"COMPARISON OF PROPOFOL AND THIOPENTONE ON HAEMODYNAMIC RESPONSES TO MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CONTROLLED TRIAL"

By

Dr. RAHUL DESAI.

DISSERTATION

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KLE UNIVERSITY, BELGAUM
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IN
ANAESTHESIOLOGY

Under the Guidance of

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MAY – 2009

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"COMPARISON OF PROPOFOL AND THIOPENTONE ON HAEMODYNAMIC RESPONSES TO MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CONTROLLED TRIAL"** *is a bonafide and genuine research work carried out by me under the guidance of* **Dr. C. S. SANIKOP** **M.D.., D.A.** *Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.*

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ABBREVIATIONS

DBP	Diastolic blood pressure
ECT	Electroconvulsive therapy
HR	Heart Rate
IP No.	Inpatient number
MAP	Mean arterial pressure
Pre op	Preoperatively
SBP	Systolic blood pressure
Sl.No.	Serial Number
Wt	Weight in kilograms

ABSTRACT

INTRODUCTION: With administration of ECT, blood pressure & heart rate steeply increase secondary to rise in plasma adrenaline and nor adrenaline. Deaths reported to have occurred with ECT, are most often, due to the alteration in these parameters. Various induction agents are being used with varying efficacy of attenuating these responses. In this study we compare the efficacy of propofol and thiopentone in attenuating these responses.

TYPE OF STUDY: Randomized control trial

METHODS AND MATERIALS: 50 patients between age of 18 and 45 years of either gender, belonging to ASA Grade-I and II scheduled for modified ECT were included. Patients were allocated randomly, into two groups. Anaesthetic technique was standardized for all patients.

Pre induction base line values of HR, SBP, and DBP were recorded using a pulse oximeter and automated non invasive blood pressure measuring device.

Induction with one of the study drug, Inj. thiopentone 4 mg. /kg (group T) or inj. propofol 1.5mg./kg (group P), over 15 seconds was carried out. Electrical stimulus was applied by bilateral electrodes to the temporal regions.

HR, SBP, DBP and mean arterial pressure were recorded soon after induction, after application of stimulus and at 1 minute interval after electric shock for 5 minutes and then at 5 minutes interval. Data are presented as mean and standard deviation Statistical

analysis was done by using the unpaired Student's 't' test for quantitative data $p<0.05$ was considered significant.

RESULTS: There was significant increase in the heart rate in both groups but the rise was lesser in the group P than the group T. There was a rise in the mean systolic blood pressure of approximately 10 mmHg in the group P. In comparison, in the group T the rise was 30 mmHg. The mean diastolic blood pressure rise in the propofol group was 7 mmHg as compared to 24 mmHg in the group T.

The mean arterial pressure in the group P increased by 8 mmHg in comparison to the rise in group T of 27 mmHg.

From our study we conclude that, the induction agent propofol could blunt the sympathetic response to electro-convulsive therapy more effectively than thiopentone.

KEYWORDS: *Electroconvulsive therapy, thiopentone, propofol, haemodynamic responses.*

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INTRODUCTION

Electroconvulsive therapy (ECT) is a biological therapy, wherein seizures are induced under medical supervision by passage of an electrical current through the brain. It has now developed into a widely recognized treatment modality in psychiatric practice. It is one of the most effective and safe treatments for depression, but has also been found to beneficial in mania, schizophrenia, catatonia and other neuropsychiatric conditions.[1] ECT is now also found to be effective in treatment of secondary psychiatric illness associated with various other diseases.[2]

For the safe conduct of ECT, an effort to avoid or minimize the physiologic sequelae and the attendant complications of ECT, a technique of modified ECT has evolved gradually, featuring use of muscle relaxation and induction agents without the concomitant abolition of the beneficial effects.[3] The commonly used muscle relaxant is a short acting depolarizing agent succinylcholine. Various induction agents were tried viz diazepam, ketamine, etomidate, methohexitone, thiopentone. Preferred is thiopentone, which is an ultra short acting barbiturate[3]. However the attendant cardiovascular effects are inadequately attenuated with its use.

Following application of the electric stimulus during ECT, there is a vagally mediated short lived bradycardia which is replaced by a sympathetically mediated tachycardia and rise in blood pressure.[4,5] Accordingly there is a sharp rise in the plasma catecholamine levels.[6] This produces a short lived sharp increase in myocardial workload which may pose significant risk for patients with coronary artery disease (CAD), dysrhythmias, or congestive cardiac failure.[7] Hence use of agents which would attenuate this adverse physiologic consequence would be preferred.

Propofol, a phenol derivative, is associated with rapid induction and recovery hence commonly used in day care surgeries.[8] Administration of propofol produces decrease in systemic blood pressure and sometimes bradycardia.[8] It is also more effective than thiopentone in attenuating the stress response to tracheal intubation.[9] Hence with the hypothesis that it can attenuate the cardiovascular responses to ECT more effectively than thiopentone this study was undertaken.

OBJECTIVES

The aim of this study was, to evaluate the efficacy of propofol, compared to thiopentone administered as induction agent to modified electro-convulsive therapy, in attenuating the haemodynamic responses namely heart rate (HR), systolic blood pressure (SBP), diastolic pressure (DBP) and mean arterial blood pressure (MAP).

REVIEW OF LITERATURE

During 16th century, one of the treatment modalities for psychiatric diseases was induction of seizures, which was achieved by use of certain agents. Until late 1930s, Metrazol was the agent used worldwide to induce convulsions.[18] It was an Italian neuropsychiatrist Ugo Cerletti, who had been using electric shock to produce seizures in animal experiments, and his colleague Lucio Bini developed the idea of use electricity in convulsive therapy.

By 1940s and 1950s use of electroconvulsive therapy became widespread. ECT then was usually given in "unmodified" form without muscle relaxants and seizures resulted in a full convulsion. However this was associated with serious complications, like fracture of bones and dislocation of joints most of them attributed to vigorous tonic contraction of skeletal muscles and sometimes-even death. To overcome this, in 1940s, Bennet introduced use of muscle relaxant, Curare, which was a plant extract found in South America. In 1951, use of succinylcholine, a safer synthetic alternative to curare, synthesized by Holmgern and Thesleff led to the more widespread application of "modified" ECT.[19]

To overcome the asphyxial feeling following muscle relaxation of the respiratory system, patients were induced with a general anaesthetic agent. By early 1960s, anaesthesia for ECT composed of use of induction agent, muscle relaxant, oxygenation and ventilation.

Several clinical observational studies indicated that Electroconvulsive therapy was associated with adverse physiological alterations especially with respect to cardiovascular system, which at times even resulted in death. Brown, in 1952, showed that there was initial bradycardia following application of electric shock which was due to transient stimulation of cardio-inhibitory centre or nerves.[20] Following the brief bradycardia, Brown reported a prolonged tachycardia, where in he observed cardiac arrhythmias and ascribed it to competitive influences of vagal and sympathetic activities.

In 1965, Gravenstein showed that, following administration of electric current there was a sharp increase in the heart rate and blood pressure with a corresponding increase in the plasma catecholamine levels.[21]

As the medical care and anaesthesia for electroconvulsive therapy was in the phase of evolution there were evidences to the fact that whenever deaths occurred in relation to electroconvulsive therapy [23], Bodley showed that it was the cardiovascular system which fails.[22]

Tewik and Wells reported that, out of 90 cases of death from electroconvulsive therapy 66 cases were due to cardiovascular complications. Kendell has also verified that death when it occurs in conjunction to electroconvulsive therapy was usually due to either myocardial infarction or ventricular arrhythmias.[24]

Since then various induction agents have been used with different benefits and drawbacks viz benzodiazepines, ketamine, barbiturates.

Friedman reported use of methohexitone, a short acting barbiturate, for modification of seizure activity.

Pitts et al studied induction of anaesthesia using methohexitone and thiopentone; a then recently introduced ultra short acting barbiturate, in electroconvulsive therapy[25]. The effect on electrocardiogram in 500 consecutive treatments with each agent was monitored. It was found that methohexitone was not only clinically superior but also caused fewer post convulsion ECG abnormalities than thiopentone.

Based on Martin studies in 1970s diazepam were used as the anaesthetic agent for induction during electroconvulsive therapy for sometime. But the study by Pitts and Allen showed that diazepam use was associated with postictal ECG abnormalities, and hence diazepam lost favour.[26]

Works in 1970s on substituting derivatives of phenol with hypnotic properties resulted in development of 2, 6 diisopropyl phenol (propofol). The first clinical trial by Kay and Rolly reported in 1977, confirmed the potential of propofol as an induction agent.[27]

Mackenzie N, Grant IS compared propofol with methohexitone and thiopentone for induction of anaesthesia in day case patients.[28] The conclusion of the study was, propofol was a suitable agent for day case with smooth and rapid induction and recovery. During the study, it was found that, propofol caused more marked decreases in systolic arterial blood pressure in the first 2 minutes after induction, with more than half of the patients experiencing a decrease of more than 20%. The mean decrease in the systolic blood pressure in the propofol group was 30 mmHg, compared to18mmHg in the other groups.

