. The dose recommended by the Royal College of Psychiatrists is 0.5 mg/kg, but larger dosages (0.75-1.5 mg/kg) are often used in clinical practice. It is given after loss of consciousness during the procedure. The electrical stimulus should be applied only after fasciculations have ceased. Pseudocholinesterase deficiency, neuromuscular disease, the presence of cholinesterase inhibitors, a history of malignant hyperthermia, neuroleptic malignant syndrome, catatonia or major burns may preclude its use and suggest conversion to a non-depolarising agent. Coexisting

conditions such as severe cachexia, osteoporosis or skeletal injury indicate the need to increase the dose of muscle relaxant. Use of larger doses of Succinlylcholine should be avoided in patients with a history of bradyarrhythmias.

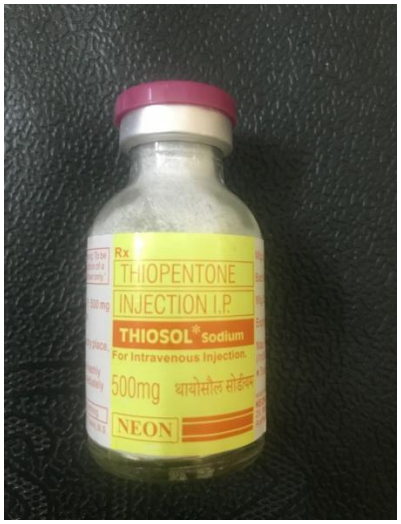


Figure 8 : Thiopentone

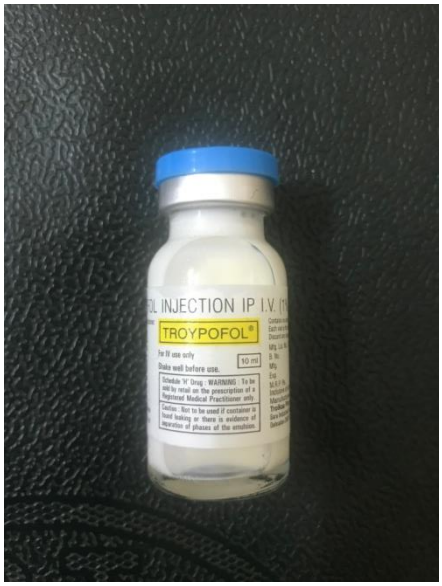


Figure 9 : Propofol

Figure 10: Succinylcholine

Figure 11: Brief Pulse Wave ECT machine

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The backbone of our study were the following observations and conclusions drawn by eminent anaesthesiologists and psychiatrists in their widely accepted clinical studies

Boey WK, Lai FO (1990) compared Propofol and Thiopentone as anaesthetic agents in their study for electroconvulsive therapy in 31 patients on four occasions in a repeated measure crossover study and concluded that hemodynamic stability was more with Propofol compared to Thiopentone but duration of seizure was shorter, discomfort on injection and apnea time was more common with Propofol compared to Thiopentone.[55]

Villalonga A, Bernado M, Gomar C, Fita G, Escobar R, Pacheo M (1993) assessed cardiovascular response and anaesthetic recovery in electroconvulsive therapy with Propofol and Thiopental in seven women (22-67 years of age). and observed that ECT induced increase in Diastolic blood pressure and Heart rate were less marked with Propofol than with Thiopental.[56]

Saito S et al (2000) compared cerebral blood flow velocity at the middle cerebral artery during ECT , using Propofol versus Thiopental anaesthesia. They concluded that Propofol anaesthesia may be suitable for patients as it has minor effect on cerebral hemodynamics might be more suitable for patients with intracranial complications, such as cerebral aneurysms.[57]

Kadoi Y et al (2003) in their comparative study between Propofol and Thiopentone on left ventricular function during electroconvulsive therapy concluded that a lesser

haemodynamic change occurs after Propofol anaesthesia (1mg/kg) compared with Thiopentone anaesthesia (2mg/kg)[58]

Bailine SH, Petrides G, Doft M, Lui G (2003) in their study, Indications for the use of Propofol in electroconvulsive therapy concluded that Propofol may be used as an useful alternative to Methohexital for the treatment of patients having excessively long seizures and / or excessive nausea and vomiting after ECT. Such seizures are more common among adolescents.[59]

Butterfield NN, Graf P, Macleod BA, Ries CR, Zis AP (2004) did a randomized, double blind study in patients receiving right unilateral ECT for depression. Patients received Propofol or Thiopental on alternating ECTs upto 6 treatments. Immediate and delayed verbal memory, motor speed, reaction speed, visuospatial, and executive functions assessed 45 minutes after each ECT. Results showed that cognitive impairments were reduced after ECT with Propofol compared to Thiopental. Emergence was quicker and EEG seizure duration was shorter after Propofol treatments.[60]

Gábor G, Judit T, Zsolt I (2007) compared Propofol and Etomidate regarding impact on seizure threshold during electroconvulsive therapy in patients with schizophrenia. 30 schizophrenic patients participated in the prospective randomized cross-over study. Anesthetic induction with 1 mg/kg of Propofol or 0.2 mg/kg of Etomidate was done alternately. For both anesthetics, seizure threshold was determined by titrating the dose of the stimulus necessary for eliciting a seizure. Seizure durations were also compared. Propofol was shown to possess significant

seizure-shortening properties, but it does not elevate seizure threshold or drop seizure duration under the minimal threshold more frequently than Etomidate does. Based on these findings, they concluded that the use of Propofol does not result in a greater electric load on the patients than Etomidate.[61]

Geretsegger C et al (2007) compared Propofol and Methohexital as anesthetic agents for electroconvulsive therapy in regard to seizure quality, therapeutic efficacy, and cognitive performance and concluded, Propofol, as compared with Methohexital, results in a more moderate increase in blood pressure and shorter seizure duration. The seizure quality did not differ significantly between the 2 groups. We detected a tendency toward improved cognitive performance after anesthesia with Propofol as compared with Methohexital, but with statistical significance in only 2 cognition trials. Therefore, Propofol is a safe and efficacious anesthetic for ECT treatment.[62]

Ingram A, Schweiter I, Ng CH, Saling MM, Savage G (2007) compared Thiopentone and Propofol administration for electroconvulsive therapy (ECT) in terms of associated efficacy and cognitive side effects in the immediate and medium term. Participants comprised 30 depressed patients who were administered either Propofol or Thiopentone as an anesthetic agent for ECT. Clinical rating scales and a battery of neuropsychological tests were administered at baseline, after 6 treatments, 1 to 3 days after treatment end point and at 1-month follow-up. They concluded that Thiopentone has advantages for use as an anesthetic agent in efficacy and cognitive side effects for ECT compared with Propofol.[63]

Hooten WM, Rasmussen KG Jr (2008) compared the effects of general anesthetic agents in adults receiving electroconvulsive therapy.They observed that, the relationship between ECT seizure length and efficacy remains unclear, all of the available induction agents would be appropriate for ECT. When the clinician needs to prolong seizure length, Methohexital or the addition of a short-acting Opioid to Methohexital or propofol should be considered. The small variations in emergence and recovery times should not govern the choice of an induction agent.[64]

Bauer J et al (2009) compared Propofol and Thiopental as anaesthetic agents for electroconvulsive therapy: a randomized, blinded comparison of seizure duration, stimulus charge, clinical effect, and cognitive side effects. They concluded, Propofol significantly decreases seizure duration without significant difference in the clinical outcome. Using the employed treatment algorithm, patients anesthetised with Propofol received higher electrical charge. Mini-Mental State Examination scores suggest that this results in more severe cognitive side effects. Results, however, might be confounded by the differences in age distribution in the groups[65]

Shah PJ, Dubey KP, Watti C, Lalwani J (2010) compared the effectiveness of Thiopentone, Propofol and Midazolam as an ideal intravenous anaesthetic agent for modified ECT. Study was conducted among 90 patients of ASA I and II of either sex who were having major depressive illness and were randomly allocated into three groups (n = 30) based on iv induction agent to be used. Group I, Group II and Group III patients were induced with iv Thiopentone 5 mg/kg, Propofol 2 mg/kg and Midazolam 0.2 mg/kg, respectively. They concluded that Propofol at a dose 2mg/kg body weight had significantly early and smooth recovery, better hemodynamics and

uncompromised therapeutic outcome which makes it an agent of choice for day care procedure.[2]

Daria Usha, Vinod Kumar (2012) compared Thiopentone and Propofol for modified ECT. Hundred patients in the age group above 18 years with ASA grade I and II of both sexes, scheduled to undergo electroconvulsive therapy under general anaesthesia were included in the crossover study. Thiopentone (2.5%) in dosage of 5 mg/kg and Propofol (1%) in dosage of 2 mg/kg were given intravenously for anaesthesia. Concluded that Propofol is a better choice for modified ECT where minimum hospitalisation is needed and for ambulatory patients as it cause rapid smooth induction and early recovery.[5]

Kumar A, Sharma DK, Mani R (2012) did a randomized, blinded study between Propofol and Thiopentone for electroconvulsive therapy on patients of depression and observed that Propofol significantly increases number of ECT required to treat the patients.[7]

Vaidya PV et al (2012) conducted A within-subject comparison of Propofol and Methohexital anesthesia for electroconvulsive therapy. Records from all patients who had undergone separate ECT courses with Methohexital and Propofol between 1992 and 2008 (n = 48) were reviewed for a retrospective within-subject comparison of outcome measures. The clinical outcomes were examined were number of treatments required in a course of ECT, changes in the Montgomery-Åsberg Depression Rating Scale and Mini Mental Status Examination, and length of stay in the hospital after initiation of ECT. Additionally, they compared treatment delivery between

Methohexital and Propofol treatment courses, measuring rate of restimulation for brief seizures, seizure duration, percentage of treatments that were bilateral, and average charge administered and concluded, Methohexital as the induction agent of choice for ECT, especially with right unilateral placement.[66]

Omosofe FO, Bolaji BO, Kolawole IK, Makanjuola AB (2012) conducted a study to Compare haemodynamic effects of Propofol and Thiopentone in modified electroconvulsive therapy in Nigerians. They concluded that Propofol at 1 mg/kg and Thiopentone at 5 mg/kg used for modified ECT in this study resulted in significant increases in heart rates. However, a significant increase in mean arterial pressure with Thiopentone and a significantly greater increase in diastolic blood pressure when the two agents are compared confer some superiority on Propofol over Thiopentone in attenuating haemodynamic responses to ECT.[67]

Zahavi GS, Dannon P (2014) Compared anaesthetics Propofol, Etomidate and Thiopental in electroconvulsive therapy. The objective of this study was to evaluate the effects of the anaesthetics used in ECT on seizure threshold and duration, hemodynamics, recovery from ECT, and immediate side effects. They observed that, Patients who were anesthetized with thiopental received a lower electrical treatment dose without an unwanted decrease in seizure duration. Thiopental might be the anaesthetic of choice when it is congruent with other medical considerations.[68]

Martínez-Amorós E et al (2014) compared Propofol and thiopental as anaesthetic agents in electroconvulsive therapy, a retrospective study in major depression. To

determine the influence of Propofol and Thiopental as anesthetics in electroconvulsive therapy (ECT), as regards, seizure duration, electrical charge, clinical efficacy, cardiovascular profile, and presence of adverse cognitive effects. They concluded, anesthetic agent used in ECT might determine differences in parameters such as seizure duration or electrical charge. However, this does not seem to be translated into differences in clinical efficacy or the pattern of adverse effects observed.[69]