In 1985, Grounds and colleagues compared hemodynamic effects of thiopentone and propofol and noted greater hypotensive effect with propofol than thiopentone.[29] A similar conclusion was also drawn by Rolly and Versichelen when they compared propofol and thiopentone for induction in unpremedicated patients.[30]

Rouse in 1988 compared propofol and methohexitone for electroconvulsive therapy and found that Propofol prevents the increase in arterial blood pressure after seizure.[31]

Villalonga et al compared hemodynamic responses of thiopentone and propofol for electroconvulsive therapy at 1 and 5 min following electric shock and found that shock induced increases in diastolic blood pressure and heart rate were less marked with propofol than with thiopentone.[32]

McCleave and Blakemore, in a study comparing induction agents' methohexitone and thiopentone found no difference between the two agents with respect to induction and awakening times.[26]

Boey and Lai in 1990 compared propofol and thiopentone anaesthetic agents for electroconvulsive therapy. The duration of seizure was shorter in the propofol group and ability to walk 10 meters, after 20 min after anaesthesia was significantly better with propofol.[33]

In a comparative study between propofol and thiopentone done by Gerald in 1993 in out-patient surgery it was noted that, propofol caused a decrease in pulse rate and decrease in systolic, diastolic and mean blood pressures and was significantly greater than the thiopentone.[34]

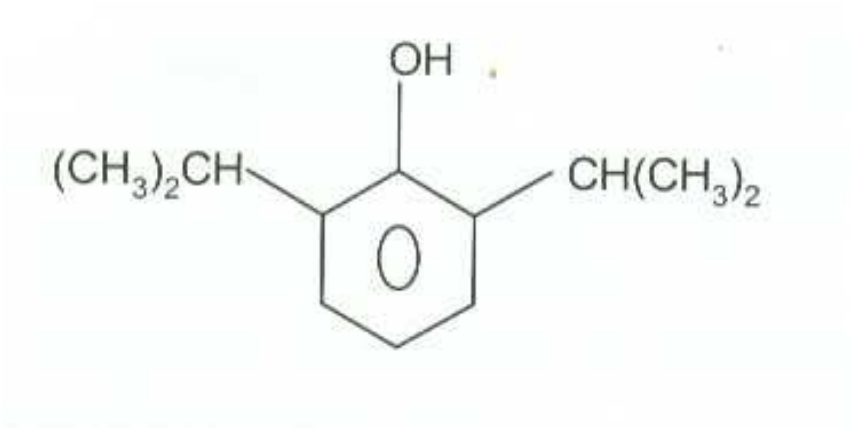
Lindgren and colleagues in1993 studied the hemodynamic and catecholamine responses to induction and tracheal intubation with propofol and thiopentone.[9] It was seen that systolic arterial pressure and QT interval responses to intubation were significantly greater with thiopentone than with propofol. Concentration of plasma adrenaline increased after induction with thiopentone only.

In 1995, Michel et al compared methohexitone, propofol and etomidate for electroconvulsive therapy on the seizure duration and concluded that etomidate was associated with longer seizures and should be considered in patients with inadequate seizure durations. It was observed that propofol provides better protection against an untoward hypertensive effect to electroconvulsive therapy.[35]

In 2000 Zaida and khan FA, did similar comparison of thiopentone and propofol for ECT and found that propofol offered superior hemodynamic stability during the procedure and quick recovery from sleep.[36]

PROPOFOL[10]

Structure



Chemical name:

2-6, di-isopropyl phenol

History:

Propofol was first introduced clinically by Ray and Rolly in 1977A lot of work in the early 1970's on substituted derivatives of phenol with hypnotic properties, resulted in the development of 2-6, di-isopropyl phenol.

Propofol is insoluble in water and therefore was initially prepared in with cremophor EL. Because of anaphylactoid reactions associated with cremophor EL, the drug was reformulated using soya been oil emulsion.

Propofol was first marketed in UK in 1986 and since then, has been accepted world wide as a general anaesthetic agent both in developed and developing countries.

Physiochemical Properties:

Chemical formula:	$C_{12}H_{18}0$.	Milky white liquid
Molecular weight:	178.27,	Oil at room temperature
Melting point:	19^0C	highly lipid soluble
Boiling point:	242^0 C	
pH range:	7-8.5	

Formulations:

Each ml. of propofol 1 % (w/v) formulation contains

Propofol : 10 mg (Active ingredient)

Soya bean oil : 10 % Lipid base.

Egg lecithin : 1.2 % Emulsifier

Glycerol : 2.25 % to maintain iso-tonicity.

Distilled water for injection: q.s.

Sodium hydroxide to maintain pH

In USA: Metabisulfite or disodium EDTA added as an anti microbial agent

In Europe: 2% propofol available is compatible with 5% dextrose if dilution is required.

Mechanism of action:

Propofol is primarily a hypnotic. The exact mechanism of action is not known. However evidence suggests that hypnotic actions are mediated by potentiating the Gama-amino butyric acid (GABA) induced chloride current through binding to β-submit of $GABA_A$ receptor sites on β_1, β_2 and β_3 sub-units of trans membrane domains have been shown to be critical for the hypnotic action of propofol.

The α_2 - adrenoceptor system plays an indirect role in the sedative effects of propofol. Propofol also causes widespread inhibition of N-methyl D-aspartate (NMDA) subtype of glutamate receptor through modulation of sodium channel gating, an action which may also contribute to the CNS effects of the drug.

Studies have demonstrated that propofol also has a direct depressant effect on neurons of the spinal cord.

The pharmacokinetics of propofol has been evaluated by numerous investigations and it has been described by both two and three compartment models.

After a single injection whole blood propofol levels decrease rapidly as a result of both redistribution and elimination. In studies using two compartments the initial distribution half life of propofol is 2-8 mins and elimination half life varies from 1.0 to 3 hrs.

An open three compartment model, describes distribution of propofol as:-

i. Rapid initial distribution from the blood to highly perfused tissues (Viz., brain, heart, lung, liver) $t_{½}\ \alpha$ - 1.8 –4.1mins

ii.Redistribution and metabolic clearance, $t_{½}$ β - 21 – 69 mins.

iii.Slow return from poorly perfused tissues to blood $t_{½}$ 184 - 834 mins

The context sensitive half life of propofol is less than 40 mins. More than 98 % of propofol is plasma protein bound and so it has a large central distribution of 20 - 40L. Clearance of propofol is extremely high 1.5 to 2.2 L min^{-1}. The time of peak effect is 90-100 sec. The pharmacokinetics of propofol may be altered by a variety of factors viz. gender, weight, pre-existing diseases, age and concomitant medications.

Propofol is rapidly metabolized in the liver by conjugation with glucuronide sulphate to produce soluble compounds, which are excreted by kidneys.

Less than 1 % of propofol is excreted unchanged in urine and only 2 % is excreted in faeces. The metabolites of propofol are not thought to be active.

Since clearance of propofol (1.5 to 2.2 l/min) exceeds hepatic blood flow, extra hepatic metabolism or extra renal elimination has been suggested. This explains the faster and clear headed recovery of its use.

Propofol itself results in concentration dependent inhibition of cytochrome P_{450} enzyme system complex and thus may alter the metabolism of other drugs.

Pharmacodynamics:

1) Central Nervous system:

Propofol is primarily a hypnotic. The onset of hypnosis after doses of 2.5 mg kg^{-1} is rapid (one arm brain circulation), with a peak effect seen at 90-100 sec. The median effective dose (ED50) of propofol for loss of consciousness is 1-1.5 mg kg-1 after a

bolus. The duration of hypnosis being dose dependant, propofol provides sedation and amnesia. It alters the mood to a lesser extent than thiopentone after short surgical procedures. Propofol also tends to produce a general state of well being. Hallucinations, sexual fantasies and opisthotonus have been reported after propofol administration.

Effects of propofol on EEG are dose dependant. Infusion of propofol demonstrates an initial increase in alpha rhythm, followed by a shift to gamma and theta frequency. High infusion rates produce burst suppression.

Propofol causes a concentration dependant decrease in the bispectral index with 50 % and 90 % patients unable to respond to verbal commands at BIS values of 63 and 51 respectively

Effect of propofol on epileptogenic EEG activity is controversial. Some report dose dependant anticonvulsant effect of propofol. But propofol is also associated with grandmal seizures and has been used for cortical mapping of epileptogenic foci.

2) Cardiovascular system:

The most prominent effect of propofol is a decrease in arterial blood pressure during induction of anesthesia independent of the presence of cardiovascular disease. An induction dose of 2 to 2.5 mg kg^{-1} produces a 25-40 % reduction in systolic blood pressure similar changes are seen in mean and diastolic blood pressure.

This is associated with a decrease in Cardiac Index (15 %), systemic vascular resistance (15-25 %), left ventricular stroke work index (30 %), mean PAP and PAOP.

The effect is maximal at 2 mins after induction due to -

i. Direct myocardial depression and

ii. Decreased peripheral resistance and preload.

The hypotensive effect of propofol is potentiated by -

1. Hypovolaemia or cardiovascular decompensation.
2. Advanced age
3. Large doses of propofol
4. Pre medication with opioids
5. Pre- existing cardiovascular disease

An infusion of propofol result in significant reduction in both myocardial blood flow and myocardial 0_2 consumption, a finding that suggest preservation of the global myocardial oxygen supply demand ratio

3. Respiratory system:

Propofol acts as a moderate respiratory depressant and can cause apnea in upto 25-30 % population after an induction dose.

The incidence and duration of apnea is dependent on dose, speed of injection and concomitant pre-medication. The onset of apnea is usually preceded by marked tidal volume reduction and tachypnea.

Propofol is mild bronchodilator and causes bronchodilatation in patients with chronic obstructive pulmonary disease.

In animal models propofol significantly reduced free radical mediated and cyclo-oxygenase catalyzed lipid peroxidation so it is proposed that propofol may have an impact on adult respiratory distress syndrome (ARDS)

4. Effect on liver and kidney function:

Post-operative hepatic function tests are not altered following propofol anesthesia. No evidence of any altered renal function has been reported following use of propofol

5. Effect on uterus:

Propofol has little or no effect on pregnant uterus propofol readily crosses the placenta but usual induction does not appear to depress neonates, propofol has no adverse effects on the uterine contraction or intra-operative blood loss.

6. Effect on adrenocortical function:

Propofol is not an analgesic but, does not cause ant-analgesia. Propofol causes minimal inhibition of cortisol production unlike other anaesthetic agents. It tends to decrease cortisol levels during infusion period shows no impairment of adrenal-steroidogenesis

Other miscellaneous effects

a) Anti-Emetic effect:

At low (sub – hypnotic) doses, propofol possesses a significant anti – emetic effect. The exact cause is not known. Studies suggest that it may occur as a result of direct depression of chemoreceptor trigger zone (CTZ), may also be due to anti – serotonergic ($5HT3_)$ properties of propofol.

b) Anti-pruritic effect:

At sub – hypnotic doses, propofol has been reported to relieve cholestatic pruritis and is found to be as effective as naloxone in treating pruritis induced by spinal opioids.

c) Anti-oxidant activity:

Propofol has been found to possess anti oxidant effects and thus acts as free radical scavenger. This suggests that propofol can be useful in conditions such as multi – organ failure and acute respiratory distress syndrome.

d) Anxiolysis:

Sub – hypnotic doses of propofol possess anxiolytic properties strengthening the cause for its use during sedation and as an adjuvant to local or regional anaesthesia.

e) Other effects:

1 Does not interfere with coagulation

2 Does not trigger malignant hyperthermia

3 Can be used in patients with porphyrias

4 Decrease polymorphonuclear leukocyte chemotaxis, but not adherence, phagocytosis and killing.

5 Also inhibits the ability of cancer cells to invade by modulating Rho-A

Side effects:

- Pain on injection
- Pro-convulsant activity viz., myoclonus
- Thrombophlebitis
- Hypotension and apnea

- Supports growth of E-Coli, hence unused infusions should be discarded within 12 hours
- Propofol infusion syndrome
- Rarely anaphylactic reaction.

Presentation:

Propofol is available as 1% i.e. 10 mg/ml emulsion in 10ml and 20 ml vials for induction and 50ml, 100 ml vials for infusion. In Europe, 2 % formulation is also available, as well as a formulation in which emulsion contains medium and long chain triglycerides.

Dosage: Induction of anesthesia – Child: 2.5- 3.5 mg/kg

Adult: 1.0 –2.5 mg/kg

Sedation: 25 to 75 $\mu g\ kg^{-1}$ min

Maintenance of anesthesia: 50 to 150 $\mu g\ kg^{-1}\ min^{-1}$

Uses:

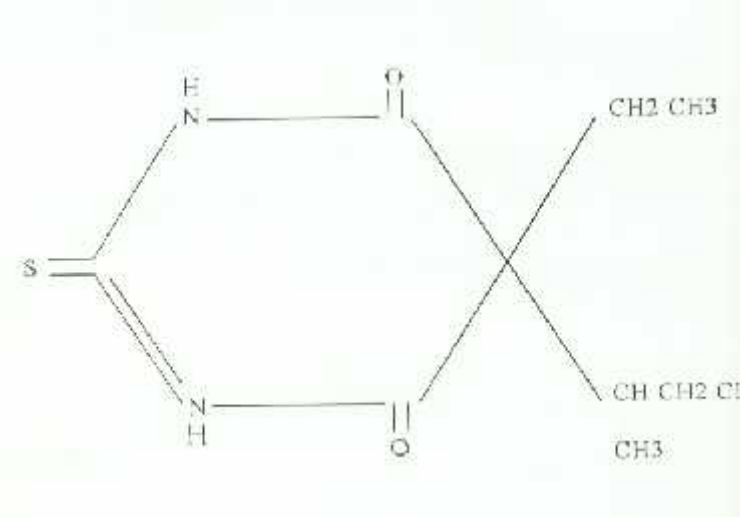
1. For induction and maintenance of general anaesthesia
2. In ICU for IV sedation and total intra-venous anaesthesia (TIVA)
3. For day care surgery as it has rapid recovery
4. In patients with bronchial asthma, porphyria and in those patients where thiopentone is contraindicated
5. In patients with malignant hyperthermia
6. As an anticonvulsant
7. As an antiemetic

Contraindication:

- Patient hypersensitive to propofol formulation
- Hypovolemia
- Epilepsy and dyslipidemia.

THIOPENTONE[11]

Structure



CH CH2 CH

Chemical name:

5-ethyl 5-(methyl,butyl) 2-thiobarbiturate

History:

The thiobarbiturates were first described in 1903. However, because of fatal experiments in dogs, their use was not further explored until the 1930.

In 1935, Tabern and Volwiler synthesized a series of sulfur containing barbiturates, of which thiopental became the most widely used.

Thiopental was introduced clinically by Ralph Water and John Lundy and became preferred clinically because of the rapid onset of action and short duration, without the excitatory effects of hexobarbital. Even though many other barbiturate derivatives have been synthesized throughout the past several decades, none has enjoyed the clinical success and popularity of thiopental. Thiopental has survived the test of time as an intravenous anaesthetic agent.

Chemistry and Physical Properties:

Thiopentone is an ultra short acting barbiturate. It is a derivative of barbituric acid and is a sulphur analogue of pentobarbitone, which accounts for its rapid induction and recovery.

It is a pale yellow powder, hygroscopic with bitter taste and sulphur smell, resembling that of hydrogen sulphide. It is soluble in water and alcohol, but not very stable and may remain so for 24-48 hours. Commercial preparations contain sodium carbonate 6% which acts as a buffer and prevents precipitation of free acid by atmospheric carbon dioxide and resulting in an alkaline solution (pH 10.5-11). It is largely in unionized form at body pH, a fact which facilitates its diffusion through membranes. The oil/gas solubility ratio is 4.7%, molecular weight 264.3 and pKa 7.6.

Dosage and Administration:

Thiopentone is supplied in vials of 0.5 gm and 1gm which are made up into a 2.5%, solution. The usual induction dose is 4-7 mg kg^{-1} body weight.

Pharmacokinetics:

Thiopentone is highly lipid soluble. Following a bolus iv injection, 60-80 % of the drug becomes bound to plasma proteins. Its high lipid solubility makes it to diffuse rapidly into the brain. EEG changes with loss of consciousness occur in 10-20 sec (one arm brain circulation time). Rapid redistribution into muscles is responsible for rapid recovery from small doses. Thiopentone is metabolized by the liver and virtually none is excreted unchanged. Three pathways of hepatic extraction and metabolism are.

1. Oxidation of C_5 side chain

2. Oxidative replacement of sulphur at C_5 to form pentobarbitone.

3. Cleavage of barbiturate to form urea and three carbon fragments.

$t_{½}\ \alpha_1$ → 2 to 6 min → corresponds to diffusion into tissues of high blood flow

$t_{½}\ \alpha_2$ → 30 to 60 min → diffusion into adipose tissue

$t_{½}\ \beta$ → 3 to 23 hr → elimination phase (due to hepatic metabolism and excretion)

Factors affecting pharmacokinetics:

- Pregnancy has little effect on the pharmacokinetics of thiopentone, although the clearance is greater in pregnant patients. The elimination half life is longer. The drug

diffuses freely across the placental barrier. Renal failure reduces the dose requirement of thiopentone. Liver failure may also lead to hypoproteinemia and reduces the dose requirement.

Increasing age is associated with a lower induction dose of thiopentone probably on the basis of lower cardiac out put and failure to compensate for the effects of the drug in the circulation.

Pharmacodynamics:

1) Central Nervous system:

Thiopentone rapidly diffuses across the blood brain barrier, causing cortical depression, the cerebral metabolic requirement of oxygen ($CMRO_2$) falls by about 50% with an infusion of thiopentone. Thiopentone is not an analgesic and small doses may increase sensitivity to pain (antanalgesia)

- It is an anticonvulsant.
- Sympathetic system is depressed more than the parasympathetic system.
- Intra cranial tension is reduced.

2). Cardiovascular system:

Thiopentone when given as a bolus dose causes a reduction in arterial blood pressure with marked peripheral vasodilatation. There is some degree of tachycardia (10-20 %), which contributes to the maintenance of blood pressure and C.O. (cardiac output).

Ability for haemodynamic stability is impaired in hypovolaemic patients and induction is hazardous in patients with compensated shock.

Thiopentone has been shown to increase myocardial oxygen consumption in healthy patients but reduces it by 39 % in those with ischaemic heart disease. The latter effect is due to reduced oxygen requirements and even in patients with ischaemic heart disease there is no evidence that it cause adverse effect.

3) Respiratory system:

It depresses spontaneous respiratory rate and tidal volume, decreases the sensitivity of respiratory centre to CO_2. Laryngeal reflexes are not depressed until deep levels of anesthesia are reached. Minor stimuli frequently cause laryngospasm during light anesthesia. Bronchospasm is common in asthmatics.

4) Action on kidney & liver:

Kidney: Decreases renal blood flow, increases secretion of antidiuretic hormone, urine out put is decreased.

Liver: It causes enzyme induction leading to increased drug metabolism and also liver dysfunction in hypoxia and reduced hepatic blood flow conditions.

5) Eye :

Loss of eyelash, conjunctival and corneal reflexes, sensitivity to light reflex is lost in deeper anaesthetic levels but preserved till the patient reaches the surgical plane. It reduces intraocular tension.

6) Pregnant uterus:

It readily crosses placental barrier and maximum concentration in fetus is seen soon after injection. There is no effect on the tone of the uterine musculature.

1. Miscellaneous effects:

Acid base and electrolyte disturbances can occur secondary to hyperventilation, skin rashes and urticarial responses are also reported. Hypersensitivity and anaphylactic responses occasionally occur.

Complications:

Local:

1) Perivenous injection: pain, redness, swelling etc.
2) Intra–arterial injection: Arterial spasm, white hand, and cyanosis, skin discoloration, edema and gangrene.
3) Thrombophlebitis
4) Nerve injury

General:

1. Respiratory depression , apnea, laryngospasm, bronchospasm
2. Circulatory collapse and dysrrythmia
3. Hiccoughs and coughing
4. Euphoria and disorientation
5. Severe anaphylactic reaction

Contra indications:

1. Anaphylaxis to thiopentone
2. Porphyria
3. Fixed low cardiac out put syndrome
4. Hypovolemic shock
5. It is also not indicated in patients with gross dyspnoea due to respiratory obstruction, asthma and acute inflammation of mouth, jaw and neck.

Indications:

1. For induction of general anaesthesia
2. As sole induction agent for short surgical procedures
3. Supplementation of regional anaesthesia
4. For electro convulsive therapy
5. As an anticonvulsant following local anaesthetic toxicity, eclampsia, epilepsy, tetanus etc.
6. Used in cerebral protection.

ELECTROCONVULSIVE THERAPY

DEFINITION

Electroconvulsive therapy is the application of electric current through bitemporal or unilateral non dominant (electrode on non dominant fronto temporal area) electrode. The current is given with an aim to achieve a seizure of greater than 25-30 seconds duration by behavioral or electrophysiological criteria.