Manjula BP, Nagaraja PS (2015) compared anaesthetic effects of Thiopentone and Propofol for modified ECT and concluded that Propofol when compared to Thiopentone is superior in attenuating physiological response to ECT.[70]

Jarineshin H et al (2015) compared Seizure Duration and Hemodynamic State during Electroconvulsive Therapy: Sodium Thiopental Versus Propofol. They concluded that Propofol provides a more stable hemodynamic state for the ECT procedures, and its use is highly preferred over sodium thiopental in patients with cardiovascular disease.[71]

Canbek O et al (2015) Compared Propofol, Etomidate and Thiopental in Anesthesia for Electroconvulsive Therapy: A Randomized, Double-blind Clinical Trial. The study was aimed to compare the effects of Propofol, thiopental, and Etomidate, which are routinely used in anesthesia for electroconvulsive therapy (ECT), on the cardiovascular system, seizure variables, recovery, cognitive functions, and response to treatment. They concluded that Propofol, Etomidate and Thiopental are associated with similar safety and efficacy profiles.[72]

Patel JD, Upadhya R, Shah H, Patel D, Sharma T (2015) compared effects of Thiopentone Sodium and Propofol for anaesthesia for modified ECT. Thirty patients of ASA grade I and II were randomized into two groups. (Group T) patients were induced with Thiopentone 3-5mg/kg and (group P) with 1.5-2mg/kg Propofol and concluded that, fast, smooth induction, better hemodynamics, early smooth recovery, antiemetic property and uncompromised therapeutic outcome makes Propofol as an the agent of choice for day care procedure .And that reduced seizure duration seen with Propofol has no effect on outcome of therapy or effectiveness of ECT.[3]

Altaf Hussain Mir et al (2017) conducted a study to compare the effects of intravenous (IV) Sodium Thiopentone, Propofol, and Etomidate, used as IV anesthetic agents in modified ECT as regards, induction time and quality of anesthesia, alteration of hemodynamics, seizure duration, and recovery time. Total 90 patients in between age group of 16–60 years of either sex, who had to undergo ECT therapy were divided randomly into three equal groups. Group A received Propofol 1% – 1.5 mg/Kg, Group B received Etomidate – 0.2 mg/Kg, and Group C received Thiopentone 2.5% – 5 mg/Kg They concluded that, Propofol had the advantage of smooth induction, stable hemodynamic parameters and rapid recovery as compared to Etomidate and Thiopentone. Thiopentone had the advantage over Propofol of having longer seizure duration at the cost of a relatively prolonged recovery period. Etomidate had a definite advantage of longer seizure duration.[1]

METHODOLOGY

METHODOLOGY

MATERIALS AND METHODS

7.1 SOURCE OF DATA :

This study was carried out in the Department of Anaesthesiology, B.L.D.E(DEEMED TO BE UNIVERSITY) Shri B.M Patil Medical College, Hospital and Research Centre, Vijayapur.

7.2 METHOD OF COLLECTION OF DATA:

Study Design: Randomized control interventional study.

Study Period: One and half years from December 2016 to August 2018.

Sample Size: With anticipated mean difference of recovery from anaesthesia between 2 study groups as 1.5 and anticipated standard deviation as 1.7 [5] , with 95% confidence level and 80 % power , minimum sample size per groupwas 29, using the formula,

$$n = \frac{(Z_\alpha + Z_\beta)^2 * SD^2 * 2}{MD^2}$$

where, Z_α = Z value at α level=95%

Z_β = Z value at β level=80%

MD = Difference between two parameters.

SD = Anticipated standard deviation.

Hence, 30 cases were included in each group.

Study group : Study was conducted on 60 ASA grade I or II adult patients, of either sex, aged between 18-60 years undergoing electroconvulsive therapy.

Patients were randomly divided using chit method into 2 groups containing 30 patients each, to receive either Inj. Propofol (Group P) or Inj. Thiopentone (Group T) for induction during Electroconvulsive therapy.

Statistical analysis was done using appropriate tests like

- Mean +/- Standard deviation
- Student 't'test
- Mann whitney U test

Inclusion criteria :

- Age between 18 to 60 years.
- Patients of either sex.
- ASA grade I & II.
- Patients undergoing modified Electroconvulsive therapy.
- Patients and relatives willing to sign informed consent.

Exclusion criteria :

Refusal of patient or relatives or both

- ASA grade III and above.
- Patients who received Diazepam 48 hours and Lithium 24 hrs prior to the procedure.
- Pregnancy.
- Allergy to any of the study drugs.
- Patient with H/O full stomach, Uncontrolled Hypertension, Epilepsy.

Investigations done;

- Complete hemogram, Total leucocyte count , Differential Count.
- Random blood sugar, Blood urea and Serum creatinine.
- Chest X-ray (when age >35 years or if necessary)
- ECG
- HIV, HBsAg (In accordance with universal safety precautions)

Preliminaries :

- Written informed consent.
- Intravenous access with a 20 gauge I.V cannula under aseptic precautions.

Study materials : Inj. Propofol , Inj. Thiopentone , Inj. Succinyl choline.

Procedure:

- 60 patients posted for modified ECT were assigned randomly to 2 groups containing 30 patients each.

- All patients were examined the day before surgery and thoroughly investigated according to institute protocol and was counselled with regards to anaesthesia as well as procedure.

- Patient's meeting the above criteria were asked to participate in the study and informed consent was taken. Patients were instructed to fast for 6-8 hours.

- All the resuscitation and monitoring equipments like, bag-valve-mask system, laryngoscope, endotracheal tubes and emergency drugs were kept ready in the operation theatre for management of any adverse event.

- On the day of procedure, patient was taken to procedure room. Baseline values of Blood pressure , Heart rate and oxygen saturation were recorded.

- Intravenous line was secured with 20 G cannula and premedication i.e Inj. Glycopyrolate 0.02 mg/ kg and Inj. Ondansetron 0.15 mg/kg was given and patient was pre-oxygenated for 3 minutes.
- Patients in group P were given Inj. Propofol 1.5mg/kg IV as induction agent and in group T were given Inj. Thiopentone 3mg/kg, till loss of eyelash reflex. BP cuff was applied to the leg and mercury raised up to 250 mm Hg to prevent circulation of Succinylcholine in that leg for monitoring of seizure duration(cuff method for monitoring of seizure duration). Then Inj. Succinyl choline 0.5mg/kg for neuromuscular blockade to reduce muscle contraction associated with ECT induced seizure activity.
- Controlled ventilation was given with facemask and Bains circuit with 100% Oxygen.
- Bitemporal ECT electrodes were placed and connection to ECT machine with proper setting was done. When fasciculations subsided, adequate muscle relaxation obtained, patient was ready to receive ECT.
- A bite block was placed before application of the electrical stimulus to protect patient's teeth and minimize the risk of laceration of the tongue and patient held tight for immobilization to prevent fracture and other complications.
- ECT was given in range of 60Hz-120Hz using brief pulse wave ECT machine. Positive pressure ventilation was resumed after stimulation and continued throughout the seizure till the patient resumed spontaneous and regular respiration.

- Following parameters will be monitored-

A) Induction characteristics - Time and the dose of the induction agent required for loss of eye lash reflex/loss of verbal contact for Propofol and Thiopentone.

B) Hemodynamic parameters - Non invasive blood pressure, heart rate, SpO_2, ECG were monitored prior to induction and after induction at zero, five, ten and fifteen minutes after ECT convulsions.

C) Seizure characteristics -

- Duration of seizure
- Seizure threshold

D) Recovery characteristics -

- Time for return of spontaneous ventilation after apnea.
- Time of eye opening on command.
- Orientation to the time, place and person
- Nausea and vomiting.

Patient was shifted to recovery room once consciousness and spontaneous ventilation was regained.

RESULTS

RESULTS

Statistical analysis

For results on continuous variables, the summary statistics of mean, standard deviation (SD) were used.

For categorical data, the number and percentage were used in the data summaries. The difference of the means of analysis variables between two independent groups was tested by unpaired t test/Mann whitney test.

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant.

Data were analyzed using SPSS software v.23.0. and Microsoft office.

A total of sixty patients participated in the study.

COMPARISON OF PATIENT CHARACTERISTICS

Table 4 : Comparison Of Patient Characteristics Between The Study Groups

Patient characteristics	Group P	Group T	P value
Number of patients	30	30	
Age in years	28.13±7.745	27.73±7.956	P=0.760 NS
Gender-Male	18(60%)	21(70%)	
Gender-Female	12(40%)	9(30%)	
Weight(kg)	64.07±19.73	63.43±15.53	P=0.514 NS
ASA grade-I	24	24	P=1 NS
ASA grade-II	6	6	

NS: Not Significant

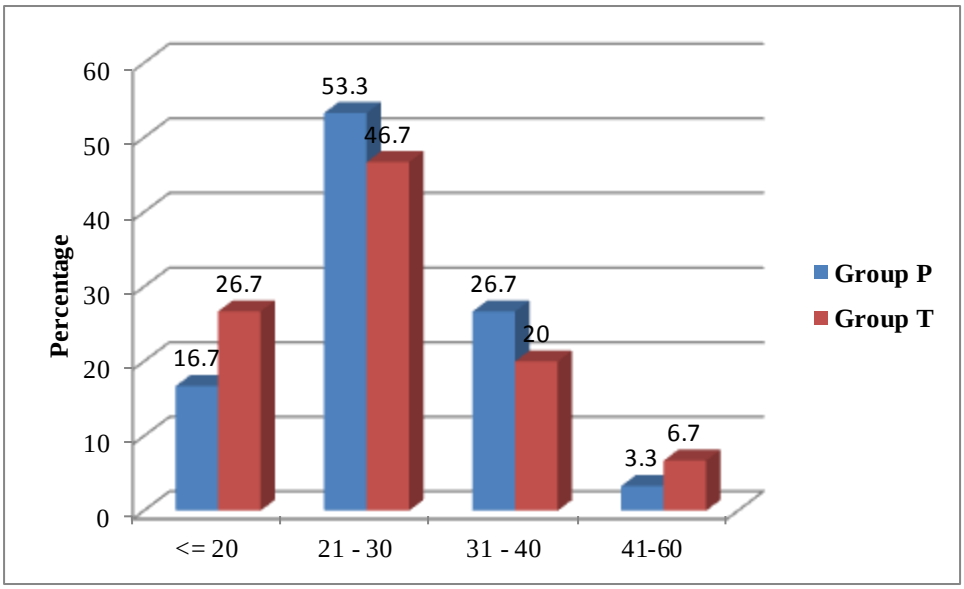
PATIENT CHARACTERISTICS

In both groups there was no significant statistical difference in age, weight, sex and ASA grade.

Hence, both groups were comparable with respect to the patient characteristics.