Techniques used for electroconvulsive therapy administration are of two types -

1. Direct - Electroconvulsive therapy is given in the absence of muscular relaxation and general anaesthesia.
2. Modified - Electroconvulsive therapy is modified by drug induced muscular relaxation and general anaesthesia.

MECHANISM OF ACTION

Generalized electrically induced seizures of the central nervous system are responsible for the therapeutic effects of electroconvulsive therapy.

The psychobiological mechanisms remain largely unknown. Biochemical changes at the regional and sub cellular levels currently offer possible explanations. Neurophysiological changes include alterations in permeability of blood brain barrier, a regional cerebral blood flow, cerebral microcirculation, neurometabolic activity, brain electrical activity[12, 13].

Neuroendocrinal changes include release of adrenocorticotropin hormone, prolactin and hypothalamic peptides. Neurochemical changes include release of brain neurotransmitters and biogenic amines.

PHASES OF ELECTROCONVULSIVE THERAPY [14] :

The electroconvulsive therapy has been divided into six phases on the clinical basis as follows :

1. Preparational phase - before electrical dose
2. Stimulatory phase - immediately at and after the stimulus dose
3. Kinetic phase-between stimulus and tonus state
    a. Atonic -following stimulus
    b. Tonic - similar to decerebrate posture
    c. Clearly recognizable movements
4. Tonus phase - Generalized rigidity
5. Clonus phase - starts from eyes and proceeds down the feet 6. Recovery phase - includes transient atony, brief decerebrate state, normal respiration

SEIZURE TIME AND THRESHOLD

Preceded by a latent period of 2 - 3 seconds, a bilateral grand mal convulsion ensues a tonic phase of 10 -12 seconds followed by clonic phase of 30 - 50seconds. The seizure pattern of the individual patient varies only slightly regardless of stimulus characteristics.

Because seizure is the therapeutic agent, the duration of seizure is a significant variable of therapeutic efficacy. But it has certain limitation, since it only gives an incomplete description of the amount of seizure activity, and it does not reliably correspond to the therapeutic outcome.

Electrical stimulation in excess of what is needed can cause greater post - ictal confusion and memory loss without any therapeutic advantage. The seizure duration does not vary with sex of the patient, is inversely related to age and is reported to increase slightly as number of treatment increase. Increased oxygenation just prior to and during seizure, hypocapnia, drugs like Ketamine increase the duration of seizure, whereas hypoxic condition, hypercapnia, barbiturates decrease the duration of seizure.

For maximal effectiveness, the electrical stimulus must be of sufficient magnitude (approximately 70 - 150 volts for 0.3 to 1.0 seconds) to suppress the patient's variable seizure threshold and head resistance (200 to several thousand ohms)

Seizure threshold varies with age, sex, drugs and physiologic condition of the patient.

It is higher in females, old patients. It can rise with coma, acute excitement, dehydration, previous seizure, and in cold dry days. Drugs like barbiturates, benzodiazepines, and local anaesthetics increase the seizure threshold in the dose related manner.

Threshold is lower in males and younger patients. It declines with water retention, vasospasm and hypoglycemia.

PHYSIOLOGICAL EFFECTS

Electroconvulsive therapy activates non-adrenergic system, enhances dopamine receptor sensitivity and reduces serotonin uptake. Electroconvulsive therapy activates peripheral autonomic nervous system and causes release of secretions from many endocrine glands. Neuroendocrine responses 2 to electroconvulsive therapy include an

immediate release (Peak Plasma level at 2 - 5 mins) of Adrenocorticotropin hormone, which returns to normal by 45 minutes, an increase in plasma epinephrine concentration to 15 times the baseline by 1 minute, which return to normal in 10 minutes, an increase in plasma norepinephrine to three times the baseline at 1 minute which returns to normal by 20 minutes.

The marked increase in levels of circulating catecholamines occasioned by electroconvulsive therapy is a result of their release from the adrenal medulla and to a lesser extent from sympathetic nerve endings. These increased levels are responsible for the hypertensive response.' The post seizure hypertension, tachycardia and cardiac dysrhythmias decline in parallel with the falling plasma concentration of catecholamines.

Transient increase in release of glucagon and inhibition of glucose mediated insulin secretion leads to hyperglycemia.

Cardiovascular Changes: [15]

Immediate changes are due to parasympathetic stimulation which are manifested as bradycardia and hypotension.

Later (After 1 min) changes are due to sympathetic stimulation which are manifested as tachycardia, hypertension and arrhythmias like asystole, bradycardia or tachycardia, ventricular premature complexes, ventricular escape. Because of these changes, cardiac output and myocardial oxygen consumption is increased.

Cerebral Changes :[16]

There is an increase in cerebral oxygen consumption and cerebral blood flow and this leads to increase in intracranial pressure.

Miscellaneous

Increase in intragastric pressure.

Increase in intraoccular pressure

INDICATIONS

Major depressive disorders Schizophrenia

Mania and Bipolar mood disorders

CONTRAINDICATIONS

Absolute:

Phaeochromocytoma, recent Myocardial Infarction, recent cerebrovascular accident, Intracranial surgery, Intracranial mass lesion

Relative:

Angina, congestive cardiac failure, cardiac pacemaker, severe pulmonary disease, severe osteoporosis, major bone fractures, glaucoma, retinal detachment, pregnancy.

COMPLICATIONS

- Damage to teeth, tongue, eyes, cutaneous structures. Muscle aches, headaches.
- Memory disturbances - complete retrograde amnesia.
- Fractures of long bones and vertebrae were the complications of unmodified electroconvulsive therapy, but have not been reported in past 10 years. '3

MORTALITY

Directly attributable to electroconvulsive therapy is very low. [17] But in the past, deaths were reported due to pulmonary embolism and cardiac arrest.

METHODOLOGY

The study was conducted after approval from institutional ethics committee. The study was conducted in fifty adult patients belonging to ASA grade I and II, taking ECT for first time, of either gender and with no absolute contraindication to ECT. The study was conducted in between the age group of 18-45 years. Informed written consent was obtained from the patient`s close relative.

A sample size of 25 in each group was calculated. It was calculated by taking a difference of 25mmHg in blood pressure as significant, with confidence interval of 95% (Z_{α} =1.96) and the power of study as 80% (Z_{β}=0.84)[9].

Following patients were excluded from the study.

EXCLUSION CRITERIA:

1. Pregnant women.
2. Hypertensive patients
3. Heart rate less than 60 bpm.
4. History of allergy to any drug.

PRE ELECTROCONVULSIVE THERAPY WORK UP:

Each patient was evaluated for medical and surgical illness in the past and previous anaesthetic exposure and experience.

Following investigations were carried out for all patients.

INVESTIGATIONS:

Hb %:

Urine routine: (Sugar, Albumin, Micro.)

Blood sugar

Serum creatinine

ECG

Chest X-RAY

CONDUCT OF ANAESTHESIA AND ECT:

On the day of ECT, each patient`s investigations verified and were found to be within normal limits. Antipsychotic drugs were omitted on the day of ECT.

Over night fasting was confirmed. Patients were randomly allocated into two groups according to the computer generated randomization listing with 25 patients in each group viz: Group Thiopentone and group propofol.

On arrival of the patient in the ECT room, ECG, pulse oxymeter and non invasive blood pressure monitors were attached and baseline heart rate, systolic, diastolic and mean arterial pressures were recorded using a non invasive blood pressure monitor (Larsen and Turbo model star 50). An intravenous line was secured on the dorsum of left hand using a 20 G intravenous cannula.

All patients were premedicated with Inj. glycopyrrolate 0.2 mg i.v.

Each patient was preoxygenated for 3 minutes.

Induction was done using thiopentone (4 mg/kg) or propofol (1.5 mg/kg) depending on the group allocated.

Group T (thiopentone):

Patients in this group received thiopentone (4 mg/kg) slowly over 15 seconds. Induction was confirmed by loss of eye lash reflex.

Group P (propofol):

Patients in this group received propofol (1.5mg /kg) slowly over 15 seconds. Induction was confirmed by loss of eye lash reflex.

After confirming the patient could be ventilated. Injection suxamethonium 1.0 mg / kg was given for muscle relaxation. Patients were ventilated with 100 % O_2 until fasciculations subsided.

As soon as the patient is relaxed, a mouth prop was inserted and a bitemporal ECT was administered by the psychiatrist. The mouth prop was changed to guedel airway after the seizure and ventilation was assisted with the fask mask and 100% oxygen until return of spontaneous respiration. The patient was observed for 10 minutes in the ECT room and later was monitored in the recovery room for an hour.

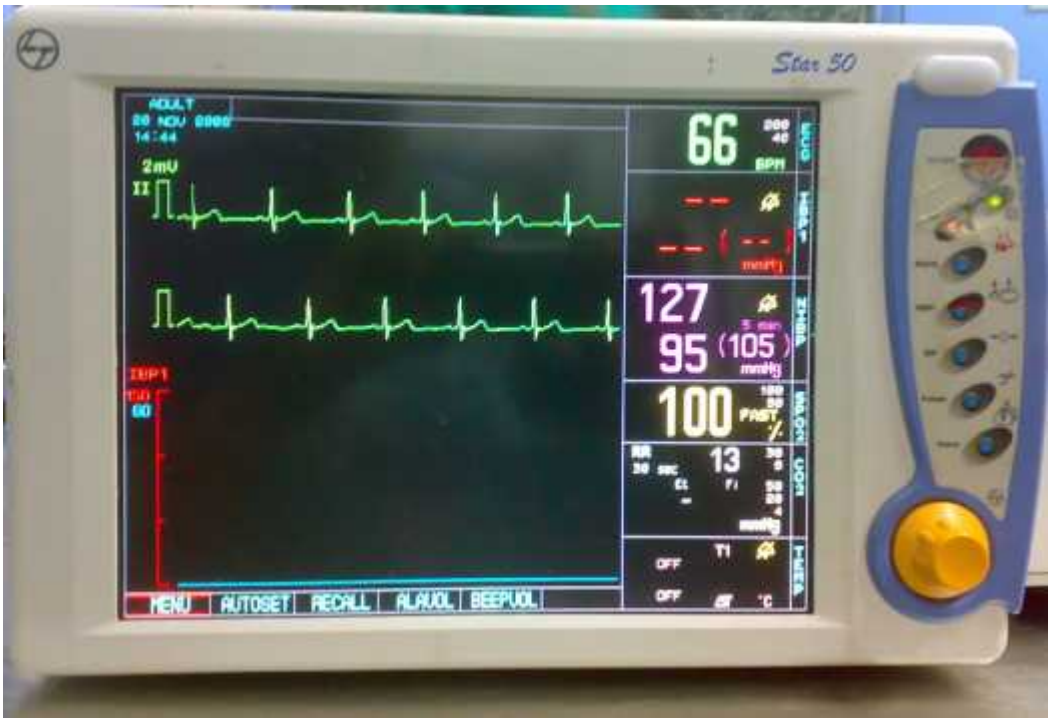
MONITORING:

All patients had continuous pulse oxymeter; ECG monitoring and systolic diastolic and mean arterial pressures were recorded and monitored using an automated blood pressure machine set to record every minute.

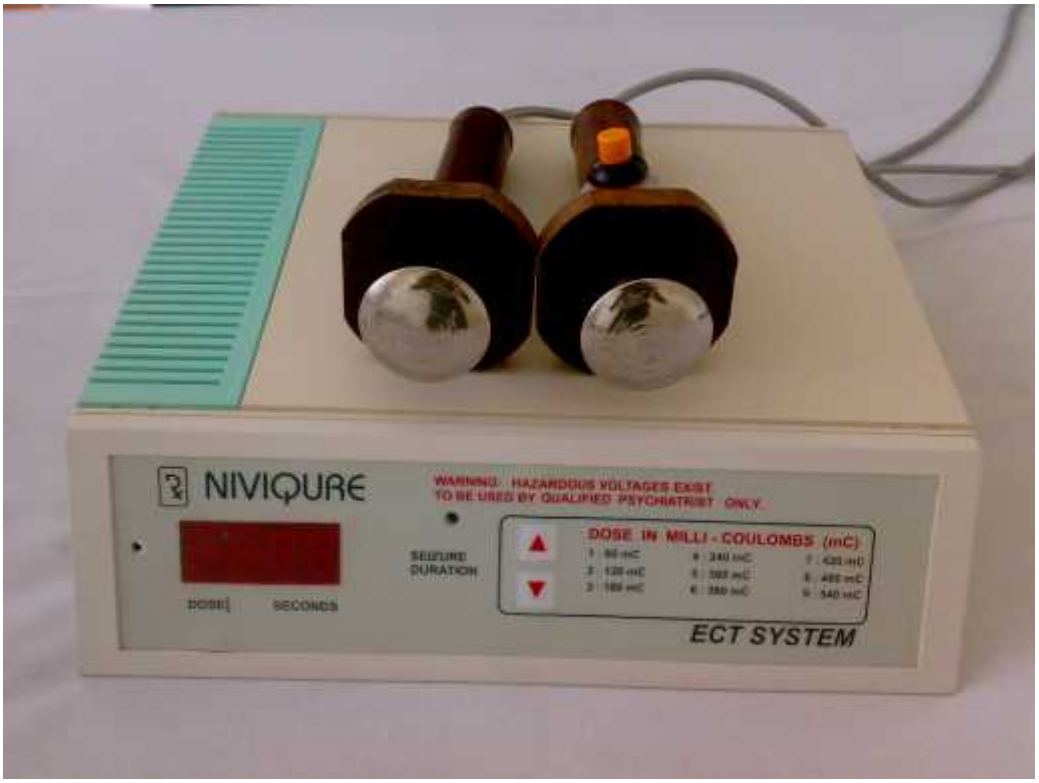
Baseline Heart rate, systolic, diastolic and mean arterial pressures were noted just before securing the intravenous cannula. The same parameters were noted after loss of eyelash reflex following induction, immediately after seizure cessation following delivery of the electric shock and at 1 minute interval for 5 minutes and once after 5 minutes (10 min post ECT).

STATISTICAL ANALYSIS:

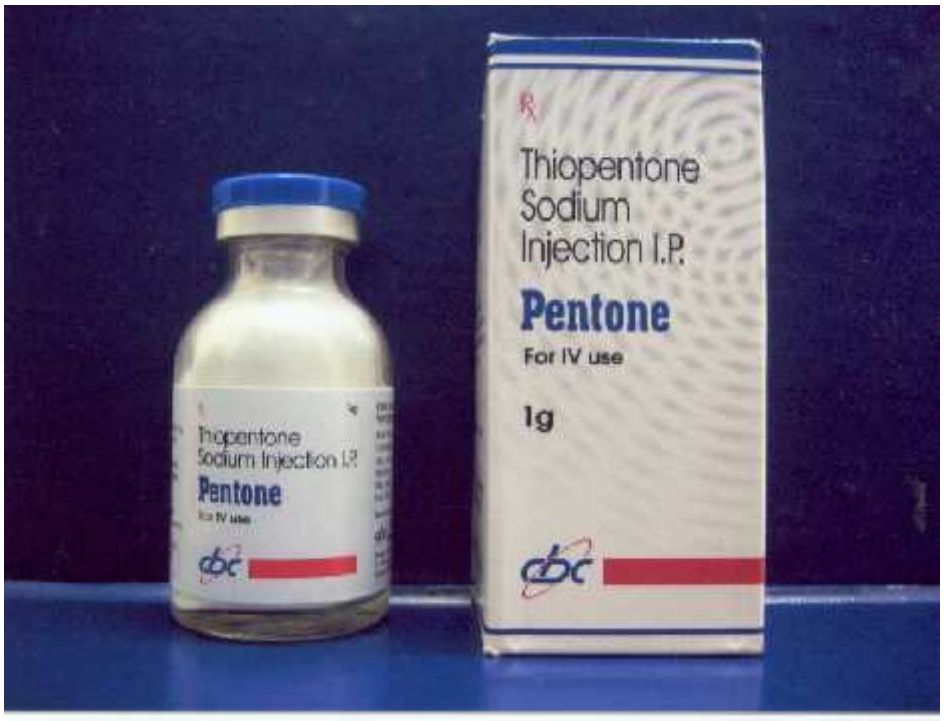
Data are presented as mean and standard deviation Statistical analysis was done by using the unpaired Student's't' test for quantitative data. Comparison of proportions (percentage) of the two groups was done using test for proportions was done using data analysis and $p<0.05$ will be considered significant. The statistical analysis was performed using Microsoft office (2007).



Larsen and Toubro Monitor (Star 50)



ECT Machine



Thiopentone vial (1 gm)

Propofol 1% Vial (10 ml)

RESULTS

In this comparative study, 50 patients (25 each) undergoing ECT for the first time were randomly selected. All patients in both the groups got induced with the calculated dose of the induction agents. Duration of seizure activity was adequate and none of the patients required a repeat shock.

TABLE I: MEAN AGE AND WEIGHT IN THE TWO GROUPS:

	Group P (Mean ± SD)	**Group T** (Mean ± SD)	**P VALUE**
Age (years)	26.6 ± 7.09	27.44 ± 7.12	0.6780
Weight(kg)	55 ± 6.9	53.88 ± 7.49	0.5848

The mean age and mean weight of the patients in both the groups is presented in the table I. There is no significant difference between the two groups.

TABLE II: DISTRIBUTION OF GENDER IN THE TWO GROUPS

	Group P		**Group T**	
Male	7	28%	11	44%
Female	18	72%	14	56%

TABLE III: DISTRIBUTION OF DIAGNOSIS IN THE TWO GROUPS

	Group P		**Group T**	
Schizophrenia	14	56%	11	44%
Depression	6	24%	10	40%
Bipolar mood disorder	1	04%	0	00%
Mania	4	16%	2	08%
OCD	0	00%	2	08%

The distribution of the gender and the cases in both the groups is presented in the table II and III and shows that both the groups are comparable.

TABLE IV: MEAN HEART RATE VALUES IN BOTH GROUPS:

EVENTS	GROUP P	GROUP T	P VALUE	
PRE INDUCTION	90.60 ± 14.12	91.12 ± 17.46	0.9083	NS
POSTINDUCTION	93.28 ± 11.14	97.20 ± 14.54	0.2901	NS
POST SHOCK	96.40 ± 16.05	114.36 ± 27.75	0.0073	S
1 min	101.60 ± 16.73	115.60 ± 15.63	0.0036	S
2 min	101.08 ± 15.49	111.24 ± 16.39	0.0289	S
3 min	10I.16 ±16.92	111.56 ± 17.74	0.0391	S
4 min	98.48 ± 15.42	108.28 ± 18.02	0.0443	S
5 min	97.16 ± 13.60	106.56 ± 17.10	0.0365	S
10 min	94.40 ± 10.91	100.12 ± 16.12	0.1483	NS

TABLE V: COMPARISON OF HEART RATE IN THE TWO GROUPS WITH THE BASELINE.

GROUP T	P VALUE	GROUP P	P VALUE
91.12 ± 17.46		90.60 ± 14.12	
97.20 ± 14.54	0.007	93.28 ± 11.14	0.20
114.36 ± 27.75	0.0002	96.40 ± 16.05	0.09
115.60 ± 15.63	0.0001	101.60 ± 16.73	0.01
111.24 ± 16.39	0.00001	101.08 ± 15.49	0.006
111.56 ± 17.74	0.00001	10I.16 ±16.92	0.010
108.28 ± 18.02	0.0001	98.48 ± 15.42	0.032
106.56 ± 17.10	0.0003	97.16 ± 13.60	0.047
100.12 ± 16.12	0.003	94.40 ± 10.91	0.11

The mean heart rates in the two groups are shown in the table V. The heart rate in the group T significantly increased after application of electric shock, the increase continued for 10 minutes after the electric shock. The maximum heart rate was observed 1 minute after the electric shock. In the group P, the heart rate increased significantly only upto 5 minutes and at 10 minutes there was no significant difference from the baseline. The heart rate trend in the group T and that in the group P were significantly different and the values immediately after applications of electric shock were significantly higher the group T compared with the group P upto 5 min (table IV, graph 1).