Table 5 : Distribution Of Cases According To Age Among The Study Groups

Age(Years)	Group P		Group T	
	No. of patients	Percent	No. of patients	Percent
<= 20	5	16.7	8	26.7
21 - 30	16	53.3	14	46.7
31 - 40	8	26.7	6	20.0
41+	1	3.3	2	6.7
Total	30	100.0	30	100.0



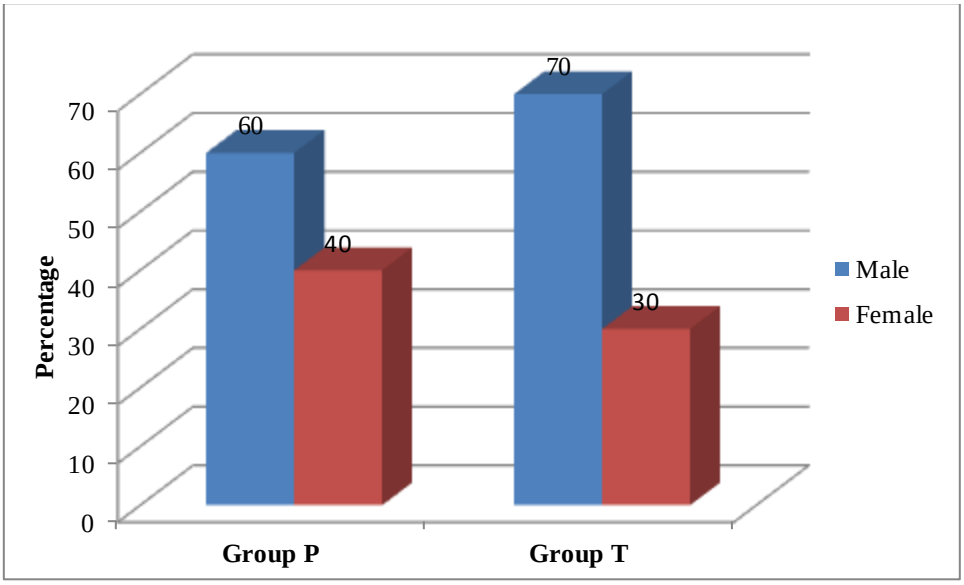
Graph 1: Distribution of Cases According To Age among The Study Groups

Group P comprised of 17%(16.7), 53%(53.3), 27%(26.7), 3%(3.3) patients with their age between <=20 years, 21-30 years, 30-40 years and 40+ years respectively. The mean age of patients in group P was 28.13±7.745.

Group T comprised of 27%(26.7), 47%(46.7), 20%, 7%(6.7) patients with their age between <=20 years, 21-30 years, 30-40 years and 40+ years respectively. The mean age of patients in group T was 27.73±7.956.

Table 6 : Distribution Of Cases According To Sex Among The Study Groups

Sex	Group P		Group T	
	No. of patients	Percent	No. of patients	Percent
Male	18	60.0	21	70.0
Female	12	40.0	9	30.0
Total	30	100.0	30	100.0



Graph 2: Distribution Of Cases According To Sex Among The Study Groups

There were 60% of males in the group P as compared 70% in the group T. Females were 40% in group P and 30% in group T. The p value was 0.4168 therefore, there was no significant difference in the sex distribution in both the groups This implies that sex matching was done between the two groups.

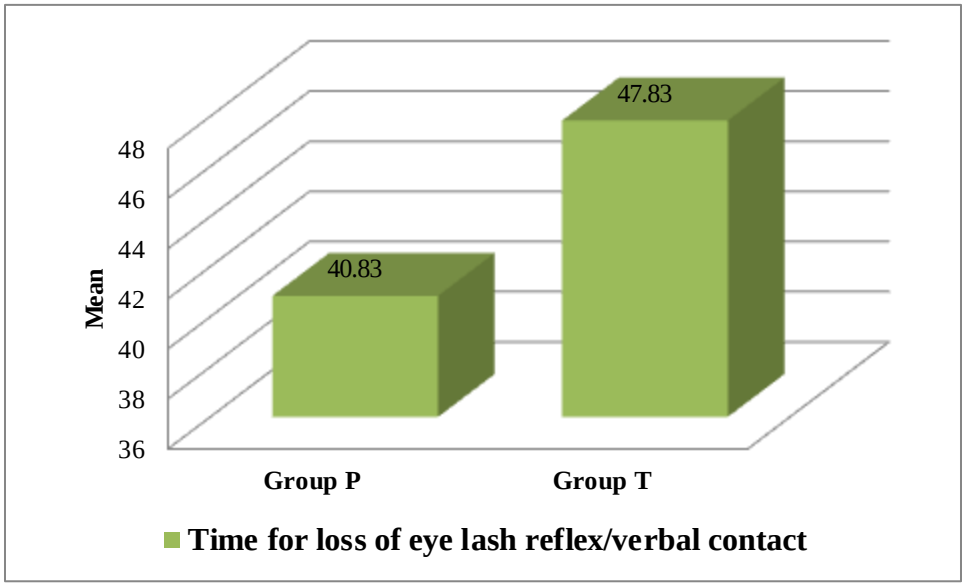
So, The patients in both groups were similar in respect to age and sex distribution.

INDUCTION CHARACTERISTICS

Table 7 : Comparison of Time for loss of eyelash reflex/verbal contact between Study Groups.

Parameter	Group P	Group T	P value
Time for loss of eyelash reflex/ verbal contact(sec)	40.83±1.464	47.83±1.802	P<0.001*

Note: *Significance at 5% level of significance (p<0.05)



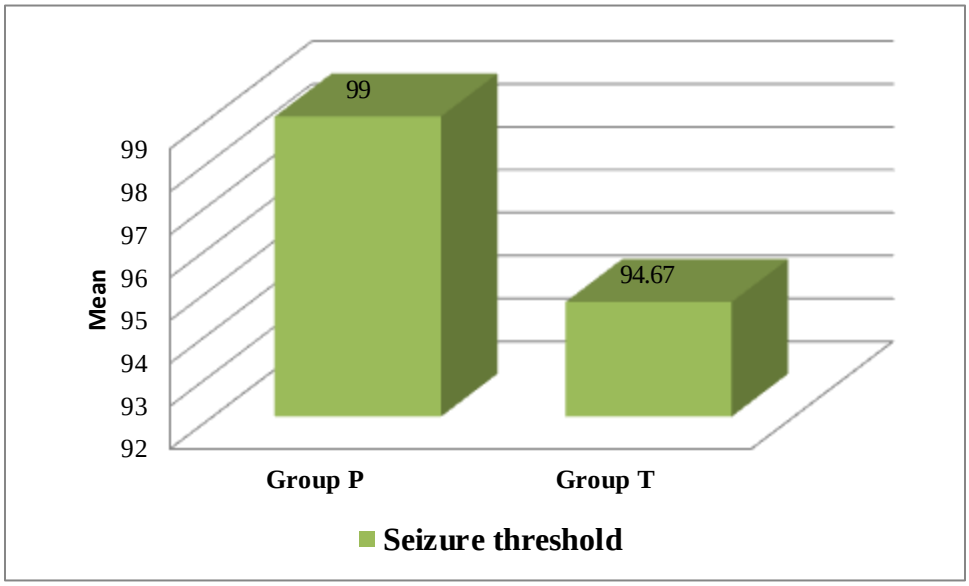
Graph 3: Comparison Of Induction Characteristics Between Study Groups

Comparing the time for loss of eyelash reflex/verbal contact for induction showed (Group T) Thiopentone took longer time (47.83 sec) than Propofol(Group P) that was (40.83 sec) which was statistically significant with (p<0.001*).

SEIZURE DURATION AND SEIZURE THRESHOLD

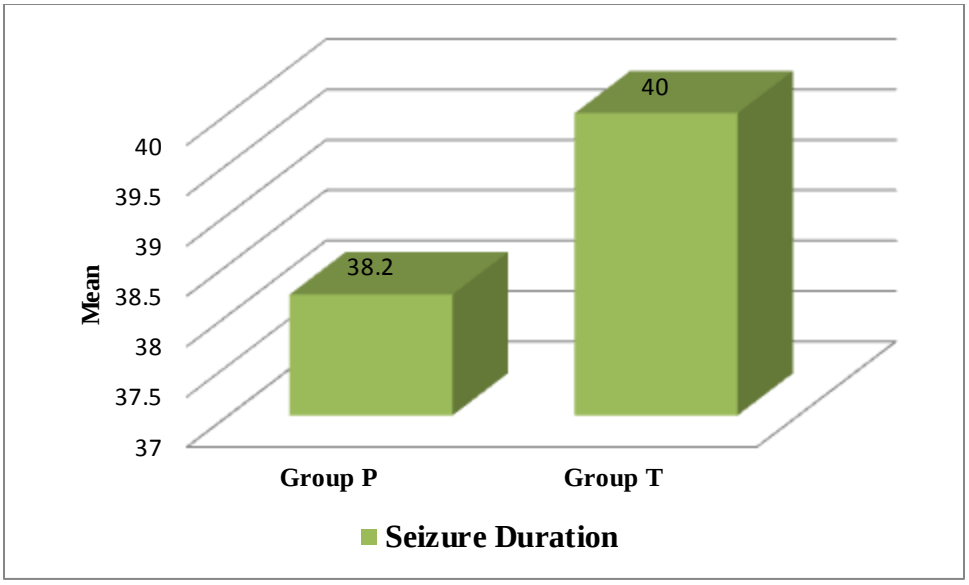
Table 8: Comparison of Seizure Parameters between Study Groups

Parameter	Group P	Group T	p value
Seizure Duration	38.20±2.89	40±5.57	P=0.123 NS
Seizure Threshold	98.00±16.89	94.67±16.55	P=0.443 NS



Graph 4: Comparison of seizure Threshold

Seizure threshold was almost same with both groups showing no statistical significance



Graph 5: Comparison of seizure duration

Seizure duration was less with Propofol (38.20 sec) than Thiopentone (40 sec) but was not statistically significant.

Comparing the effects of induction agents on seizure duration and seizure threshold did not show any statistical significance.

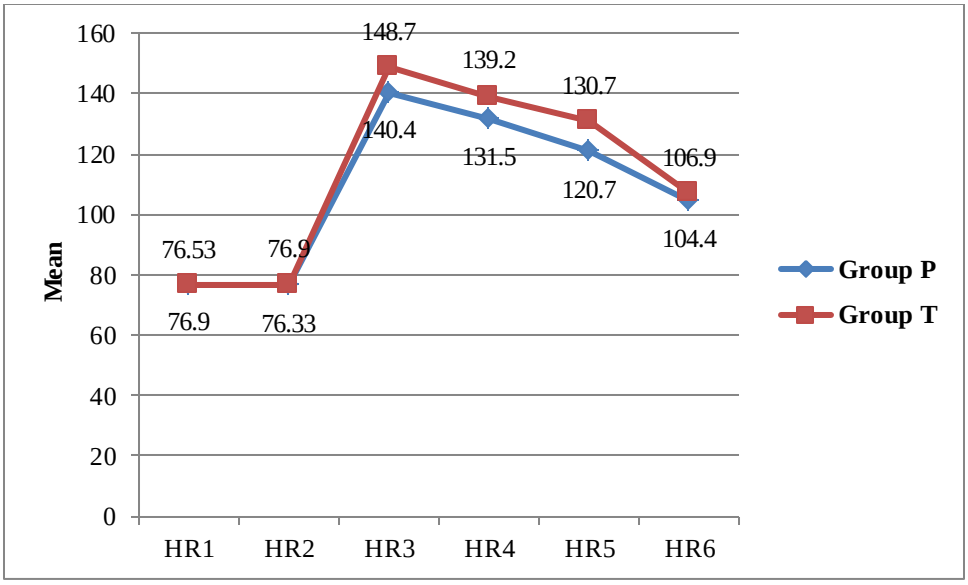
HAEMODYNAMIC PARAMETERS

Heart Rate

The heart rates were not significantly different between the two groups prior to induction and post induction.