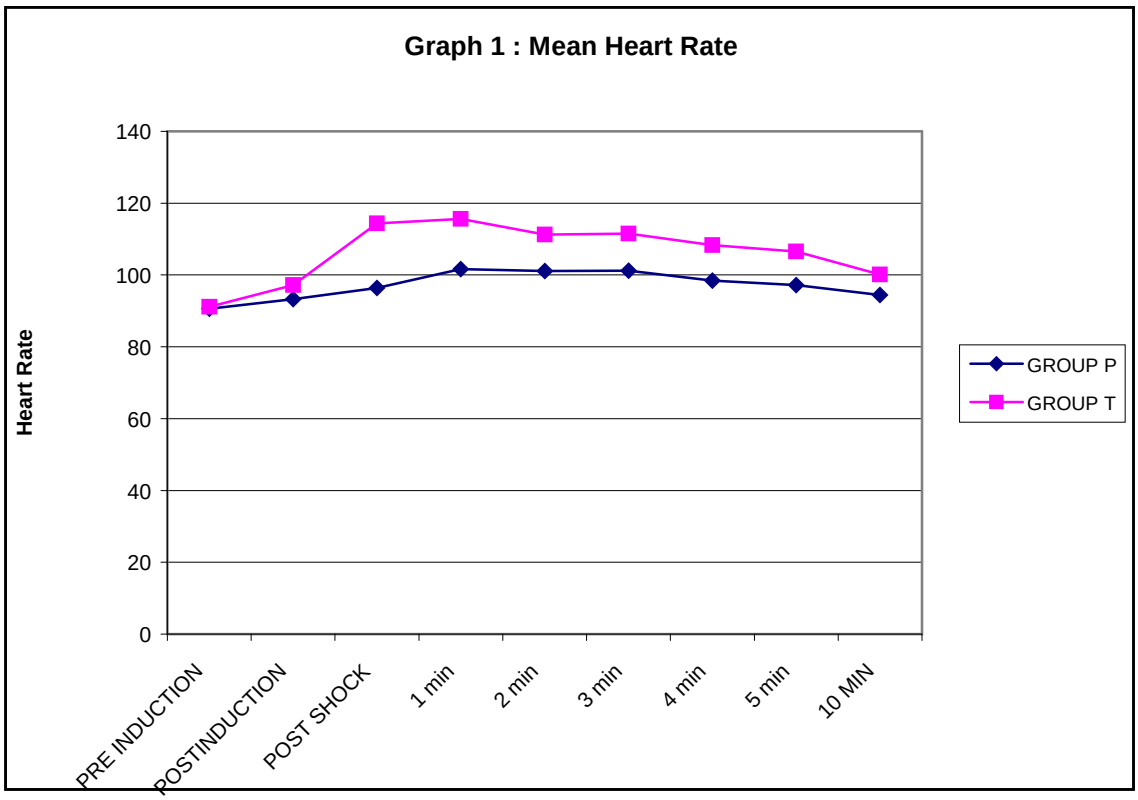

Graph 1 : Mean Heart Rate
Heart Rate
140
120
100
80
60
40
20
0
PRE INDUCTION
POSTINDUCTION
POST SHOCK
1 min
2 min
3 min
4 min
5 min
10 MIN
GROUP P
GROUP T

TABLE VI: SYSTOLIC BLOOD PRESSURE VALUES OF THE TWO GROUPS

EVENTS	GROUP P	GROUP T	P VALUE	
PRE INDUCTION	110.44 ± 9.39	116.52 ± 11.97	0.0514	NS
POSTINDUCTION	108.4 ± 10.36	114.72 ± 16.28	0.1080	NS
POST SHOCK	116.64 ± 14.87	143.68 ± 21.73	0.0000	S
1 min	118.24 ± 13.69	150.52 ± 25.30	0.0000	S
2 min	116.04 ± 12.11	144 ± 29.71	0.0001	S
3 min	112.08 ± 10.67	144.16 ± 22.99	0.0000	S
4 min	110.4 ± 8.97	137.4 ± 21.15	0.0000	S
5 min	111.36 ± 8.95	131.44 ± 17 .61`	0.0000	S
10 min	111.32 ± 7.00	122.84 ± 16.78	0.0027	S

TABLE VII: COMPARISON OF SYSTOLIC BLOOD PRESSURE IN THE TWO GROUPS WITH THE BASELINE.

GROUP T	P VALUE	GROUP P	P VALUE
116.52 ± 11.97		110.44 ± 9.39	
114.72 ± 16.28	0.177	108.4 ± 10.36	0.19
143.68 ± 21.73	.0001	116.64 ± 14.87	0.02
150.52 ± 25.30	0.0001	118.24 ± 13.69	0.01
144 ± 29.71	0.0001	116.04 ± 12.11	0.03
144.16 ± 22.99	0.0001	112.08 ± 10.67	0.25
137.4 ± 21.15	0.0001	110.4 ± 8.97	0.49
131.44 ± 17 .61`	0.0001	111.36 ± 8.95	0.35
122.84 ± 16.78	0.015	111.32 ± 7.00	0.35

The systolic blood pressure in the group T increased after application of electric shock and the increase continued until 10 min after the application of electric shock (table VII). In the group P, there was an increase in the SBP until 3 min of application of electric shock. The increase was greater at 1 min of application of electric shock in the two groups. The trends of the SBP in the group T and that in the group P were significantly increased in the group T compared with the group P (table VI, graph 2).

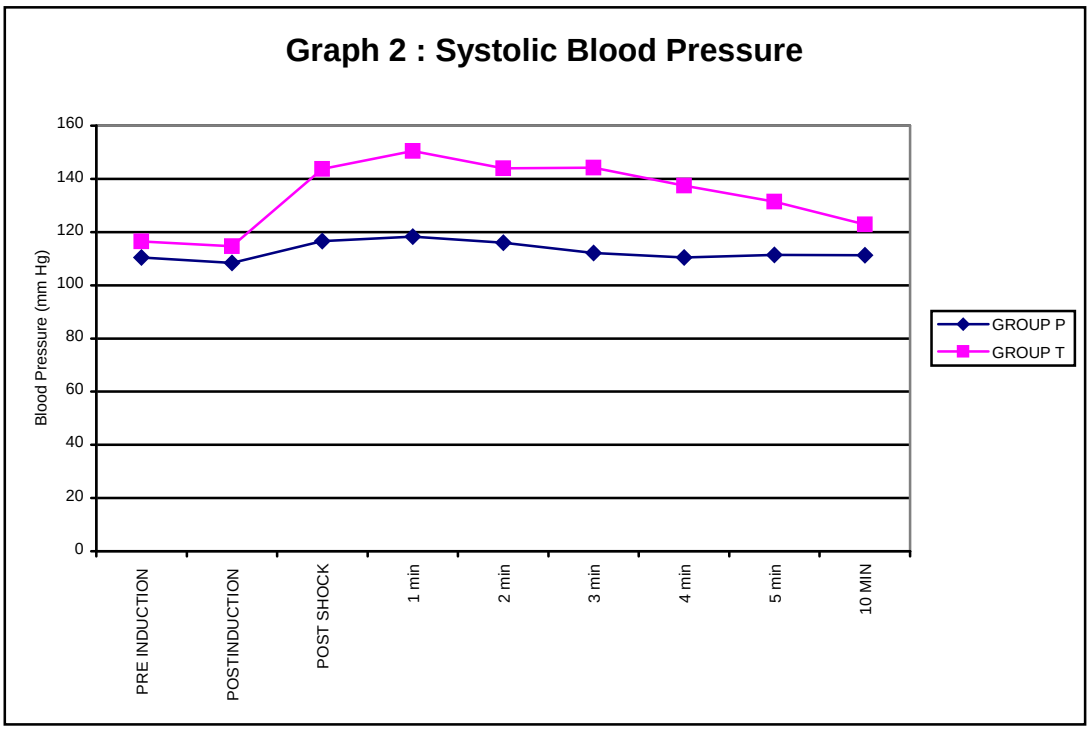

Graph 2 : Systolic Blood Pressure
Blood Pressure (mm Hg)
160
140
120
100
80
60
40
20
0
PRE INDUCTION
POSTINDUCTION
POST SHOCK
1 min
2 min
3 min
4 min
5 min
10 MIN
GROUP P
GROUP T

TABLE VIII: MEAN DIASTOLIC BLOOD PRESSURE IN THE TWO GROUPS

EVENTS	GROUP P	GROUP T	P VALUE	
PRE INDUCTION	71.64 ± 8.92	76.8 ± 9.57	0.0543	NS
POSTINDUCTION	70.56 ± 11.77	77.48 ± 12.24	0.0472	S
POST SHOCK	77.92 ± 13.96	92.8 ± 16.39	0.0012	S
1 min	76.92 ± 12.20	101.12 ± 17.53	0.0000	S
2 min	74.8 ± 10.32	97.04 ± 14.42	0.0000	S
3 min	71.88 ± 9.19	93 ± 14.09	0.0000	S
4 min	69.96 ± 8.26	89 ± 12.02	0.0000	S
5 min	69.8 ± 7.4	84.88 ± 11.88	0.0000	S
10 min	73.08 ± 8.73	81.16 ± 10.56	0.0049	S

TABLE IX: COMPARISON OF DIASTOLIC BLOOD PRESSURE IN THE TWO GROUPS WITH THE BASELINE.

GROUP T	P VALUE	GROUP P	P VALUE
76.8 ± 9.57		71.64 ± 8.92	
77.48 ± 12.24	0.307747	70.56 ± 11.77	0.327107
92.8 ± 16.39	0.0001	77.92 ± 13.96	0.019737
101.12 ± 17.53	0.0001	76.92 ± 12.20	0.030061
97.04 ± 14.42	0.0001	74.8 ± 10.32	0.097381
93 ± 14.09	0.0001	71.88 ± 9.19	0.456619
89 ± 12.02	0.0001	69.96 ± 8.26	0.237448
84.88 ± 11.88	0.000169	69.8 ± 7.4	0.187474
81.16 ± 10.56	0.01564	73.08 ± 8.73	0.216139

The diastolic blood pressure (DBP) in the thiopentone group increased after application of electric shock and the increase continued until 10 min after the application of electric shock (table IX). In the group P, there was an increase in the DBP until 1 min of application of electric shock. The increase was greater at 1 min of application of electric shock in the two groups. . The trends of the DBP in the group T and that in the group P were significantly increased in the group T compared with the group P (table VIII, graph 3).

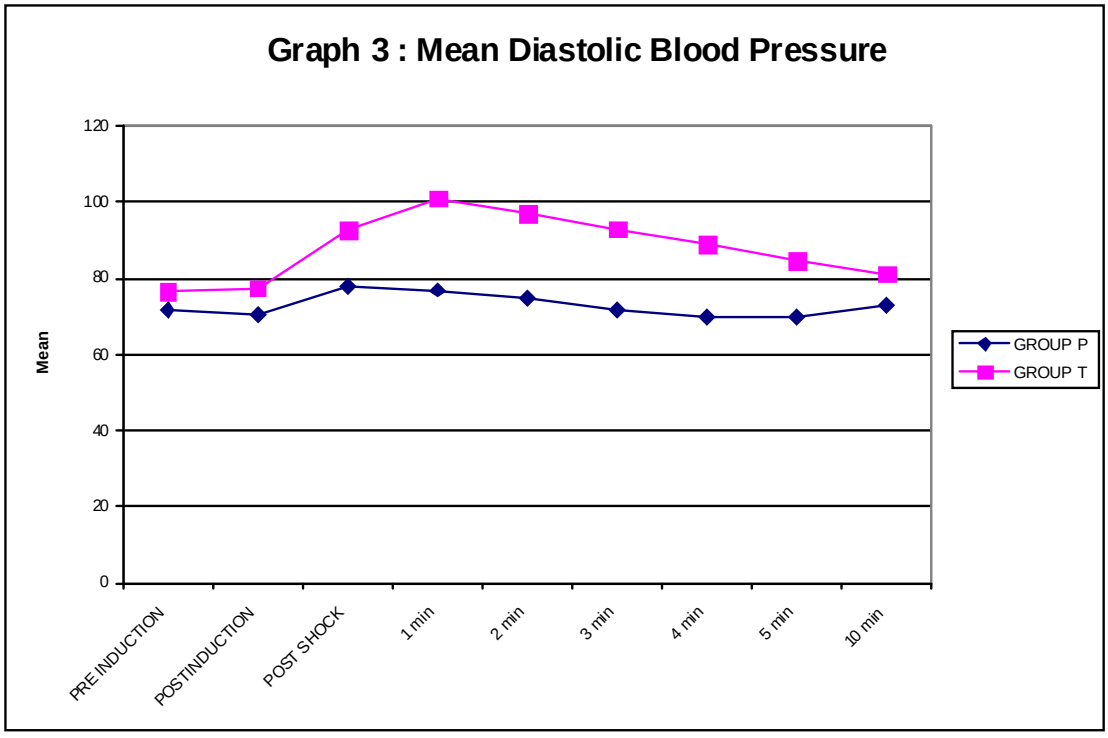

Graph 3 : Mean Diastolic Blood Pressure
Mean
120
100
80
60
40
20
0
PRE INDUCTION
POSTINDUCTION
POST SHOCK
1 min
2 min
3 min
4 min
5 min
10 min
GROUP P
GROUP T

TABLE X: MEAN ARTERIAL PRESSURE IN THE TWO GROUPS.

EVENTS	GROUP P	GROUP T	P VALUE	
PRE INDUCTION	85.76 ± 8.14	90.68 ± 9.32	0.0524	NS
POSTINDUCTION	83.72 ± 11.13	90.92 ± 13.3	0.0433	S
POST SHOCK	90.88 ± 14.12	108.28 ± 17.36	0.0003	S
1 min	91.92 ± 12.65	114.64 ± 20.95	0.0000	S
2 min	89.04 ± 11.11	117 ± 29.75	0.0001	S
3 min	85.48 ± 9.23	106.8 ± 16.11	0.0000	S
4 min	84.76 ± 8.98	103.6 ± 14.88	0.0000	S
5 min	83.68 ± 7.15	99.56 ± 12.99	0.0000	S
10 min	85.12 ± 8.6	95.8 ± 11.41	0.0005	S

TABLE XI: COMPARISON OF MEAN ARTERIAL PRESSURE IN THE TWO GROUPS WITH THE BASELINE.

GROUP T	P VALUE	GROUP P	P VALUE
90.68 ± 9.32		85.76 ± 8.14	
90.92 ± 13.3		83.72 ± 11.13	0.162307
108.28 ± 17.36	0.0001	90.88 ± 14.12	0.042645
114.64 ± 20.95	0.0001	91.92 ± 12.65	0.013588
117 ± 29.75	0.0001	89.04 ± 11.11	0.097947
106.8 ± 16.11	0.0001	85.48 ± 9.23	0.448619
103.6 ± 14.88	0.0001	84.76 ± 8.98	0.337316
99.56 ± 12.99	0.000251	83.68 ± 7.15	0.130323
95.8 ± 11.41	0.014041	85.12 ± 8.6	0.378521

The mean arterial pressure (MAP) in the group T increased after application of electric shock and the increase continued until 10 min after the application of electric shock (table XI). In the group P, there was an increase in the MAP until 1 min of application of electric shock. The increase was greater at 1 min of application of electric shock in the two groups. . The trends of the MAP in the group T and that in the group P were significantly increased in the group T compared with the group P (table X, graph 4).

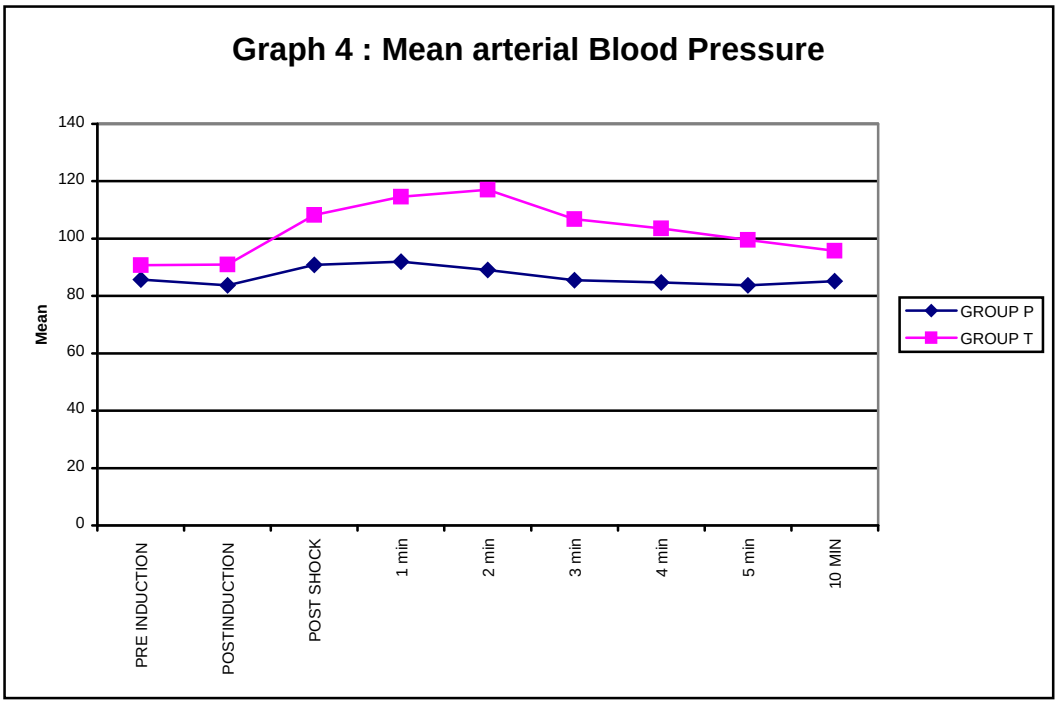

Graph 4 : Mean arterial Blood Pressure
Mean
140
120
100
80
60
40
20
0
PRE INDUCTION
POSTINDUCTION
POST SHOCK
1 min
2 min
3 min
4 min
5 min
10 MIN
GROUP P
GROUP T

TABLE XII: INCIDENCE OF SIDE-EFFECTS.

	Group P	**Group T**
Pain on injection	5	0
Vomiting	0	0
Hiccoughs	0	2
Involuntary movements	0	0

In the group P the incidence of pain on injection was 20 % and none had pain in the group T. Two patients had hiccough on group T induction and none in group P.

DISCUSSION

Electroconvulsive therapy has become a widely accepted treatment modality in psychiatric practice and its application is on a rise, especially when drug treatment fails to show appreciable progress. Safety of this treatment modality is improved by use of muscle relaxants after anaesthetizing patients with induction agents to which we refer to as “modified” electroconvulsive therapy. The attendant adverse cardiovascular consequences, in the form of sympathetic system stimulation, are yet poorly attenuated with the currently used induction agents, more commonly thiopentone.

The induction agent, propofol which has become a preferred induction agent in day care surgeries is known to produce hypotension on administration. The hypotensive effect of propofol is greater than that produced by thiopentone. This effect could be used to mitigate the hypertensive effect during electroconvulsive therapy following application of electric shock.

In this study we have compared the hemodynamic responses to electroconvulsive therapy with thiopentone and propofol as induction agents. The results of our study indicate that there a difference in the hemodynamic responses on induction with those two agents.

In our study we found that the mean heart rate in the propofol group and the thiopentone increased from the baseline after application of electric shock. However the rise was lesser in the propofol group than the thiopentone group. The heart rate reached the almost baseline in the propofol group after 10 min.