Table 9: Comparison Of Heart Rate Between Study Groups

Heart rate	**Group P**		**Group T**		**Unpaired t test/ Mann whitney U test**
	Mean	SD	Mean	SD	
HR1	76.90	8.189	76.53	9.49	P=0.8733 NS
HR2	76.33	9.54	76.97	11.50	P=0.8173 NS
HR3	140.30	3.73	148.73	5.47	P<0.001*
HR4	131.57	4.77	139.2	5.05	P<0.001*
HR5	120.77	4.55	130.73	3.73	P<0.001*
HR6	104.43	5.24	106.93	2.86	P=0.025*



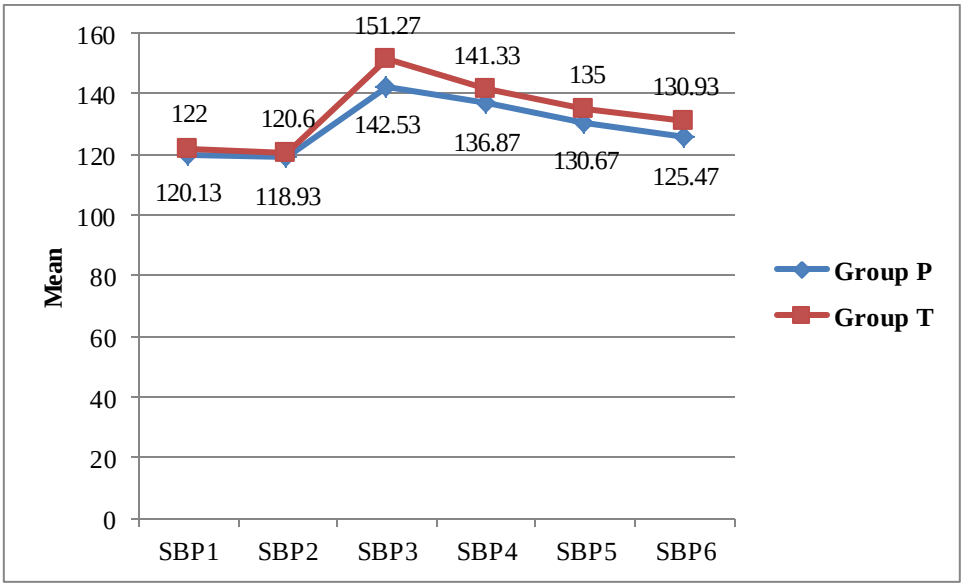
Graph 6: Comparison of Heart rate Between Study Groups

Heart rate was recorded at 0 min, 5 min, 10 min and 15 min after ECT convulsions between the two groups.

The heart rates in the Propofol group were less during the above intervals compared to Thiopentone group showing statistical significance (P<0.001*, P<0.001*, P<0.001*,P=0.025* respectively}

Table 10: Comparison of Systolic Blood Pressure Between Study Groups

Blood pressure	Group P		Group T		Unpaired t test/ Mann whitney test
	Mean	SD	Mean	SD	
SBP1	120.13	8.016	122.00	6.215	P=0.3176 NS
SBP2	118.93	8.283	120.60	6.038	P=0.2147 NS
SBP3	142.53	8.153	151.27	7.638	P<0.0001*
SBP4	136.87	7.569	141.33	7.053	P=0.0158*
SBP5	130.67	6.177	135.00	6.19	P=0.0136*
SBP6	125.47	5.557	130.93	5.192	P=0.0005*

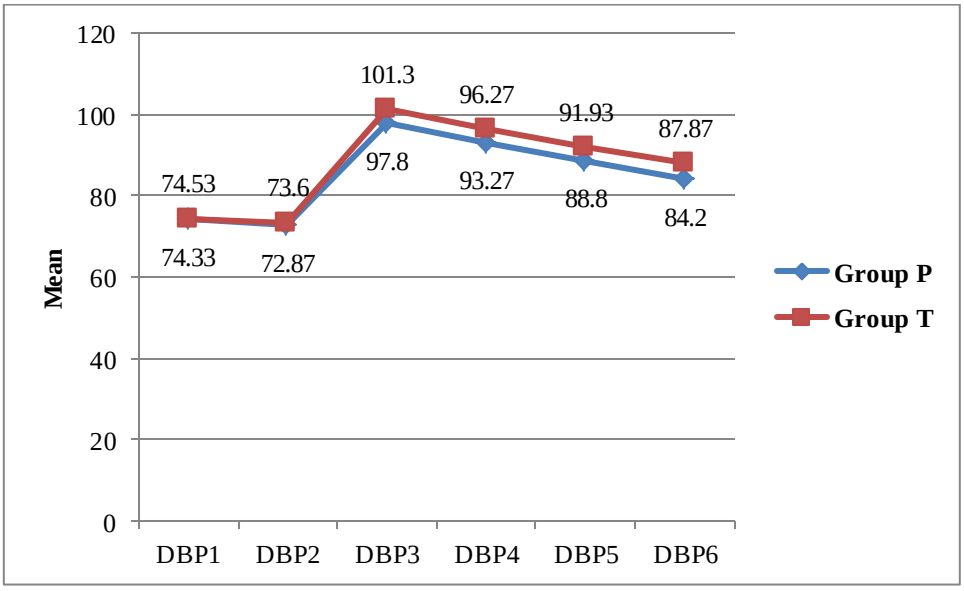


Graph 7: Comparison of Systolic Blood Pressure Between Study Groups

The Systolic blood pressures were not significantly different between the two groups prior to induction and post induction. There was significant difference in the systolic blood pressures recorded at 0 min and 5 min, 10 min, 15 min after ECT convulsions between the two groups with p values (p<0.0001*, p=0.0158*, p=0.0136*,p=0.0005*) respectively.

Table 11 : Comparison of Diastolic Blood Pressure Between Study Groups

Blood pressure	Group P		Group T		Unpaired t test/ Mann whitney test
	Mean	SD	Mean	SD	
DBP1	74.33	6.541	74.53	7.181	P=0.9106 NS
DBP2	72.87	7.403	73.60	7.744	P=0.7091 NS
DBP3	97.80	5.47	101.33	7.25	P=0.038*
DBP4	93.27	4.4	96.27	7.04	P=0.044*
DBP5	88.8	3.8	91.93	6.88	P=0.034*
DBP6	84.20	4.01	87.87	7.56	P=0.023*



Graph 8: Comparison of Diastolic Blood Pressure Between Study Groups

The Diastolic blood pressure were not significantly different between the two groups prior to induction and post induction.

There was significant difference in the diastolic blood pressures recorded at 0 min, 5 min, 10 min, 15 min after ECT convulsions between two groups with p values of (p=0.038, p=0.044, p=0.034, p=0.023) respectively.

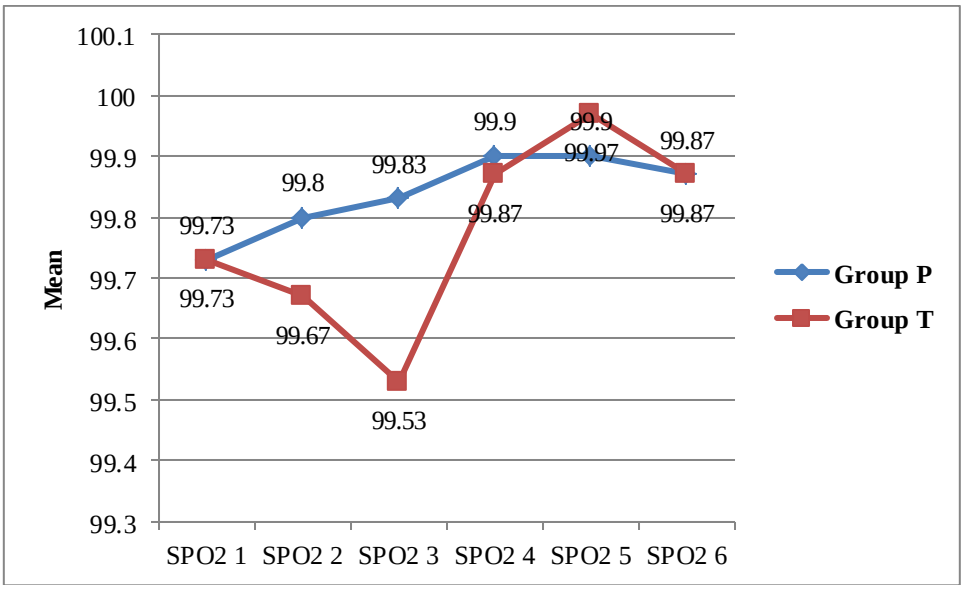
ECG

No ECG changes were observed in any of the patients throughout the ECT sessions

Oxygen Saturation

Table 12 : Comparison of SPO_2 between study groups

SPO2	Group P		Group T		Unpaired t test/ Mann whitney U test
	Mean	SD	Mean	SD	
SPO2 1	99.73	0.640	99.73	0.640	p=0.9909 NS
SPO2 2	99.80	0.551	99.67	0.758	P=0.4869 NS
SPO2 3	99.83	0.592	99.53	0.73	P=0.086 NS
SPO2 4	99.90	0.403	99.87	0.571	P=0.9999 NS
SPO2 5	99.90	0.305	99.97	0.183	P=0.3129 NS
SPO2 6	99.87	0.346	99.87	0.346	P=0.9900 NS



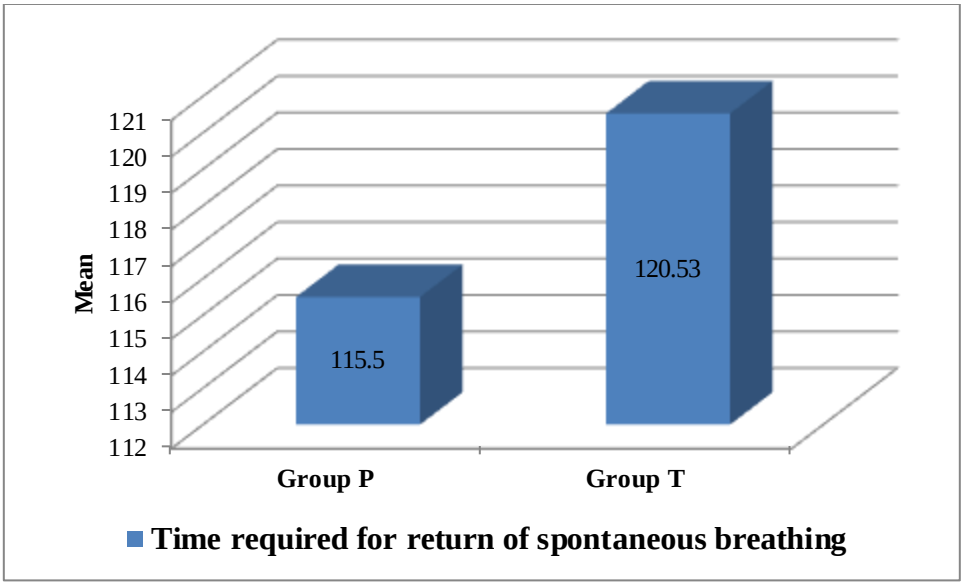
Graph 9: Comparison of SPO_2 between study groups

There was no significant difference in oxygen saturation between the two groups. There was no incidence of hypoxia (oxygen saturation of < 90%) in any of the patients

RECOVERY CHARACTERISTICS

Table 13: Comparison of Recovery characteristics between study groups

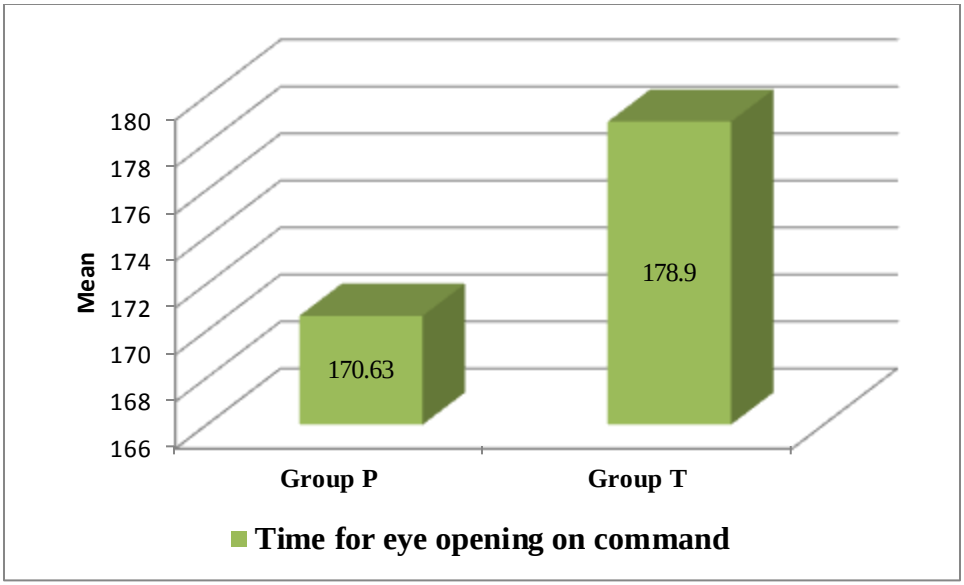
Parameters	Group P	Group T	p value
Time required for return of spontaneous breathing	115.50±4.45	120.53±5.92	P=0.001*
Time for eye opening on command	170.63±13.34	178.90±11.37	P=0.012*
Time for orientation to time, place or person	429.27±20.02	457.57±24.89	P=0.001*



Graph 10: Comparison of Time required for return of spontaneous breathing

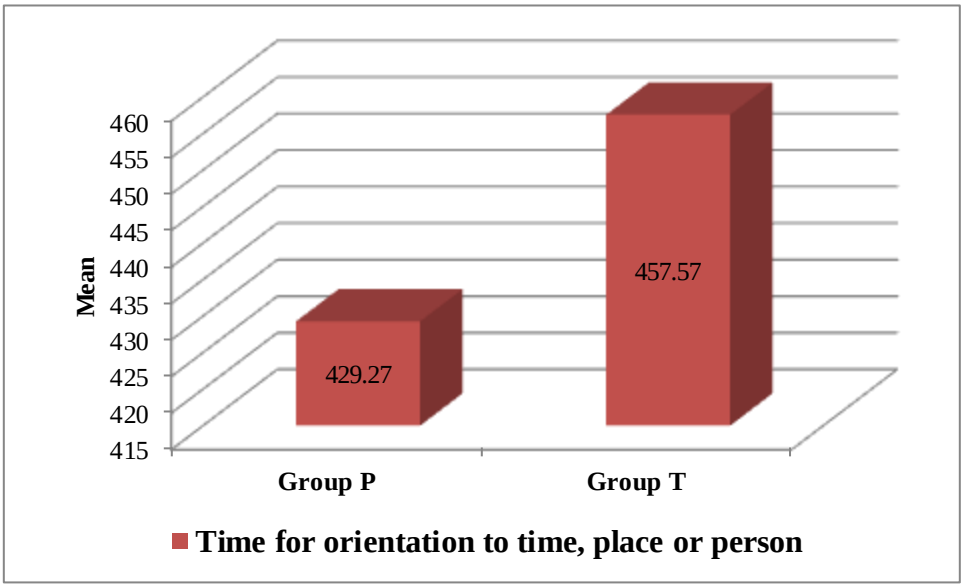
Comparison study of recovery characteristics in both groups, showed all the three recovery parameters compared were statistically significant.

This clinical investigation we observed that, time required for return of spontaneous breathing was less with Propofol (115.50 sec) compared to Thiopentone (120.53 sec) which was statistically significant (p=0.001*).



Graph 11: Comparison of Time of eye opening on command between study groups

Time for eye opening on command was less with Propofol (170.63 sec) compared to Thiopentone (178.80 sec) had statistical significance (p=0.012*).



Graph 12: Comparison of Orientation to Time, Place or Person between study groups

Time for Orientation to time, place or person was less with Propofol (429.27 sec) than Thiopentone (457.57 sec) had statistical significance (p=0.001*).

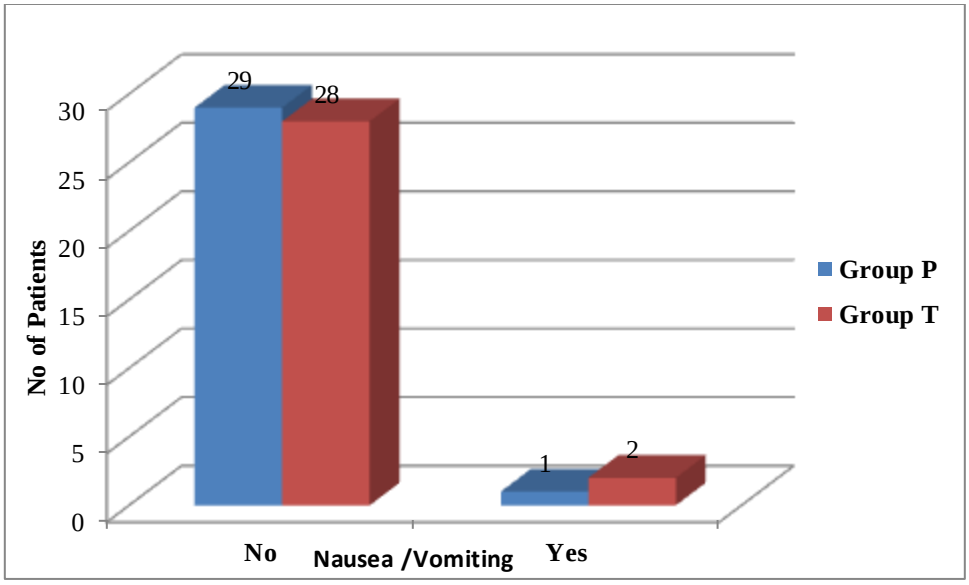
Table 14 : Comparison of Adverse effects between Study groups

Adverse effects	Group P		Group T		Chi square test
	No. of patients	Percent	No. of patients	Percent	P=0.5536 NS
Yes	1	3.3	2	6.7	
No	29	96.7	28	93.3	
Total	30	100.0	30	100.0	

Nausea/Vomiting

Table 15: Comparison of Nausea or Vomiting between Study groups

Nausea or Vomiting	Group P		Group T		Chi square test
	No. of patients	Percent	No. of patients	Percent	P=0.5536 NS
No	29	96.7	28	93.3	
Yes	1	3.3	2	6.7	
Total	30	100.0	30	100.0	



Graph 13 : Comparison of Nausea/vomiting between Study groups

Out of 60 ECT sessions,3 sessions had nausea or vomiting or both during recovery. One in Propofol group and two in Thiopentone group which was not of statistical significance (p=0.5536).

Among 60 patients, none of them in any group had Awareness of the procedure.

DISCUSSION

DISCUSSION

Anesthetic agents used for ECT should have characteristics that include rapid induction, short duration of action, minimal side effects, rapid recovery, and no interference with the ECT efficacy. Because of its rapid induction and rapid recovery, Propofol was recently introduced for ECT anesthesia. Previous studies have compared the use of Propofol for ECT with barbiturates, which have long been used for ECT anesthesia.

In this clinical study we aimed to compare between Propofol and Thiopentone by observing their induction and recovery characteristics, haemodynamic stability during the therapy and their effects on seizure characteristics.

INDUCTION CHARACTERISTICS

The induction characteristics were compared in relation to time required for loss of eyelash reflex/verbal contact and the results showed Induction was rapid with Propofol (40.83 ± 1.464 in seconds) as compared to Thiopentone (47.83 ± 1.802 in seconds) which was statistically significant (P<0.001*). This suggests that Propofol has faster induction than Thiopentone.

This was comparable to the study conducted by, **Mir *et al* (2017)**[1] to compare the effectiveness of Sodium Thiopentone, Propofol and Etomidate as an ideal intravenous anaesthetic agent for modified electroconvulsive therapy. It was found that, Induction time with Propofol was quicker i.e ,41.9 ± 3.5 s than that for Thiopentone i.e 48 ± 3.9 s which was statistically significant (P < 0.001*).

Shah *et al* (2010)[2] Compared Effectiveness of Thiopentone, Propofol and Midazolam as an ideal intravenous anaesthetic agent for modified electroconvulsive therapy. Induction was quicker in Propofol group i.e., (41.03 ± 6.11sec) than in Thiopentone (50.6 ± 6.32 sec) and was found to statistically significant with p(<0.05*)

Daria *et al* (2012)[5] conducted a study to compare Thiopentone and Propofol to see better anaesthetic agent for modified electroconvulsive therapy**.** They found that mean induction time was significantly less in Propofol 40.4 seconds, in compared to Thiopentone 49.4 seconds with (p=0.044*).

Jignesh D. Patel *et al* (2015)[3] conducted a study to compare the effects of Thiopentone sodium and Propofol as an intravenous anaesthetic agent in modified ECT. Induction was rapid with Propofol (41.9 ± 5.21 in seconds) as compared to Thiopentone (47.40 ± 5.68 in seconds) which was statistically significant (P<0.05*).

Arya *et al* (2008) [73]conducted a study to compare Thiopentone, Midazolam , Propofol for ECT. They found, Induction with Propofol was significantly faster (41.13± 6.11 sec) compared to Thiopentone sodium (51.06 ± 6.82 sec)

HEMODYNAMIC PARAMETERS

The hemodynamic changes during ECT involve sequential increases in parasympathetic and sympathetic nervous system activity. The anesthetic used during ECT has an important impact on the hemodynamic response. These results confirm that Propofol provides the better protection against an untoward hypertensive response to ECT, while Thiopentone is less effective in blunting the hyperdynamic response.

The haemodynamic parameters including heart rate and blood pressure were not significantly different between the two groups prior to induction HR1(p=0.8733), SBP1(p=0.3176), DBP1(p=0.9106) and post induction HR2(p=0.8173), SBP2(p=0.2147), DBP2(p=0.7091). It can be concluded that induction characteristics of both were comparable. Studies also support us, **Health PJ *et a1*[74]** observed that both Propofol and Thiopentone provided high quality induction in their study. **Boey WK** and **Kumar A**[75] in their study found that induction times were similar for both groups.

There was significant difference in heart rate recorded at 0 min, 5 min, 10 min and 15 min after ECT convulsions between the two groups (P<0.001*, P<0.001*, P<0.001*,P=0.025* respectively) . There was significant difference in the systolic blood pressures recorded at 0 min and 5 min, 10 min, 15 min after ECT convulsions between the two groups with p values (p<0.0001*, p=0.0158*, p=0.0136*, p=0.0005*) respectively. There was significant difference in the diastolic blood pressures recorded at 0 min,5 min, 10 min, 15 min after ECT

convulsions between two groups with p values of {p=0.038*, p=0.044*, p=0.034*, p=0.023*} respectively.

Kumar *et al* (2012)[7] noted, an increase in all hemodynamic parameters after the procedure, mean heart rate (80 ± 14 bpm vs. 76 ± 14 bpm), systolic blood pressure (98 ± 17 mmHg vs. 91 ± 11 mmHg) in group P. In group T too, a similar trend of increase in all hemodynamic parameters was seen after the procedure, Heart rate (81 ± 12 bpm vs. 70 ± 11 bpm), systolic blood pressure (119 ± 11 mmHg vs. 100 ± 12 mmHg) However, the percentage increase was significantly greater in group T as compared to group P ($P < 0.05$*).

Jignesh D Patel *et al*(2015)[3]found In P group, an increase in all hemodynamic parameter seen after the procedure, mean heart rate (94.00± 10.52 vs 107.17 ± 11.58), SBP (121.93 ±10.35 vs 132.47 ±11.50), DBP (75.87 ± 6.69 vs 85.67 ± 7.95). In T group too, a similar trend of increase in all hemodynaemic parameters was seen after the procedure, mean heart rate (98.20 ± 14.94 vs 115.03 ± 12.71), SBP (130.10 ± 10.99 vs 140.33 ±8.53), DBP (84.13 ± 9.31 vs 90.27 ± 8.49). However, the percentage increase in each of the variables following the procedure was significantly greater in T group as compared to P group.

The significant rise in HR after ECT with Thiopentone compared to Propofol was also noted by **Mir *et al* [1], Boey and Lai [55], Arya *et al* [73], Shah *et al* [2] and Singhal *et al* [76].**

No significant difference was observed in SpO_2 with Propofol and Thiopentone following induction and ECT.

No ECG changes were observed in any of these patients throughout the ECT sessions.

SEIZURE PARAMETERS

In the present study, seizure duration was less in the Propofol group (38.20±2.89) compared to Thiopentone group (40±5.57) but not statistically significant. The potent anticonvulsive property of Propofol might be a potential mechanism for the less duration of seizures with the electrical stimulus[75].

This result was similar to study conducted by **Jignesh D Patel *et al*** [3]in which, duration of seizure was less in P group (17.07sec) than in T group (19.53sec) but was not statistically significant(P >0.05)[3]. There is no effect of reduced seizure duration with Propofol on outcome of the therapy or effectiveness of ECT[2].

This result was also similar to **Daria *et al*** [5](Mean seizure duration was found less in propofol as 25.6seconds while in Thiopentone it was found 28.1 seconds and on comparison this difference was found nonsignificant).

Mir *et al* [1] The mean duration of seizure was 27.6±4.7sec with Propofol compared to Thiopentone i.e 30.2±5.4 sec (p>0.05) which was not statistically significant.

Zaidi *et al* [77] The mean duration of seizure was 31.08 ± 4.13 seconds with Thiopentone and 23.76 ± 3.38 seconds with Propofol (p<0.001*)

Omprakash *et al* [4] Propofol had shorter seizure duration as compared to Thiopentone group, which was statistically significant.

Shah *et al* [2] The seizure duration was found less with Propofol (26.36 ± 2.79sec) compared to Thiopentone(36.26 ± 4.83sec) which was statistically significant. This did not effect the therapeutic outcome.

Although seizure duration has been considered crucial for ECT therapeutic efficacy, two psychiatric reports conclude that the efficacy of ECT using Propofol did not differ significantly from those using barbiturates.[78,79] They found magnitude of improvement in the patients' depression symptoms was unrelated to the total duration

of seizure activity during the series of ECT treatments. Even though the seizure duration was consistently shorter with Propofol (versus Methohexital), the Hamilton Rating Scale for Depression scores were improved to a similar degree in both anesthetic groups after they completed a standard series of ECT treatments.[78,79]

Shortening of seizure duration in Propofol was in agreement with finding of , **Arya *et al* [73], Singhal *et al* [76], Boey *et al* [55]**

Seizure threshold was almost same with both groups, In group P 98.00±16.80 and in group T 94.67±16.55 showing no statistical significance (p=0.443).

RECOVERY PARAMETERS

In this study we observed that time for return of spontaneous breathing was less with Propofol (115.50±4.45 sec) compared to Thiopentone (120.53±5.92 sec) with statistical significance {P=0.001*}. Time for eye opening on command was less with Propofol (170.63±13.34 sec) compared to Thiopentone (178.90±11.37 sec) had statistical significance. Time for orientation to time, place or person was less with Propofol (429.27±20.02) than Thiopentone (457.57±24.89 sec) and showed statistical significance.

Many studies support our findings of faster recovery.

Jignesh D. Patel *et al* [3] observed that, regaining of reflexes was earlier in P group (6.93minutes) than in T group (6.07minutes) with (P=0.002)statistically significant. Responds to pain in P group is significantly early (7.33min) than T group (8.70 min). (P=0.001*) highly significant. Following verbal commands in P group is significantly early (10.5 min) than T group (14.07 min) and (P=0.001*) highly significant.

Kumar *et al* [7] observed that recovery time for Propofol (4.2 ± 1.2) was compared to Thiopentone (5.7 ± 2.9 4.41) which was statistically significant (p<0.0001*).

Mir *et al* [1] in the study also found that ,the recovery of cognition, orientation, and neuromuscular coordination was significantly fast in Propofol group ($P < 0.001$*)

Daria *et al* [5] in the study also found that, recovery time was significantly less in Propofol group(22.1±2.5) compared to Thiopentone group (28.9±3.2) with (p=0.015*).

Shah *et al* [2] found a significant difference in recovery time among the groups Propofol group which had faster recovery compared to Thiopentone group (P<0.05*).

Boey WK [55] Many other studies support our findings of faster recovery and study concludes that time for eye opening on command and to sit up unaided were same for both drugs but the ability to walk 10 meters after 20 minutes after anesthesia was significantly better with Propofol.

Zaidi *et al* [77] Recovery features showed that the ability to obey vocal commands like opening of eyes took a mean of 5.04 ± 1.36 minutes with Thiopentone and 3.28 ± 0.89minutes with Propofol ($p<0.001$*) concluding that, Propofol offered quick recovery compared to Thiopentone for electroconvulsive therapy.

Ingram A *et al* [63] in their study suggest that Thiopentone has advantages for use as an anesthetic agent in efficacy and cognitive side effects for ECT compared with Propofol. The apparent discrepancies in the predicted course of early recovery can be attributed to the effect of the seizure itself (i.e., smaller anesthetic doses allowed longer seizures and were associated with a more prolonged recovery). Thus, the duration of the ECT induced seizure may be the primary determinant of early recovery rather than the hypnotic drug.

The more rapid and pleasant recovery after Propofol in comparison with Thiopentone , Methohexital and Etomidate has made it a drug of choice for short procedures.

ADVERSE EFFECTS

Out of 60 ECT sessions 3 sessions had nausea or vomiting or both during recovery. The nausea and vomiting is 50% more with Thiopentone group than Propofol group but was not statistically significant. This may be because Propofol, in small doses, possesses direct antiemetic properties.[80] The precise mechanism by which Propofol acts as an antiemetic remains unclear, but there is a possibility that Propofol may have a weak serotonin antagonistic effect.

Shah *et al* [2] found that the incidence of nausea and vomiting was almost nil in Propofol due to antiemetic property as compared to 23.33% in Thiopentone.

Among 60 patients included in the study, none of them in any group had awareness of the procedure

SUMMARY

SUMMARY

In this clinical study, we compred between Propofol and Thiopentone by observing their induction and recovery characteristics, haemodynamic stability during the therapy and their effects on seizure characteristics.

We compared 60 ECT sessions for this study under two groups, group P and group T.

- The induction characteristics compared in relation to time required for loss of eyelash reflex/verbal contact showed, Induction was rapid with Propofol (40.83 ± 1.464 in seconds) as compared to Thiopentone (47.83 ± 1.802 in seconds) which was statistically significant (P<0.001*). Suggesting that Propofol has faster induction than Thiopentone.
- There was significant difference in heart rate recorded at 0 min, 5 min, 10 min and 15 min after ECT convulsions between the two groups (P<0.001*, P<0.001*, P<0.001*,P=0.025* respectively) .
- There was significant difference in the systolic blood pressures recorded at 0 min and 5 min, 10 min, 15 min after ECT convulsions between the two groups with p values (p<0.0001*, p=0.0158*, p=0.0136*, p=0.0005*) respectively.
- There was significant difference in the diastolic blood pressures recorded at 0 min,5 min, 10 min, 15 min after ECT convulsions between two groups with p values of (p=0.038*, p=0.044*, p=0.034*, p=0.023*) respectively.

So this study showed Propofol is superior in offering stable hemodynamics than Thiopentone during the therapy.

- Seizure duration was less in the Propofol group (38.20±2.89) compared to Thiopentone group (40±5.57) but not statistically significant. The potent anticonvulsive property of Propofol might be a potential mechanism for the less duration of seizures with the electrical stimulus.
- Seizure threshold was almost same with both groups, In group P 98.00±16.80 and in group T 94.67±16.55 showing no statistical significance (p=0.443).
- Time needed for return of spontaneous breathing was less with Propofol (115.50±4.45 sec) compared to Thiopentone (120.53±5.92 sec) with statistical significance (P=0.001*).
- Time for eye opening on command was less with Propofol (170.63±13.34 sec) compared to Thiopentone (178.90±11.37 sec) had statistical significance (P=0.012*).
- Time for orientation to time, place or person was less with Propofol (429.27±20.02) than Thiopentone (457.57±24.89 sec) and showed statistical significance (p=0.001*) .

  Thus concluding that Propofol offers a faster recovery with less Cognitive impairment than Thiopentone.
- Out of 60 ECT sessions 3 sessions had nausea or vomiting or both during recovery. The nausea and vomiting is 50% more with Thiopentone group than Propofol group but was not statistically significant.

CONCLUSION

CONCLUSION

Finally from the observations made we conclude that,

- Propofol had smooth and faster induction compared to Thiopentone
- Propofol attenuated the haemodynamic responses of ECT compared to Thiopentone.
- Interference with seizure parameters at a dose given for ECT was similar for Thiopentone and Propofol.
- Propofol offered superior recovery profile compared to Thiopentone
- Nausea / Vomiting was less with Propofol but, was not statistically significant.

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BIBLIOGRAPHY

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ANNEXURES

ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

BIJAPUR 586 103.
OUTWARD
No. 611/2016
Date. 06/10/16
B.L.D.E.U's Shri B.M. Patil Medical College

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04/10/2016 *at* 3-00pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title A comparative study of thiopentone and Propofol as induction agents for modified electroconvulsive therapy

Name of P.G. student Savita.B.Patil
Dept in Anaesthesiology

Name of Guide/Co-investigator Dr Vijaykumar T.K
Professor in Anaesthesiology

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-II

INFORMED CONSENT FORM

TITLE OF THE PROJECT: "A COMPARATIVE STUDY OF THIOPENTONE AND PROPOFOL AS INDUCTION AGENTS FOR MODIFIED ELECTROCONVULSIVE THERAPY"

PRINCIPAL INVESTIGATOR : **Dr. SAVITA.B.PATIL**

Department of Anaesthesiology,

Email: savitabpatilc@gmail.com

PG GUIDE : **Dr. VIJAYKUMAR T.K**,

Professor,

Department of Anaesthesiology,

B.L.D.E.(DEEMED TO BE UNIVERSITY) Shri B.M.Patil Medical College, Hospital and Research Centre Vijayapur, Karnataka.

I have been informed that this study is **"A COMPARATIVE STUDY OF THIOPENTONE AND PROPOFOL AS INDUCTION AGENTS FOR MODIFIED ELECTROCONVULSIVE THERAPY"**. I have been explained about this study in the language which I understand. I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have been told that my participation in the above study is voluntary and I am aware that I can opt out of the study at any time without having to give any reasons for doing so. I am also informed that my refusal to participate in this study will not affect my treatment by any means.

I agree to participate in the above study and cooperate fully. I agree to follow the Doctor's instructions about my treatment to the best of my ability.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time and Dr.Savita.B.Patil is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for my careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr.Savita.B.Patil will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/ my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have been explained about the purpose of this research, the procedures required and the possible risks and benefits, in my own language.

I have been explained all the above in detail and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

Patient's Signature: Witness Signature

Name : Name :

Date : Date :

Dr. VIJAYKUMAR.T.K **Dr. SAVITA.B.PATIL.**

(Guide) (Investigator)

ANNEXURE III

SCHEME OF CASE TAKING :

PROFORMA

STUDY: "A COMPARATIVE STUDY OF THIOPENTONE AND PROPOFOL AS INDUCTION AGENTS FOR MODIFIED ELECTROCONVULSIVE THERAPY."

Name of the patient : I.P. No. :

Age : Sex: | M | F |

Weight : Date of Admission:

Diagnosis:

Consent taken for | Y | N | study:

ECT No.

Group | P | T | allocated :

Pre anaesthetic evaluation :

Chief complaints :

Past History :

a) Presence of any comorbid condition - Diabetes/ Hypertension/ Ischemic heart disease/ Cerebrovascular accident / Asthma/ Epilepsy/ Bleeding disorder/ Drug allergy/ any other .

b) Drug Therapy

c) H/o previous anaesthetic exposure :

Family History :

General Physical Examination:

- General condition :
- Pallor / Icterus / Cyanosis / Clubbing / Lympadenopathy / Pedal edema.
- Temperature:
- Pulse rate:
- Respiratory rate:
- Blood Pressure :

Mallampati grade :

Systemic Examination :

- Cardiovascular system
- Respiratory system
- Central nervous system
- Others

Investigations :

- Complete blood picture

  Total Leucocyte count :
  Differential count :
  - Neutrophils :
  - Lymphocytes :
  - Basophils :
  - Eosinophils :
  - Monocytes :

  Platelet count :

- Random Blood sugar :

- Urine routine:

- ECG :

- Chest X ray:

- Any other :

ASA Grade :

Diagnosis:

ANAESTHESIA PROTOCOL :

- Premedication :

  Inj.Glycopyrolate 0.02mg/kg IV [ ]

  Inj Ondansetron 0.15mg/kg IV [ ]

INDUCTION CHARACTERISTICS :

Dose of induction agent:

Time required for loss of eye lash reflex:

Hemodynamic Variables:

	Before induction	Immediately after induction	Immediately after ECT convulsions	5 minutes after ECT convulsions	10 minutes after ECT convulsions	15 minutes after ECT convulsions
HR						
BP						
SPO_2						

SEIZURE CHARACTERISTICS :

Duration of seizure : Adequate: YES/ NO

Seizure threshold:

RECOVERY CHARACTERISTICS :

Return of spontaneous ventilation:

Eye opening on command:

Awareness of procedure: Yes/No

Any nausea or vomiting: Yes/No

Orientation to time, place or person:

Adverse effects, if any:

Signature of Anaesthesiologist

Name:

Designation:

KEY TO MASTER CHART

sl.no	→	Serial number
IP.No	→	Inpatient Hospital Number
ASA	→	American Society of Anaesthesiologists
HTN	→	Hypertension
ECT.no	→	Electroconvulsive therapy number
Kgs	→	Kilograms
mg	→	Milligrams
HR1	→	Heart rate before Induction
HR2	→	Heart rate immediately after Induction
HR3	→	Heart rate immediately after ECT convulsions
HR4	→	Heart rate 5 minutes after ECT convulsions
HR5	→	Heart rate 10 minutes after ECT convulsions
HR6	→	Heart rate 15 minutes after ECT convulsions
SBP1	→	Systolic Blood Pressure before Induction
SBP2	→	Systolic Blood Pressure immediately after Induction
SBP3	→	Systolic Blood Pressure immediately after ECT Convulsions
SBP4	→	Systolic Blood Pressure 5 minutes after ECT Convulsions
SBP5	→	Systolic Blood Pressure 10 minutes after ECT Convulsions
SBP6	→	Systolic Blood Pressure 15 minutes after ECT Convulsions
DBP1	→	Diastolic Blood Pressure Before Induction
DBP2	→	Diastolic Blood Pressure immediately after Induction
DBP3	→	Diastolic Blood Pressure immediately after ECT Convulsions
DBP4	→	Diastolic Blood Pressure 5 minutes after ECT Convulsions
DBP5	→	Diastolic Blood Pressure 10 minutes after ECT Convulsions

DBP6	→	Diastolic Blood Pressure 15 minutes after ECT Convulsions
SpO_2(%)1	→	Oxygen Saturation before induction
SpO_2(%)2	→	Oxygen Saturation immediately after induction
SpO_2(%)3	→	Oxygen Saturation immediately after ECT Convulsions
SpO_2(%)4	→	Oxygen Saturation 5 minutes after ECT Convulsions
SpO_2(%)5	→	Oxygen Saturation 10 minutes after ECT Convulsions
SpO_2(%)6	→	Oxygen Saturation 15 minutes after ECT Convulsions

sl.no	Name	Age(years)	Sex	weight in Kgs	Ip.No	ASA	ECT.No	Group	Dose of Induction ahent	Dose of Scholine	Time required for loss of eyelash reflex	HR1	HR2	HR3	HR4	HR5	HR6	SBP1	SBP2	SBP3	SBP4	SBP5	SBP6	DBP1	DBP2	DBP3	DBP4	DBP5	DBP6	SPO2 1	SPO2 2	SPO2 3	SPO2 4	SPO2 5	SPO2 6	Seizure Duration	Seizure threshold	Time of return of spont. Breathing	Time for eye opening on command	Awareness of Procedure	Any Nausea or Vomiting	Orientation to Time, Place, Person	Adverse effects if any
1	Shakeelabanu	40	Female	70	32402	2(HTN)	2	P	80mg	35mg	40	74	72	142	132	114	104	136	130	160	152	138	136	92	90	96	94	92	90	100	100	100	100	100	100	35	60	112	168	no	no	438	no
2	Chandrashekar	35	Male	58	34535	1	2	P	70mg	30mg	38	72	70	138	132	125	102	116	112	152	146	138	128	78	70	88	84	84	80	100	100	100	100	100	100	42	60	114	166	no	no	420	no
3	Vishwanath	18	Male	50	23420	1	2	P	70mg	35mg	40	90	90	144	128	120	118	120	114	140	136	130	130	80	74	88	86	86	84	100	100	100	100	100	100	40	60	110	156	no	no	410	no
4	Lalbasha	26	Male	55	24835	1	1	P	75mg	30mg	39	70	70	140	128	126	102	126	116	142	140	138	134	70	68	88	84	84	84	100	100	100	100	100	100	38	60	112	170	no	no	428	no
5	Vijeta	24	Female	52	30315	1	1	P	60mg	25mg	38	90	92	138	118	110	102	116	120	134	132	130	130	70	68	92	90	80	80	100	99	100	100	100	100	42	60	112	155	no	no	415	no
6	Anil	25	Male	53	38773	1	1	P	60mg	25mg	38	62	60	132	122	115	110	118	116	134	132	128	120	70	68	92	90	86	82	100	100	100	100	100	100	42	100	118	160	no	no	420	no
7	Raju	25	Male	61	36922	1	2	P	80mg	30mg	42	68	60	136	130	122	106	116	108	128	126	128	120	68	66	98	94	90	80	100	100	100	100	100	100	37	100	110	170	no	no	450	no
8	Laxmi	20	Female	48	40054	1	3	P	60mg	25mg	40	78	77	142	136	122	102	126	122	142	132	128	126	74	72	94	90	88	84	100	100	100	100	100	100	40	100	117	160	no	no	412	no
9	Laxmi	20	Female	48	40054	1	5	P	60mg	25mg	42	74	76	146	130	120	106	122	116	138	130	126	120	72	64	92	92	90	90	100	100	100	100	100	100	38	100	119	164	no	no	422	no
10	Sharadha	35	Female	54	41451	1	2	P	75mg	30mg	40	78	77	144	139	130	110	132	134	156	152	140	130	84	88	102	98	94	90	100	100	100	100	100	100	44	100	114	156	no	no	415	no
11	Sharadha	35	Female	54	41451	1	4	P	75mg	30mg	41	80	82	142	136	122	104	136	132	158	150	142	132	86	88	98	98	98	90	100	100	99	100	100	100	39	100	116	170	no	no	430	no
12	Ramesh	27	Male	65	945	1	2	P	90mg	35mg	40	86	85	146	134	121	108	112	110	132	128	126	118	74	74	104	96	92	86	100	100	100	100	100	100	40	100	119	168	no	no	430	no
13	Ramesh	27	Male	65	945	1	4	P	90mg	35mg	41	90	88	142	134	124	104	116	112	138	134	124	120	76	76	106	98	94	88	100	100	100	100	100	100	35	100	116	176	no	no	432	no
14	Ramesh	27	Male	65	945	1	6	P	90mg	35mg	42	88	90	142	126	114	108	112	112	138	130	122	120	70	68	94	90	88	80	100	100	100	100	100	100	32	100	120	170	no	no	432	no
15	Shankar	26	Male	105	107496	2(Obese)	2	P	110mg	55mg	41	66	63	134	128	125	102	132	130	154	148	140	134	84	82	108	100	96	92	98	98	99	99	99	99	35	120	122	200	no	no	430	no
16	Shankar	26	Male	105	107496	2(Obese)	4	P	110mg	55mg	43	68	66	132	126	122	102	128	130	156	146	142	136	80	80	106	100	92	88	98	100	100	100	100	100	32	120	123	202	no	no	440	no
17	Mainuddin	40	Male	102	10649	2(Obese)	1	P	110mg	50mg	42	70	70	140	136	116	98	122	120	138	130	128	126	74	70	102	98	90	88	98	99	100	98	99	99	40	120	118	186	no	yes	470	nausea
18	Mainuddin	40	Male	102	10649	2(Obese)	2	P	110mg	50mg	42	74	72	142	136	118	100	128	126	142	136	130	128	80	78	104	94	90	86	99	98	100	100	99	99	38	120	120	190	no	no	476	no
19	Savitri	23	Female	45	10915	1	1	P	60mg	25mg	39	72	70	144	136	116	98	124	120	142	132	128	126	74	72	98	94	88	84	100	100	100	100	100	100	38	100	110	162	no	no	404	no
20	Savitri	23	Female	45	10915	1	2	P	60mg	25mg	40	70	69	140	134	114	102	122	120	138	130	128	128	72	72	100	92	84	80	100	100	100	100	100	100	35	100	112	170	no	no	410	no
21	Mainuddin	40	Male	102	10649	2(Obese)	4	P	110mg	50mg	43	72	70	140	134	118	98	124	120	142	132	128	126	76	78	98	96	88	84	99	100	100	100	100	99	38	120	128	204	no	no	479	no
22	Rakesh	21	Male	68	11012	1	1	P	90mg	35mg	40	80	84	142	132	124	108	116	138	134	128	128	122	64	62	96	92	86	82	100	100	100	100	100	100	35	100	114	170	no	no	410	no
23	Ashwini	26	Female	45	12183	1	1	P	60mg	25mg	41	78	80	140	136	126	106	110	114	140	138	128	122	70	68	98	94	86	80	100	100	100	100	100	100	40	100	116	166	no	no	420	no
24	Ashwini	26	Female	45	12183	1	3	P	60mg	25mg	43	75	76	138	130	122	105	104	106	138	132	124	118	66	64	94	90	90	78	100	100	100	100	100	100	38	100	118	160	no	no	420	no
25	Srikanth	45	Male	68	12433	1	2	P	90mg	35mg	42	84	86	144	134	122	114	122	124	150	146	140	128	74	76	96	94	88	82	100	100	100	100	100	100	38	100	114	170	no	no	430	no
26	Mahantesh	40	Male	52	10825	1	2	P	70mg	25mg	42	80	84	140	136	124	108	118	116	148	140	134	124	70	68	100	92	90	86	100	98	100	100	100	100	40	100	110	160	no	no	410	no
27	Rahul	20	Male	68	13888	1	2	P	90mg	35mg	41	90	89	144	136	126	110	116	114	140	138	126	122	76	76	102	94	90	86	100	100	100	100	100	100	41	100	114	170	no	no	448	no
28	Rahul	20	Male	68	13888	1	4	P	90mg	35mg	42	88	87	142	130	123	106	112	110	138	134	120	118	74	76	104	96	90	84	100	100	100	100	100	100	38	100	116	178	no	no	452	no
29	Shilpa	22	Female	48	14784	1	1	P	75mg	25mg	41	68	65	135	126	122	96	110	112	140	136	128	122	64	64	96	92	86	78	100	100	97	100	100	100	40	100	110	158	no	no	410	no
30	Shilpa	22	Female	48	14784	1	3	P	75mg	25mg	42	72	70	138	132	120	94	112	114	144	140	130	120	68	66	100	94	84	80	100	100	100	100	100	100	36	100	111	164	no	no	415	no

sl.no	Name	Age(years)	Sex	weight in Kgs	IP.No	ASA	ECT.No	Group	dose of induction agent	Dose of Scholine	Time required for loss of eyelash reflex	HR 1	HR 2	HR 3	HR 4	HR 5	HR 6	SBP1	SBP2	SBP3	SBP4	SBP5	SBP6	DBP1	DBP2	DBP3	DBP4	DBP5	DBP6	SPO2 1	SPO2 2	SPO2 3	SPO2 4	SPO2 5	SPO2 6	Seizure duration	Seizure threshold	time of return of spontaneous ventilation	Time of eye opening on command	Awareness of procedure	Any nausea or vomiting	Orientation to time, place, person	Adverse effects, if any
1	Shakeelabanu	40	Female	70	32402	2(HTN)	1	T	250mg	35mg	48	68	66	150	138	132	110	130	130	156	150	140	140	86	84	102	100	100	96	100	100	100	100	100	100	35	60	124	178	no	no	470	no
2	Shekappa	36	Male	60	31955	2(HTN)	1	T	175mg	30mg	49	76	76	150	146	130	106	130	132	164	156	140	134	64	66	96	90	90	86	100	100	100	100	100	100	35	60	122	178	no	no	480	no
3	Husensab	20	Male	56	6385	1	1	T	150mg	30mg	48	72	74	150	144	126	106	122	116	134	136	126	124	70	64	92	90	88	86	100	100	100	100	100	100	30	60	124	186	no	no	490	no
4	Jayashree	22	Female	60	18884	2	1	T	200mg	30mg	45	64	60	136	138	130	102	138	126	156	154	142	130	80	90	106	104	102	98	100	100	100	100	100	100	30	60	114	180	no	no	450	no
5	Lalbasha	26	Male	55	24835	1	3	T	200mg	30mg	48	68	66	148	140	134	108	116	116	144	140	138	134	68	66	96	94	90	86	100	100	100	100	100	100	32	60	120	180	no	no	440	no
6	Vijeta	24	Female	52	30315	1	2	T	150mg	25mg	48	94	110	158	130	126	106	122	112	142	128	128	130	74	80	96	82	78	78	100	99	100	100	100	100	42	100	110	165	no	no	440	no
7	Raju	25	Male	61	36922	1	1	T	175mg	30mg	48	68	66	144	142	136	108	116	118	148	140	138	130	64	62	86	84	80	80	100	100	98	100	100	100	38	100	116	180	no	no	490	no
8	Raju	25	Male	61	36922	1	3	T	175mg	30mg	46	70	68	148	144	138	104	114	116	156	144	132	134	68	66	88	86	82	82	100	100	100	100	100	100	35	100	124	185	no	no	500	no
9	Anil	25	Male	53	38773	1	2	T	150mg	25kgs	50	62	60	144	140	132	112	124	122	160	146	144	136	80	80	100	98	90	90	100	100	100	100	100	100	47	100	120	190	no	no	426	no
10	Anil	25	Male	53	38773	1	3	T	150mg	25kgs	48	64	62	138	136	130	110	122	120	158	144	142	132	78	78	102	98	92	88	100	100	98	100	100	100	45	100	125	186	no	no	450	no
11	Laxmi	20	Female	48	40054	1	1	T	150mg	25mg	48	72	86	156	144	128	108	116	110	140	132	128	128	62	62	98	90	82	74	100	98	99	100	100	100	46	100	110	168	no	no	430	no
12	Laxmi	20	Female	48	40054	1	2	T	150mg	25mg	49	76	82	152	142	130	106	126	128	144	136	132	126	72	70	98	88	80	74	100	100	100	100	100	100	40	100	112	170	no	no	432	no
13	Laxmi	20	Female	48	40054	1	4	T	150mg	25mg	46	74	84	158	146	132	106	118	112	144	136	126	130	64	64	100	92	84	72	100	100	99	100	100	100	38	100	114	166	no	no	440	no
14	Sharadha	35	Female	54	41451	1	1	T	150mg	25mg	48	72	70	148	144	136	110	130	128	162	146	142	134	88	86	112	100	96	94	100	100	100	100	100	100	42	100	112	168	no	no	445	no
15	Sharadha	35	Female	54	41451	1	3	T	150mg	25mg	46	76	74	150	142	138	106	128	126	160	144	138	132	84	82	110	102	94	90	100	100	98	100	100	100	40	100	116	172	no	no	465	no
16	Siddu	19	Male	56	596	1	1	T	200mg	30mg	47	82	80	146	138	132	106	124	122	156	140	134	130	78	76	100	94	94	92	100	100	100	100	100	100	45	100	120	178	no	no	470	no
17	Ramesh	27	Male	65	945	1	1	T	200mg	35mg	49	88	89	156	142	134	104	118	120	146	132	126	122	80	78	104	100	96	90	100	97	100	99	100	100	48	100	117	160	no	yes	410	nausea
18	Siddu	19	Male	56	596	1	2	T	200mg	30mg	48	84	88	154	132	128	106	126	124	158	140	138	130	82	78	112	104	98	94	100	100	100	100	100	100	43	100	122	163	no	no	428	no
19	Ramesh	27	Male	65	945	1	3	T	200mg	35mg	48	90	88	152	130	126	104	116	122	144	134	130	128	76	74	106	102	98	94	100	100	100	100	100	100	50	100	119	172	no	no	446	no
20	Ramesh	27	Male	65	945	1	5	T	200mg	35mg	47	88	86	148	142	132	104	118	124	156	142	136	132	78	76	102	100	96	92	100	98	100	100	100	100	40	100	122	176	no	no	452	no
21	Shankar	26	Male	105	107496	2(obese)	1	T	300mg	50mg	48	64	62	148	136	130	102	130	130	150	148	140	136	80	82	102	100	96	94	98	99	100	100	100	99	42	120	130	204	no	no	460	no
22	Shankar	26	Male	105	107496	2(obese)	3	T	300mg	50mg	52	66	64	144	132	128	112	128	124	148	146	142	144	78	76	100	94	94	92	98	100	98	100	100	99	40	100	132	208	no	no	475	no
23	Mainuddin	40	Male	102	10649	2(obese)	3	T	300mg	50mg	50	74	72	142	140	138	108	120	118	158	156	152	142	74	72	118	114	110	98	99	100	99	97	99	99	35	120	128	200	no	yes	505	nausea
24	Rakesh	24	Male	68	11012	1	2	T	225mg	35mg	48	82	80	148	144	128	102	116	116	142	138	134	128	62	60	88	88	80	82	100	100	100	100	100	100	45	100	118	180	no	no	432	no
25	Laxmi	29	Female	51	12422	1	1	T	175mg	25mg	42	70	74	148	136	130	106	110	112	146	138	126	122	66	66	102	92	84	74	100	100	99	100	100	100	40	100	124	180	no	no	440	no
26	Srikanth	45	Male	68	12433	1	1	T	200mg	35mg	48	86	84	148	128	126	108	124	124	160	142	134	130	80	78	104	102	100	94	98	99	100	100	100	100	46	100	130	178	no	no	470	no
27	Srikanth	45	Male	68	12433	1	3	T	200mg	35mg	50	84	82	146	140	130	110	122	122	156	144	132	128	76	74	110	106	98	94	99	100	99	100	100	99	42	100	126	180	no	no	490	no
28	Mahantesh	40	Male	52	10825	1	1	T	150mg	25mg	49	80	78	142	134	128	110	122	120	152	140	132	128	74	72	102	96	94	90	100	100	100	100	100	100	44	100	118	170	no	no	438	no
29	Rahul	20	Male	68	13888	1	1	T	225mg	35mg	46	90	88	156	142	126	108	116	112	146	132	128	126	76	74	104	100	96	92	100	100	100	100	100	100	35	100	122	178	no	no	478	no
30	Rahul	20	Male	68	13888	1	3	T	225mg	35mg	48	92	90	154	144	128	110	118	116	152	136	130	128	74	72	104	98	96	90	100	100	99	100	100	100	30	100	125	188	no	no	485	no