A similar comparative study of thiopentone and propofol for ECT was done by Saito and colleagues where apart from middle cerebral artery blood flow, haemodynamic parameters viz: HR and MAP where observed.[38] They found a similar increase in the heart rate in the thiopentone group but the reached the baseline at 5 min. whereas in the propofol group there was no significant increase.

Following induction with propofol, there was slight fall the systolic, diastolic and the mean blood pressure. This is attributed to its vasodilating property of propofol, which reduces the peripheral vascular resistance.

After application of the electric shock, the SBP, DBP and MAP increased significantly upto 10 min in the thiopentone group. In the propofol group, the increase in SBP, DBP and MAP was for 2, 1 and 1 min respectively. Propofol maintained a more stable blood pressure than thiopentone. These results are in similar with that seen in the study done by Saito.[38]

After application of the electric shock, there was a rise in the mean systolic blood pressure of approximately 10 mmHg (108.4 mmHg to 118.24 mmHg) in the propofol group. In comparison, in the thiopentone group the rise was 30 mmHg (116.52 to 150.52 mmHg). This rise was greater at 1 minute. The mean diastolic blood pressure rise in the propofol group was 7 mmHg (70.56 to 77.92 mmHg) as compared to 24 mmHg (77.48 to 101.12 mmHg) in the thiopentone group.

The mean arterial pressure in the propofol group increased by 8 mmHg (83.72 to 91.92 mmHg) in comparison to the rise in thiopentone group 27 mmHg (90.92 to 117 mmHg).

A comparative study between propofol and thiopentone for electroconvulsive therapy was done by Boey and Lai.[33] The rise in the heart rate, and the blood pressure was significantly less in the propofol group than the thiopentone group and the changes were greater at 1.5 min from the application of the shock.

In a study on electroconvulsive therapy Rasmussen et al have shown that after the electrical stimulus, there is a vagally mediated short lived bradycardia following sympathetically mediated tachycardia and rise in blood pressure.[37] The initial bradycardia was not noticed in any of the patient in our study. Premedication with intravenous glycopyrrolate could have aborted that phase in our study.

Villalonga et al studied the cardiovascular responses and anaesthetic recovery in electroconvulsive therapy with propofol or thiopentone.[32] They concluded that propofol provokes a slight hypotensive effect that could mitigate the hypertensive response to electroconvulsive therapy.

Mitchell P, Smythe G and Torda T have studied neuroendocrinal responses in 25 patients undergoing ECT under propofol or thiopentone anaesthesia. [35] They found that subjects given propofol had significantly reduced ACTH and cortisol responses compared to thiopentone. These humoral responses could have resulted in the lesser rise in the hemodynamic parameters in the propofol induced subjects.

Electroconvulsive therapy causes sympathetic system stimulation leading to hypertension and tachycardia immediately following application of electric stimulus. [5, 37] Severe elevations in blood pressure and heart rate would increase cardiac work load thus predisposing individuals to myocardial ischemia/infarction and also arrhythmias in

susceptible patients.[39] The incidence of such cardiovascular complication is expected to be on the rise, as there is an increasing indication of ECT in patients with secondary depression with comorbid illnesses.[40] From our study we find that, attenuation of the accompanying cardiovascular changes can be achieved more effectively with propofol than with thiopentone.

Pain on injection of propofol is a known side-effect with varying incidence. In our study, the incidence was 25 %. Various agents have been to attenuate this pain. None of them were used in this study as they cold have altered the results of the study. 2 patients in the thiopentone had hiccoughs following induction. No other side-effect or complication occurred during the study.

CONCLUSION

From our study we conclude that, when propofol is used as an induction agent for modified electroconvulsive therapy there is a better hemodynamic stability in comparison to thiopentone induction.

For the prospective use of this beneficial property of propofol to be used in patients with co-morbid cardiac illness undergoing electroconvulsive therapy definitive clinical trials are to be carried out.

SUMMARY

It is now a standard practice to administer electro convulsive therapy after administration of anaesthesia, in an effort to minimize the physiological sequelae and attendant complications of ECT. Until now short acting barbiturates, methohexital and thiopentone were commonly used for induction. The cardiovascular responses are poorly attenuated. Propofol provokes a slight hypotensive effect that could mitigate the cardiovascular response to ECT. Hence in this study we compared thiopentone and propofol as induction agents for ECT. Fifty patients undergoing ECT for the first session of ECT were randomly divided into two groups to receive the induction agent either thiopentone or propofol. The haemodynamic parameters namely HR, SBP, DBP and MAP were monitored after electrical stimulus every minute for five minutes and at ten minutes. Any side effects were also noted. All the haemodynamic parameters increased after electrical stimulus in both the groups. The rise was lesser in the propofol group than in patients induced with thiopentone. Propofol offers the superior haemodynamic stability during the procedure. In conclusion propofol is found to be a better induction agent for ECT with respect to haemodynamic stability compared to thiopentone. Propofol can be an induction agent of choice for ECT in patients with co morbid cardiovascular illness.

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INFORMED CONSENT FORM

A study, **"COMPARISON OF PROPOFOL AND THIOPENTONE ON HAEMODYNAMIC RESPONSES TO MODIFIED ELECTROCONVULSIVE THERAPY : A RANDOMIZED CONTROLLED TRAIL"** is being conducted by Dr. Rahul Desai, post graduate in anaesthesiology at J. N. Medical College Belgaum, Karnataka. Under guidance of **Dr. C.S. Sanikop** Prof. Dept. of Anaesthesiology, J. N. Medical College, Belgaum, under K.L.E.'s academy of Higher Education, Belgaum.

Respected Sir/ Madam we request you to participate in our study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you are suppose to answer to the best of your knowledge.

Your participation in this study is voluntary. Your decision whether or, not , to participate in the study will not affect your relationship with J.N.M.C. If you decide to participate you are free to withdraw at any point of time. The purpose of the study is to compare the effectiveness of propofol in maintaining the haemodynamic stability following shock during ECT.

Procedure involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail and investigated accordingly. You will receive one of the two study drugs (Inj. Thiopentone, Inj. Propofol) during your ECT session.

Benefits and Risks:

Propofol is known to produce faster onset, smoother induction and rapid recovery. However, it is known to cause hypotension, injection is slightly painful and very rarely known to cause anaphylaxis.

Alternatives:

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

Confidentiality:

All information collected about me during the course of the study will be kept confidential to the extent permitted by law. The code numbers will identify you in this study records and the information from this study may be published but your identity will be confidential in any publication.

Compensation:

In the event of injury, related to the study, treatment will be made available at KLES Hospital & MRC, Belgaum. No reimbursement, compensation or free medical care will be given, by law. If you are injured, you may contact Dr. Rahul Desai at Department of Anaesthesiology, KLE's Hospital & MRC, Ph. No. 0831-2473777.

Queries:

If you have any queries, in future or in case of study related injury or illness, you may contact. Dr. Rahul Desai at Department of Anaesthesiology, KLES Hospital & MRC, Ph No. 0831-2473777.

If you have any queries about your rights as a study subject, you may call Dr. V.D. Patil. Principal and Chairman. J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Ph. 0831-2473777 at J.N. Medical College, Belgaum.

CONSENT TO PARTICIPATE IN A RESEARCH STUDY:

I, Mr./ Mrs. _____

voluntarily agree to take part in this study, by signing this consent form I am not giving up my legal rights. I may withdraw at any time. I am signing after having read, or been read to me in the vernacular language including risks and the benefits and having all queries cleared.

_____ _____

Signature of the study patient

_____ _____

Name of Study patient Date

_____ _____

Signature of the legally authorized representative Date

_____ _____

Relationship with the patient

Name and Signature of Witness Date

Signature of investigator/ designee obtaining Date

PROFORMA

"COMPARISON OF PROPOFOL AND THIOPENTONE ON HAEMODYNAMIC RESPONSES TO MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CONTROLLED TRIAL".

Name: Age(in years) : Gender:

Ward: IP No. Religion:

Address:

On General Physical examination:

Weight: Height Temperature:

Pallor: Cyanosis: Pedal edema: Clubbing:

Pulse: BP: RR:

CVS:

Heart Sounds:

RS:

Breath Sounds: Trachea:

CNS:

SPINE:

PREVIOUS SURGERIES:

INVESTIGATIONS:

Hb %:

Urine routine: (Sugar, Albumin, Micro.)

Blood sugar

Serum creatinine

ECG

Chest X-RAY

ASA STATUS:

ANESTHETIC PROCEDURE:

Intravenous line will be secured using appropriate IV cannula and fluids will be started. All patients were pre medicated with inj. Glycopyrrolate .2 mg. just before induction. Pre induction base line values of HR, SBP, DBP were recorded.

Induction with one of the study drug, over 15 seconds will be carried out, either with Inj. Thiopentone 4 mg./kg or inj. Propofol 1.5mg./kg.

After noticing loss of eyelash reflex, succinylcholine 1 mg./kg intravenously was administered and patient was ventilated with 100% oxygen till the disappearance of fasciculations.

Electrical stimulus of 90 to 100 volts was applied by bilateral electrodes to the temporal regions till adequate response by a psychiatrist and then the patient was manually ventilated till the regain of consciousness with 100 % oxygen.

PR, SBP, DBP and oxygen saturation were recorded soon after induction and at 1 minute interval after electric shock for 5 minutes and then once at 5 minute interval, using a pulse oxymeter and a automated non invasive blood pressure apparatus.

Any adverse effects were also noted.

INDUCTION:

Premedication: Inj glycopyrrolate 0.2 mg iv

Group P: inj propofol ___ mg(1.5mg/kg)

Inj suxamethonium ___ mg(1mg/kg)

Group T: inj thipentone ___ mg (4mg/kg)

Inj suxamethonium ___ mg(1mg/kg)

Readings were recorded in the following manner:

Variables	**Pre Induction (Baseline) recordings**	**Following induction recordings**	**Post shock recordings in mins.**						
			0	**1**	**2**	**3**	**4**	**5**	**10**
HR (/min.)									
SBP (mm Hg.)									
DBP (mm Hg.)									
MAP (mm Hg.)									

Signature of staff in charge: