"COMPARISON OF EFFECT OF INTRAVENOUS ANAESTHETIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURING MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CLINICAL TRIAL"

By

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DISSERTATION

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Under the Guidance of

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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
SD	Seizure duration
Sl. No.	Serial Number
Wt	Weight in kilograms

ABSTRACT

BACKGROUND: With administration of ECT, blood pressure & heart rate steeply increase secondary to rise in plasma adrenaline and nor adrenaline levels. 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 Etomidate and Propofol on Seizure duration and haemodynamic parameters.

TYPE OF STUDY: Randomized clinical trial

METHODS AND MATERIALS: 40 patients between age the of 18 and 58 years of either gender, belonging to ASA Grade-I and II scheduled for modified ECT were included. Patients were allocated into two groups. Anaesthetic technique was standardized for all patients.

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

Patients were induced with one of the study drugs , i.e Inj. Etomidate 0.2 mg/kg (group E) or inj. propofol 1 mg/kg (group P). Blood pressure cuff applied to the lower limb was inflated to isolate the foot & permit accurate measurement of motor seizure duration.

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

Electrical stimulus was applied by bilateral electrodes to the temporal regions. Motor seizure duration was noted. HR, SBP, DBP and MAP 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 and the heart rate did not reach the baseline even after 10 min .There was a rise in the mean systolic blood pressure by approximately 7 mm of Hg in the group P compared to

4 mm of Hg in the group E. The mean diastolic blood pressure rise in the propofol group was 6 mm of Hg as compared to 5 mm of Hg in the group E. The mean arterial pressure in the both the groups increased by 7 mm of Hg. The parameters reached the baseline earlier with group P when compared to group E.

CONCLUSION: From our study we conclude that, the induction agent propofol could blunt the sympathetic response to electro-convulsive therapy more effectively than Etomidate whereas Etomidate significantly prolongs seizure duration when compared to propofol.

KEYWORDS: *Electroconvulsive therapy, Etomidate, propofol, seizure duration haemodynamic responses.*

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INTRODUCTION

Electroconvulsive therapy (ECT), also known as electroshock, is a well-established, albeit controversial, psychiatric treatment in which seizures are electrically induced in anesthetized patients for therapeutic effect. Today, ECT is most often used as a treatment for severe major depression which has not responded to other treatment,[1] and is also used in the treatment of mania (often in bipolar disorder), catatonia and schizophrenia.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. However the attendant cardiovascular effects are inadequately attenuated with its use.

Following application of the electrical 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 and congestive cardiac failure.[7] Hence use of agents which would attenuate this adverse physiologic consequence would be preferred.

Etomidate, a imidazole derivative is a short acting intravenous anaesthetic agent used for the induction of general anaesthesia , Administration of Etomidate in ECT has variable impact on seizure duration and haemodynamic parameters, when compared to propofol .Hence we make an attempt to compare the effect of these two drugs on seizure duration and haemodynamic response when administered during ECT.

OBJECTIVES

To evaluate the efficacy of Etomidate, compared to propofol administered as induction agent during modified electro-convulsive therapy, on Seizure duration and 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, Paracelsus induced seizures by administering Camphour by mouth to treat psychiatric illness. Until late 1930s, Metrazol was the agent used worldwide to induce convulsions.[8] Convulsive therapy was introduced in 1934 by Hungarian neuropsychiatrist Ladislas J Meduna who, believing that schizophrenia and epilepsy were antagonistic disorders, induced seizures in patients first with camphor and then cardiazol.[9]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.

In the 1940s and early 1950s ECT was usually given in unmodified form, that is, without muscle relaxants, and the seizure resulted in a full-scale convulsion. An anaesthetic was used by a few psychiatrists but most considered it unnecessary as the electric shock produced instant unconsciousness.[10]

A rare but serious complication of unmodified ECT was fracture or dislocation of the long bones, caused by the violence of the muscular contractions during the convulsion. In the 1940s psychiatrists began to experiment with curare, the muscle-paralysing South American poison, in order to modify the convulsions. The introduction in 1951 of succinylcholine, a safer synthetic alternative to curare, led to the more widespread use of modified ECT. A short-acting anaesthetic was usually given in addition to the muscle relaxant in order to spare patients from the terrifying feeling of suffocation that can be experienced with muscle relaxants.[10]

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.[11] 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.[12]

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 [13], Bodley showed that it was the cardiovascular system which fails.[14]

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.[15]

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[16]. 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 Martins' studies in 1970s diazepam was used as the anaesthetic agent for induction during electroconvulsive therapy for sometime. But the study by Pitts and Allen showed that use of diazepam was associated with postictal ECG abnormalities, and hence diazepam lost favour.[16]

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.[17]

Mackenzie N, Grant IS compared propofol with methohexitone and thiopentone for induction of anaesthesia in day care patients.[18] The conclusion of the study was, propofol was a suitable agent for day care 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.[19] A similar conclusion was also drawn by Rolly and Versichelen when they compared propofol and thiopentone for induction in unpremedicated patients.[20]

Rouse in 1988 compared propofol and methohexitone for electroconvulsive therapy and found that Propofol prevents the increase in arterial blood pressure after seizure.[21]

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.[22]

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.[23]

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.[24]

In a comparative study between propofol and thiopentone done by Gerald in 1993 for 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.[25]

Lindgren and colleagues in1993 studied the hemodynamic and catecholamine responses to induction and tracheal intubation with propofol and thiopentone.[26] 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.[27]

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.[28]

In 1994 Mårtensson B, et al compared the effect of propofol and methohexital as anesthetic agents for ECT on seizure duration, therapeutic outcome, and memory. They concluded that Propofol significantly reduced the seizure duration without reducing

the therapeutic outcome There were no significant differences between the two agents in effects on recovery times after anesthesia and on anterograde memory[29].

Michail et from their study concluded that Propofol and methohexital, decreased ECT-induced seizure duration compared to etomidate, hence etomidate may be a useful alternative to propofol and methohexital for ECT therapy[27]

A comparative study was done by Stadtland C et al , in which patients were switched from propofol to etomidate during an ECT course showed an increase in EEG and motor seizure duration.[30.] .

However Gazdag et al studying the effect of same drug showed that Etomidate was associated with a smaller increase in mean blood pressure compared to propofol[31].

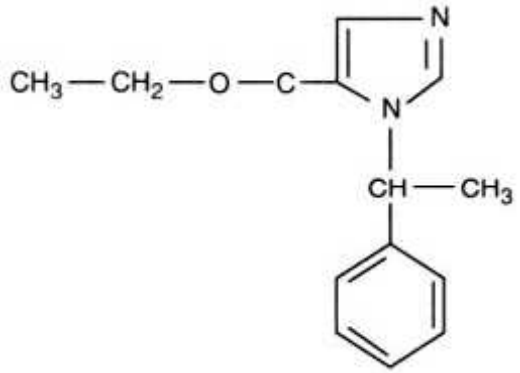
A retrospective study done by patel et al comparing effect of etomidate and propofol in ECT came to a conclusion that patients who received propofol had higher seizure threshold ,longer acute courses of ECT and consequently longer & costlier inpatient stays[32].

In 2006 khalid et al concluded that Etomidate has the distinct advantage over thiopental in producing seizures of adequate duration during ECT and should be used as first line measure in augmenting seizures in patients with high seizure thresholds[33].

A study of Rosa et al showed no haemodynamic changes in comparing ECT anaesthesia with etomidate and propofol[34]. Studies conducted so far have shown variable responses on haemodynamic parameters and seizure duration.

ETOMIDATE

Structure



Chemical name:

R-(+)-pentylethyl-1H-imidazole-5 carboxylate sulfate

History:

Etomidate (Amidate, Hypnomidate) was synthesized in 1964 and introduced into clinical practice in 1972. Its properties include hemodynamic stability, minimal respiratory depression, cerebral protection, and pharmacokinetics enabling rapid recovery following either a single dose or a continuous infusion. These beneficial properties led to widespread use of etomidate for induction, for maintenance of anesthesia, and for prolonged sedation in the critically ill. Anesthesiologists' enthusiasm for etomidate, however, was tempered by reports that the drug can cause temporary inhibition of steroid synthesis after both single doses and infusions. This effect, combined with other minor disadvantages (e.g., pain on injection, superficial thrombophlebitis, myoclonus, and a relatively high incidence of nausea and vomiting) led to several editorials questioning the role of etomidate in modern anesthetic practice. Use of the drug waned significantly following those editorials, but has been

expanding over the past several years owing to rediscovery of etomidate beneficial physiologic profile combined with a lack of any new reports describing clinically significant adrenocortical suppression

Physiochemical Properties:

Chemical formula:	C12H180.	Milky white liquid
Molecular weight:	342.36 kd.	Unstable in a neutral solution
PH range:	6.9	water insoluble

Formulations:

Each ml. of Etomidate (w/v) formulation contains

Etomidate : 2 mg /ml (Active ingredient)

Propylene glycol : 35 %

Osmolality : 4640 mOsm/L.

Mechanism of action:

Etomidate 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-subunit of GABA receptor sites on β2 and β3 sub-units of trans membrane domains have been shown to be critical for the hypnotic action of etomidate.

Pharmacokinetics

The pharmacokinetics of etomidate has been calculated following single bolus doses and following continuous infusion.

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

- Rapid initial distribution from the blood to highly perfused tissues (Viz., brain, heart, lung, liver) t ½ α - 2.7 mins
- Redistribution and metabolic clearance, t ½ β - 29 mins.
- Slow return from poorly perfused tissues to blood t ½ 2.9 – 5.3 hrs.

The context sensitive half life of etomidate is less than 10 mins. 75 % of etomidate is plasma protein bound. Clearance of etomidate by liver is extremely high 18 to 25 ml/kg min-1. The volume of distribution at steady state is 2.5 to 4.5 L/kg. Drugs affecting hepatic blood flow will alter its elimination half-life. Since redistribution is the mechanism whereby the effect of a bolus of etomidate is dissipated, hepatic dysfunction should not appreciably alter recovery from its hypnotic effect .Pathologic conditions altering serum proteins (e.g., hepatic or renal disease) vary the amount of the free (unbound) fraction and may cause a given dose to have an exaggerated pharmacodynamic effect.

In patients with cirrhosis, the volume of distribution is doubled while clearance is normal, the result being an elimination half-life that is twice normal. It is likely that the initial distribution half-life and clinical effect are unaffected. Increasing age is associated with a smaller initial volume of distribution and a decreased clearance of etomidate.

Etomidate is metabolized in the liver primarily by ester hydrolysis to the corresponding carboxylic acid of etomidate (major metabolite) or by N-dealkylation. The main metabolite is inactive.Only 2 percent of the drug is excreted unchanged; the rest being excreted as metabolites by the kidney (85 percent) and bile (13 percent).

Pharmacodynamics:

1) **Central Nervous system:**

Etomidate is primarily a hypnotic. The onset of hypnosis after doses of 0.3 mg kg-1 is rapid (one arm brain circulation).Etomidate has no analgesic activity.

Plasma levels required during the maintenance of anesthesia are approximately 300 to 500 ng/ml, those for sedation 150 to 300 ng/ml, and those for awakening 150 to 250 ng/ml. At a dose of 0.2 to 0.3 mg/kg, etomidate reduces CBF (by 34 percent) and CMRO2 (by 45 percent) without altering mean arterial pressure. Thus, cerebral perfusion pressure is maintained or increased, and there is a beneficial net increase in the cerebral oxygen supply/demand ratio.

Etomidate given in doses sufficient to produce EEG burst suppression acutely lowers ICP by up to 50 percent in patients with already raised ICP, returning raised ICP to almost normal values. The decrease in ICP is maintained in the period immediately following intubation To maintain the effects of etomidate on ICP, high infusion rates (60 mg/kg/min) are necessary. In contrast to the situation with other neuroprotective agents such as thiopental, reduction of ICP and maintenance of burst suppression are not associated with a drop in mean arterial blood pressure. Since cerebral vascular reactivity is still maintained following etomidate administration, hyperventilation theoretically may further reduce ICP when used in conjunction with

etomidate

A dose of 0.3 mg/kg rapidly reduces intraocular pressure by 30 to 60 percent. The decrease in intraocular pressure following a single dose lasts 5 minutes, but the reduction may be maintained by an infusion of 20 mg/kg/min.

Etomidate produces changes in the EEG similar to those produced by the barbiturates. There is an initial increase in a amplitude with sharp bursts followed by mixed d-u waves, with d-wave activity predominating prior to the onset of periodic burst suppression. The absence of b waves in the initial phase of induction with etomidate is the major difference in EEG changes as compared with thiopental. Etomidate has been associated with grand mal seizures and has been shown to produce increased EEG activity in epileptogenic foci. This has proved useful for intraoperative mapping of seizure foci prior to surgical ablation.

Etomidate is also associated with a high incidence of myoclonic movement, but the myoclonus is not associated with seizure-like EEG activity. The myoclonic movement is believed to result from activity either in the brain stem or in deep cerebral structures.The effect of etomidate on auditory evoked potentials is similar to that produced by the inhaled anesthetics

2) **Cardiovascular system:**

An induction dose of 0.3 mg/kg of etomidate given to cardiac patients for noncardiac surgery results in almost no change in heart rate, mean arterial pressure, mean pulmonary artery pressure, pulmonary capillary wedge pressure, central venous pressure, stroke volume, cardiac index, and pulmonary and systemic vascular resistance.

A relatively large dose of etomidate, 0.45 mg/kg (which is 50 percent larger than a normal induction dose), also produces minimal changes in cardiovascular parameters. In patients with ischemic heart disease or valvular pathology, etomidate (0.3 mg/kg) produces similar minimal alterations in cardiovascular parameters. In patients with mitral or aortic valve pathology, etomidate may produce greater changes in mean arterial pressure (an approximate 20 percent decrease) than in patients without cardiac valvular disease.

Following induction (18 mg) and infusion (2.4 mg/min), etomidate produces a 50 percent decrease in myocardial blood flow and oxygen consumption and a 20 to 30 percent increase in coronary sinus blood oxygen saturation. Myocardial oxygen/supply demand ratio is thus well maintained.

The hemodynamic stability seen with etomidate may be due in part to its unique lack of effect both on the sympathetic nervous system and on baroreceptor function. However, etomidate, because of its lack of analgesic efficacy, may not totally ablate the sympathetic response to laryngoscopy and intubation. Thus, for the smoothest hemodynamic induction/intubation sequence, a low dose (1.5 to 5.0 mg/kg) of fentanyl is often combined with etomidate.

3) **Respiratory system:**

Etomidate has minimal effect on ventilation. It does not induce histamine release either in normal patients or in patients with reactive airways disease. Ventilatory response to carbon dioxide is depressed by etomidate, but the ventilatory drive at any given carbon dioxide tension is greater than that following an equipotent dose of methohexital.

Induction with etomidate produces a brief period of hyperventilation, sometimes followed by a similarly brief period of apnea, which results in a slight (±15 percent) increase in PaCO2 but no change in PaO2.Hiccups or coughing may accompany etomidate induction, with an incidence similar to that following methohexital induction

4) **Effect on adrenocortical function:**

The specific endocrine effects manifested by etomidate are a dose-dependent reversible inhibition of the enzyme 11β-hydroxylase, which converts 11-deoxycortisol to cortisol, and a relatively minor effect on 17-α-hydroxylase . This results in an increase in the cortisol precursors 11-deoxycortisol and 17-hydroxyprogesterone as well as an increase in adrenocorticotropic hormone (ACTH). The blockade of 11-β-hydroxylase (and to a lesser extent 17-α-hydroxylase) appears to be related to the free imidazole radical of etomidate-binding cytochrome P450. This results in inhibition of ascorbic acid resynthesis, which is required for steroid production in humans.The blockade of the cytochrome P450-dependent enzyme 11-β-hydroxylase also results in decreased mineralocorticoid production and an increase in intermediaries (11-deoxycorticosterone). Vitamin C supplementation restores cortisol levels to normal following use of etomidate.

However, the universal lack of demonstrable negative effect from temporary adrenocortical suppression associated with induction doses of etomidate in any study, as well as the finding that mean cortisol levels usually remain in the low normal range after etomidate induction, suggests that the issue of temporary adrenocortical suppression following induction doses may not be clinically significant.

Other miscellaneous effects:

1 Nausea and vomiting, pain on injection, myoclonic movement and hic-cups. Superficial thrombophlebitis of the vein used may occur 48 to 72 hours after etomidate injection.

2 Etomidate reduces the ED50 of pancuronium and therefore appears to enhance the neuromuscular blockade of nondepolarizing neuromuscular blockers.

3 Hepatic function is unaltered by etomidate.

4 In vitro, etomidate inhibits aminolivulinic acid synthetase, but it has been administered to patients with porphyria without inducing an acute attack of porphyria.

Presentation:

Etomidate is available as 2 mg/ml emulsion in 10ml .In Europe, new formulation in lipid emulsion also available, in which emulsion contains medium and long chain triglycerides.

Dosage:

Induction of anesthesia: 0.2 – 0.6 mg/kg IV

Sedation: 5 to 10 µg kg–1 min

Maintenance of anesthesia: 10 µg kg–1 min–1 IV with N2O and an opiate.

Uses:

1. For induction and maintenance of general anaesthesia for patients with cardiovascular disease, reactive airways disease, intracranial hypertension, or any combination of pathologies indicating the need for an induction agent with limited or beneficial physiologic side effects

2. For cardioversion, in hemodynamically unstable patients,

3. For day care surgery as it has rapid recovery

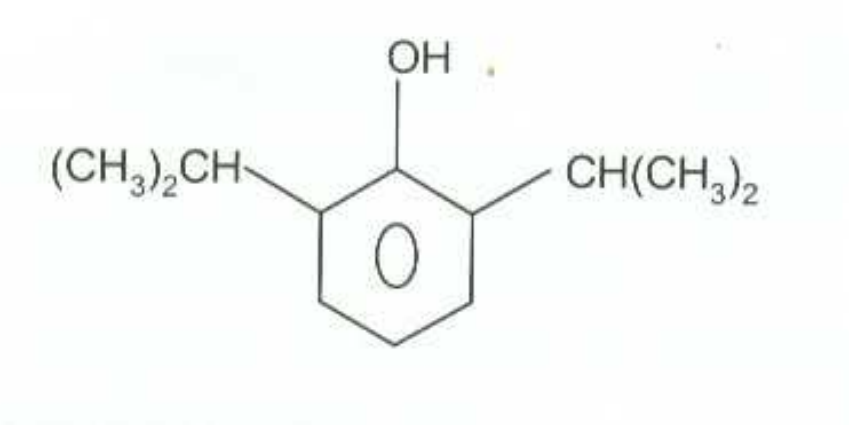
4. In patients with porphyria and in those patients where thiopentone is contraindicated

5. Short-term sedation for those requiring sedation following an acute myocardial infarction or with unstable angina for a minor operative procedure or for intubation both in the emergency room and the ICU.

6. Electroconvulsive therapy.

PROPOFOL

Structure



Chemical name:

2-6, di-isopropyl phenol

History:

Propofol was first introduced clinically by Ray and Rolly in 1977.A 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 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.

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 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.

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 at KLE'S Prabhakar kore Hospital & MRC. Forty adult patients between the age group of 18-58 years belonging to ASA grade I and II, taking ECT for first time, of either gender and with no absolute contraindication to ECT were included. Informed written consent was obtained from the patient`s close relative.

STUDY PERIOD: January 2009 –December 2009.

A sample size of 20 in each group was calculated. It was calculated by taking a difference of seizure duration of 12 seconds as significant, with confidence interval of 95% (Z_{α} =1.96) and the power of study as 80% (Z_{β}=0.84).

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 of 20 patients each (odd in patient no to Etomidate group & even in patient no to Propofol group)

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 Etomidate (0.2mg/kg) or propofol (1 mg/kg) depending on the group allocated.

Group T (Etomidate):

Patients in this group received Etomidate (0.2 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 mg /kg) slowly over 15 seconds. Induction was confirmed by loss of eye lash reflex.

After noticing of loss of eyelash reflex, blood pressure cuff applied to the lower limb was inflated to isolate the foot & permit accurate measurement of motor seizure duration.

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 face 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.

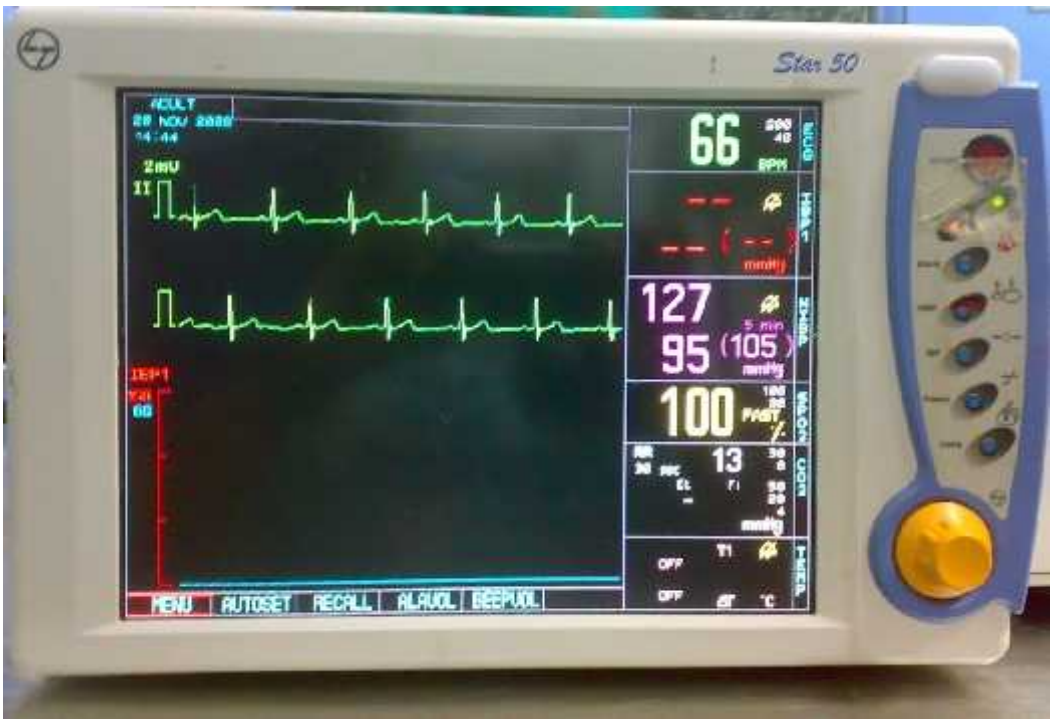
MONITORING:

Seizure duration was noted in all patients. 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).



L & T Monitor (Star 50)

ECT Machine

Etomidate ampoule (10ml)

Propofol 1% Vial (10 ml)

RESULTS

In this comparative study, 40 patients (20 in each group) undergoing ECT were randomly selected. All patients in both the groups got induced with the calculated dose of the induction agents.

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

	Group E (Mean ± SD)	**Group p** (Mean ± SD)	**P VALUE**
Age (years)	28.6 ± 10.56	34.25 ± 14.02	0.1582
Weight(kg)	48.90 ± 5.63	51.40± 12.60	0.4229

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 E		**Group P**	
		%		**%**
Male	10	50%	11	55%
Female	10	50%	9	45%

TABLE III: DISTRIBUTION OF DIAGNOSIS IN THE TWO GROUPS

	Group E		**Group P**	
		%		**%**
Schizophrenia	10	50	8	40
Depression	3	15	3	15
catatonia	3	15	2	10
Mania	2	10	3	15
Psychosis	2	10	4	20

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 SEIZURE DURATION

	Group E (Mean ± SD)	**Group P** (Mean ± SD)	**P VALUE**
Seizure duration (in seconds)	51.25± 9.01	38.30±9.92	0.00011

The mean seizure duration in Group E (51.25± 9.01 sec) is greater than in Group P (38.30±9.92 sec) and clearly statistically significant.

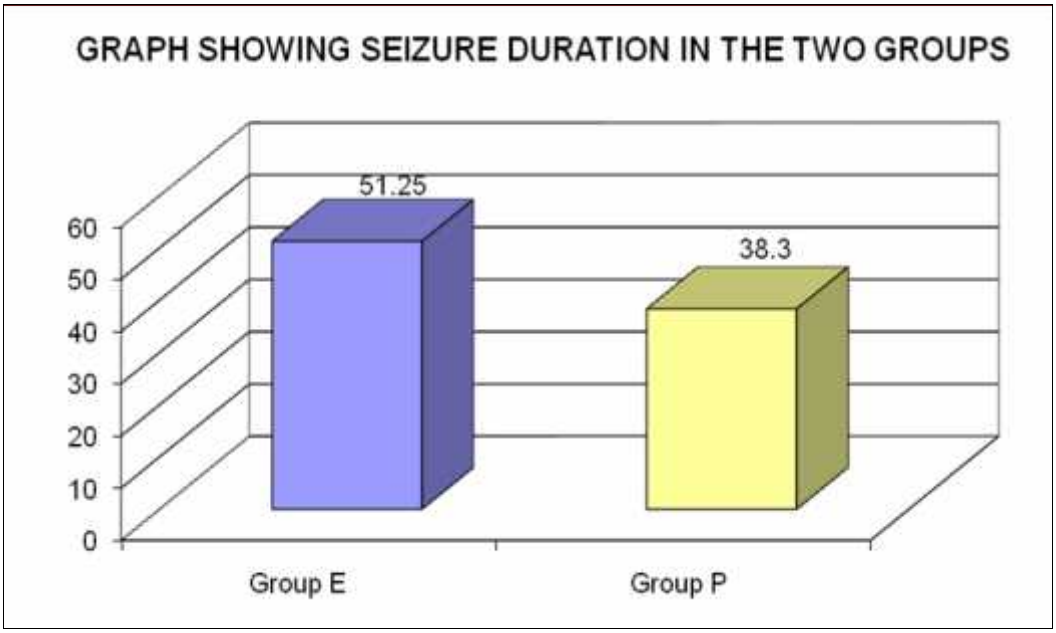


TABLE V: MEAN HEART RATE VALUES IN BOTH GROUPS:

EVENTS	GROUP E	GROUP P	P VALUE	Inference
PRE INDUCTION	78.40 ± 7.00	84.05± 13.65	0.108	NS
POSTINDUCTION	83.55± 12.12	85.25 ±16.55	0.712	NS
POST SHOCK	85.45 ±12.36	93.35 ± 20.63	0.150	NS
1 min	89.30 ± 16.21	96.70 ± 24.31	0.264	NS
2 min	87.20 ± 12.16	97.70 ± 25.49	0.104	NS
3 min	84.85±11.06	94.00 ± 20.14	0.082	NS
4 min	84.55 ± 9.21	97.70 ± 25.36	0.035	S
5 min	83.20 ± 8.22	97.00 ± 23.91	0.019	S
10 min	82.95 ± 7.78	93.60 ± 21.59	0.044	S

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

GROUP E	P VALUE	GROUP P	P VALUE
78.40 ± 7.00		84.05± 13.65	
83.55± 12.12	0.0060	85.25 ±16.55	0.1632
85.45 ±12.36	0.0014	93.35 ± 20.63	0.0054
89.30 ± 16.21	0.0027	96.70 ± 24.31	0.0014
87.20 ± 12.16	0.0005	97.70 ± 25.49	0.0021
84.85±11.06	0.0022	94.00 ± 20.14	0.0013
84.55 ± 9.21	0.0012	97.70 ± 25.36	0.0067
83.20 ± 8.22	0.0025	97.00 ± 23.91	0.0038
82.95 ± 7.78	0.0031	93.60 ± 21.59	0.0147

The mean heart rates in the two groups are shown in the table IV. The heart rate in the both groups significantly increased after application of electric shock, the increase continued for 3 minutes after the electric shock but does not reach the baseline even at 10 mins. The heart rate trend in the group E and that in the group P were significantly different and the values immediately after applications of electric shock were significantly higher with the group P compared with the group E (table V,graph 1).

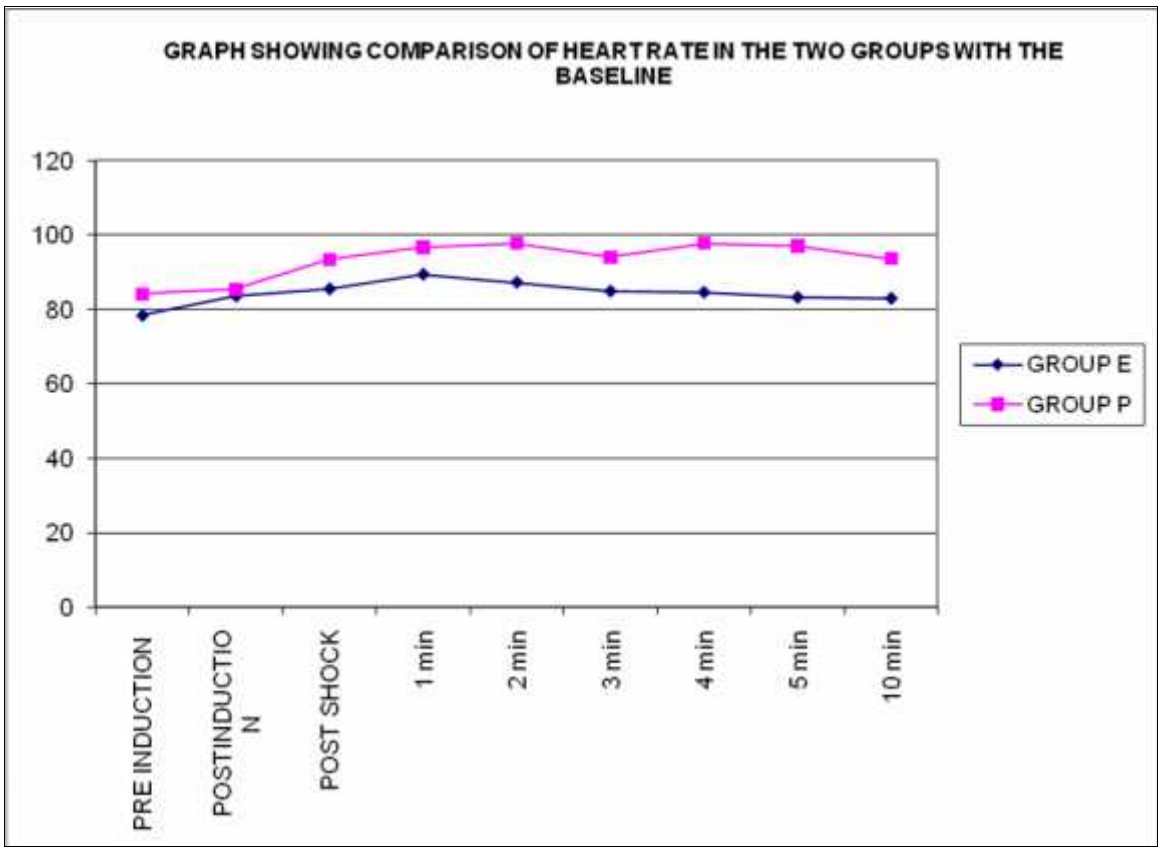


TABLE VII: SYSTOLIC BLOOD PRESSURE VALUES OF THE TWO GROUPS

EVENTS	GROUP E	GROUP P	P VALUE	Inference
PRE INDUCTION	124.35 ± 13.08	124.60 ± 17.77	0.9599	NS
POSTINDUCTION	124.80 ± 11.01	121.20 ± 17.14	0.4343	NS
POST SHOCK	128.50 ± 12.83	131.50 ± 31.65	0.6967	NS
1 min	129.90 ± 12.69	130.65 ± 22.49	0.8973	NS
2 min	131.50 ± 13.65	132.70± 24.81	08507	NS
3 min	129.55 ± 11.55	124.75 ± 20.10	0.3603	NS
4 min	127.25± 13.43	124.80± 20.25	0.6546	NS
5 min	125.35 ± 12.24	122.75 ± 18.97`	0.6096	NS
10 min	124.90± 12.15	121.80 ± 18.23	0.5306	NS

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

GROUP E	P VALUE	GROUP P	P VALUE
124.35 ± 13.08		124.60 ± 17.77	
124.80 ± 11.01	0.3836	121.20 ± 17.14	0.0412
128.50 ± 12.83	0.0030	131.50 ± 31.65	0.0222
129.90 ± 12.69	0.0146	130.65 ± 22.49	0.0473
131.50 ± 13.65	0.0103	132.70± 24.81	0.4377
129.55 ± 11.55	0.0073	124.75 ± 20.10	0.4844
127.25± 13.43	0.0423	124.80± 20.25	0.4788
125.35 ± 12.24	0.1919	122.75 ±18.97	0.3106
124.90± 12.15	0.2901	121.80 ± 18.23	0.2138

The systolic blood pressure in the group E increased after application of electric shock and the increase continued until 4 min after the application of electric shock (table VII). In the group P, there was an increase in the SBP until 2 min of application of electric shock. The increase was greater at 2 min of application of electric shock in the two groups. (table VI, graph 2).

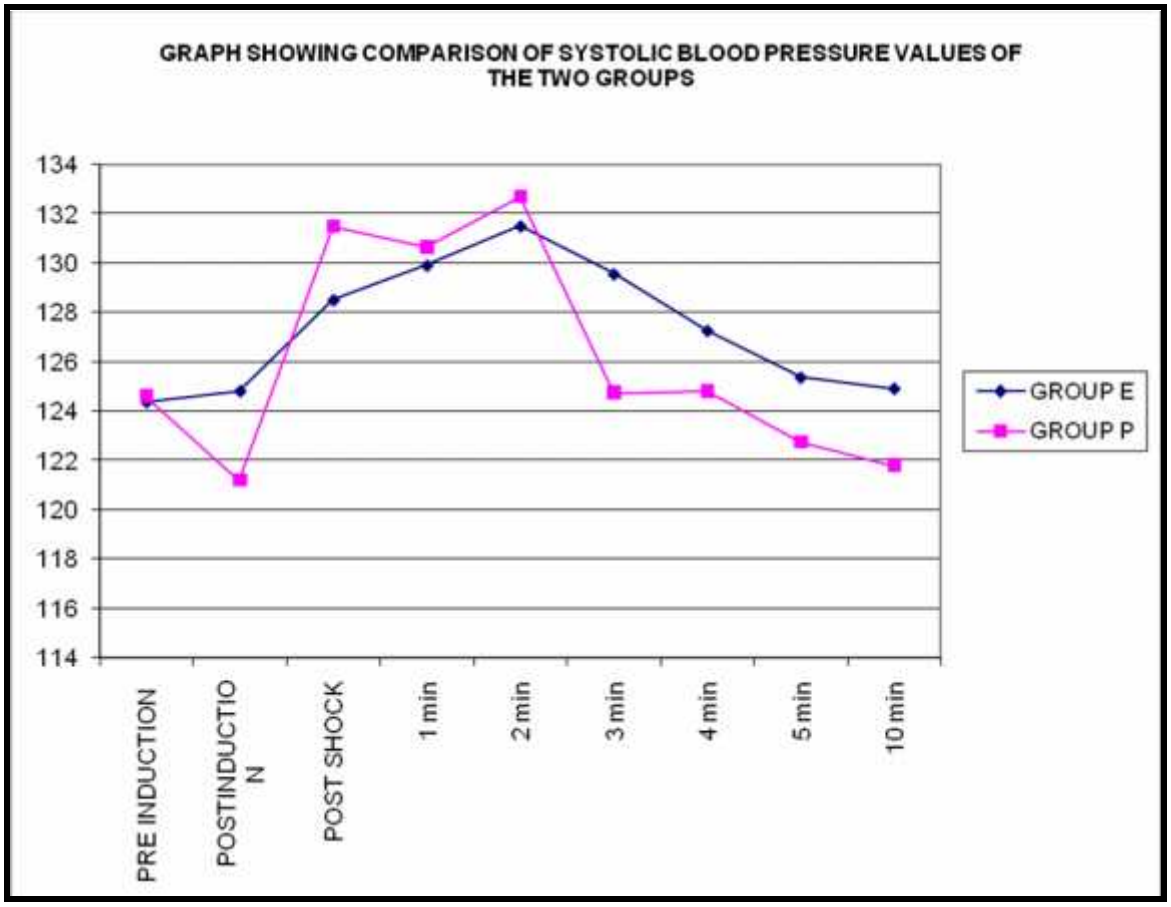


TABLE IX: MEAN DIASTOLIC BLOOD PRESSURE IN THE TWO GROUPS

EVENTS	GROUP E	GROUP P	P VALUE	Inference
PRE INDUCTION	76,40 ± 7.21	80.35 ±13.46	0.2545	NS
POSTINDUCTION	78.05 ± 7.56	77.20 ± 14.11	0.8136	NS
POST SHOCK	81.00 ± 9.51	86.25 ± 24.74	0.3813	NS
1 min	82.50 ± 10.50	85.90 ± 22.36	0.5419	NS
2 min	79.55 ± 6.87	87.20 ± 21.24	0.1336	NS
3 min	79.55 ± 5.38	76.70± 18.25	0.5070	NS
4 min	79.10 ± 5.41	75.65± 16.55	0.3812	NS
5 min	75.40 ± 8.00	75.35 ± 17.92	0.9910	NS
10 min	74.20 ± 6.41	75.65 ± 15.16	0.6958	NS

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

GROUP E	P VALUE	GROUP P	P VALUE
76,40 ± 7.21		80.35 ±13.46	
78.05 ± 7.56	0.1385	77.20 ± 14.11	0.0248
81.00 ± 9.51	0.0106	86.25 ± 24.74	0.0483
82.50 ± 10.50	0.0031	85.90 ± 22.36	0.0465
79.55 ± 6.87	0.0354	87.20 ± 21.24	0.0293
79.55 ± 5.38	0.0407	76.70± 18.25	0.1251
79.10 ± 5.41	0.0414	75.65± 16.55	0.0591
75.40 ± 8.00	0.2744	75.35 ± 17.92	0.0570
74.20 ± 6.41	0.0629	75.65 ± 15.16	0.0651

The diastolic blood pressure (DBP) in the group E increased after application of electric shock and the increase continued until 4 min after the application of electric shock (table IX). In the group P, there was an increase in the DBP until 2 min of application of electric shock .(table VIII, graph 3).

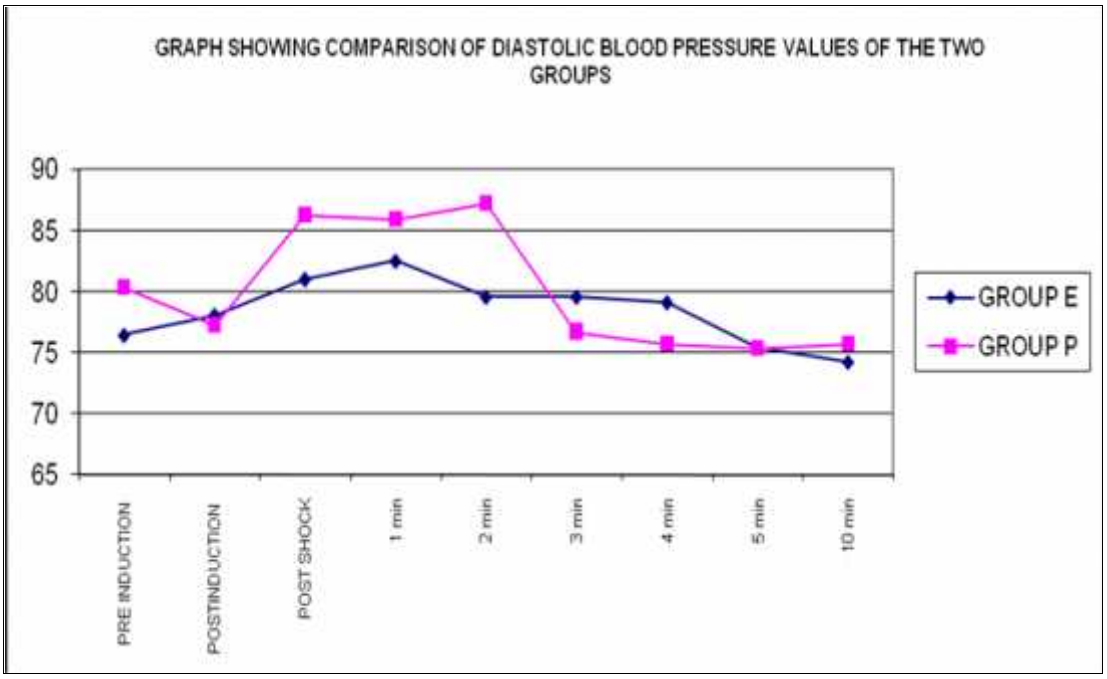


TABLE XI: MEAN ARTERIAL PRESSURE IN THE TWO GROUPS.

EVENTS	GROUP E	GROUP P	P VALUE	Inference
PRE INDUCTION	91.65 ± 12.95	92.60 ± 15.45	0.8342	NS
POSTINDUCTION	93.30 ± 9.00	90.15 ± 13.77	0.3972	NS
POST SHOCK	98.05 ± 11.28	99.00± 20.78	0.8436	NS
1 min	99.30 ± 9.27	98.30 ± 22.23	0.8537	NS
2 min	98.80 ±9.02	100.55 ± 25.79	0.7761	NS
3 min	96.30 ± 8.83	90.45 ± 19.73	0.2337	NS
4 min	94.55 ± 10.44	90.95 ± 18.92	0.4608	NS
5 min	91.60 ± 10.00	88.40 ± 19.36	0.5153	NS
10 min	91.35 ± 9.69	87.20 ± 18.21	0.3738	NS

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

GROUP E	P VALUE	GROUP P	P VALUE
91.65 ± 12.95		92.60 ± 15.45	
93.30 ± 9.00	0.2148	90.15 ± 13.77	0.0429
98.05 ± 11.28	0.0035	99.00± 20.78	0.0383
99.30 ± 9.27	0.0005	98.30 ± 22.23	0.0333
98.80 ±9.02	0.0007	100.55 ±25.79	0.0400
96.30 ± 8.83	0.0488	90.45 ± 19.73	0.2680
94.55 ± 10.44	0.0472	90.95 ± 18.92	0.3287
91.60 ± 10.00	0.4880	88.40 ± 19.36	0.1231
91.35 ± 9.69	0.4287	87.20 ± 18.21	0.0587

The mean arterial pressure (MAP) in the group E increased after application of electric shock and the increase continued until 4 min after the application of electric shock (table XI). In the group P, there was an increase in the MAP until 2 min of application of electric shock.. The trends of the MAP in the group E and that in the group P were significantly increased in the group E compared with the group P (table X, graph 4).

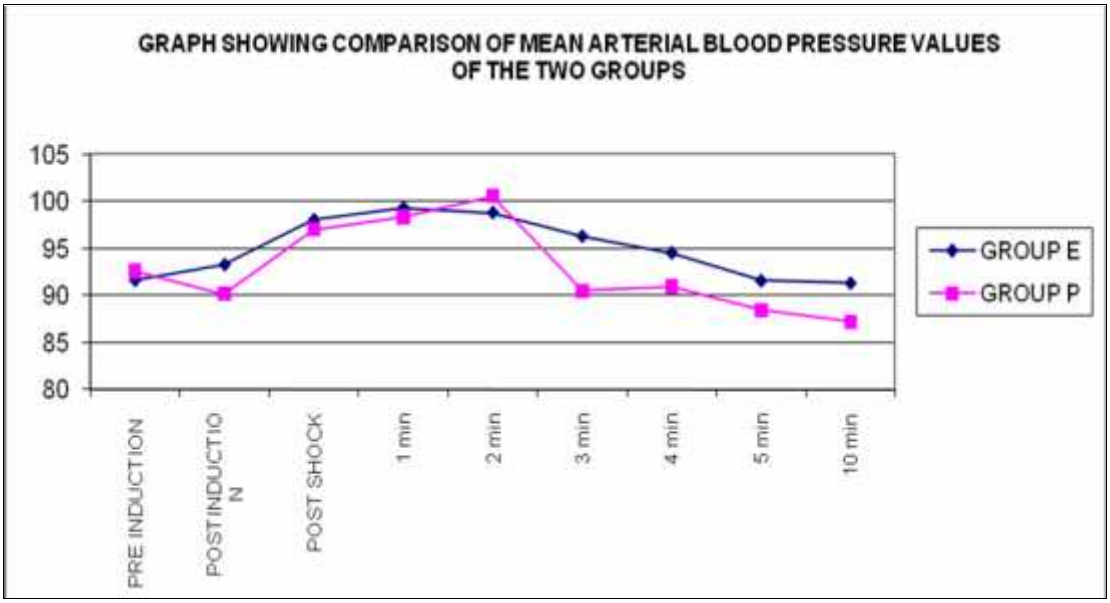


TABLE XIII: INCIDENCE OF SIDE-EFFECTS.

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

In the group P the incidence of pain on injection was 25 % and none had pain in the group E.

DISCUSSION

ECT has a well-established role in the management of patients who have not responded to psychopharmacological treatment [35,36,37]. Many studies documenting the efficacy of ECT for depressive illness have been published, finding ECT superior to medications in the treatment of patients with severe depressive illness[35], particularly those with psychotic and suicidal symptoms [38].

The procedure itself consists of programmed electrical stimulation of the central nervous system to initiate seizure activity. In terms of haemodynamic effects, seizure activity causes an initial parasympathetic discharge, later followed by sympathetic discharge.

With the introduction of intravenous anaesthetic agents, neuromuscular blockade and assisted or controlled ventilation with 100% oxygen in 1963, anaesthesia has brought ECT into a new dimension in terms of patient comfort as well as amnesia during the procedure [39]. The perfect induction agent for ECT would ensure rapid unconsciousness, be painless on injection, have no haemodynamic effects, would not affect seizure duration or amplitude, provide rapid recovery and be inexpensive [39].

The search for an ideal anaesthetic agent for ECT has been an ongoing process. Most of the anaesthetic agents used possess anticonvulsant properties because of their effects on the gamma-aminobutyric acid receptors [40,41] .

For several years, Etomidate has been under-utilized due to its feared complications of adrenal suppression and anaphylaxis. In the past decade, there has

been a resurgence of interest in etomidate, especially with the introduction of the drug in lipid formulation designed to reduce the problems of thrombophlebitis, pain on injection and haemolysis. Etomidate has good cardiovascular stability and allows rapid recovery. It has also been shown to prolong seizure duration in elderly seizure-resistant patients undergoing ECT [42] and has been suggested as an alternative anaesthetic agent for the procedure [43,44].

Propofol has been used as an induction agent for ECT, as it is an ultra short-acting anaesthetic agent with good recovery profile, including an earlier return of cognitive function [45] .Its potent anticonvulsant properties may be problematic for certain seizure-resistant individuals. Propofol which has become a preferred induction agent in day care surgeries is known to produce hypotension. The hypotensive effect of propofol is greater than that produced by thiopentone. This effect can be used to mitigate the hypertensive effect during electroconvulsive therapy following application of electric shock.

In this study we have compared the seizure duration and hemodynamic responses to electroconvulsive therapy with Etomidate and propofol as induction agents. The results of our study indicate that there are differences in seizure duration and the hemodynamic responses on induction with these two agents.

In our study the mean seizure duration was significantly prolonged in Etomidate group (51.25± 9.01 secs) when compared to propofol group (38.30±9.92 secs).The seizure duration was defined as time interval between administration of electrical stimulus and loss of visible fasciculation's in the isolated limb. The aim of ECT is to obtain generalized convulsions over 20 seconds. Although there is no

beneficial effect with only one seizure, clinical improvement can be observed with a total seizure time over 210 seconds.

In a similar study ,Grati L et al Compared the effects between etomidate & propofol for anaesthesia during ECT in which they observed that duration of seizures was significantly prolonged in former group[46].

A switch from propofol to Etomidate during ECT course increases EEG and motor seizure duration was a significant finding in a study carried out by Stadland et al as in our study[30].

Etomidate has the distinct advantage of producing seizures of adequate duration during ECT and should be used as first line measure in augmenting seizures in patients who have very high seizure thresholds was the conclusion derived from a study carried out by khaleed et al[33]

A retrospective study done by patel et al observed that patients who received propofol had longer courses of ECT and, consequently longer & costlier inpatients stays and concluded that Etomidate could be an alternative induction agent[32].

Mean seizure duration was lowest for propofol. However, mean stimulus charge was highest in the propofol group ($p<0.0001$) who required a greater increase in stimulus charge during the course of treatment and also experienced a greater proportion of failed seizures (</=15 s on EEG). Use of propofol may be associated with longer treatment course that could result in extra cost was a significant observation from a retrospective study by eranti et al[47].

Mitchell P, Smythe G and Torda T have studied neuroendocrinal responses in 25 patients undergoing ECT under propofol or thiopentone anaesthesia. [48] .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.

After application of the electric shock, there was a rise in the mean systolic blood pressure of approximately 7 mm of Hg (124.6 mmHg to 131.50 mmHg) in the propofol group. In comparison, in the etomidate group the rise was 4 mm of Hg (124.8 to 128.50 mmHg). The mean diastolic blood pressure rise in the propofol group was 6 mm of Hg (80.35 to 86.25 mmHg) as compared to 5 mm of Hg (76.40 to 81.00 mmHg) in the etoimdate group. The mean arterial pressure in the both the groups increased by 7 mm of Hg.

Although significant increases in mean blood pressure values were observed after ECT with both the agents, increase in blood pressure was slightly higher with propofol, when compared with etomidate but the values reached the base line earlier i.e. by 2 mins in Group P when compared 4 mins in Group E following administration of electrical stimulus. Analysis of the data suggested that propofol was more effective in controlling hemodynamic response to ECT than Etomidate

In our study we found that the mean heart rate in both the group increased from the baseline after application of electric shock. However the rise was lesser in the Etomidate group than the Propofol group.

A similar comparative study of propofol & Etomidate for ECT was done by Avramou and colleagues where apart from seizure duration, cognitive recovery profiles, haemodynamic parameters viz: HR and MAP where observed. Their obseravtions were similar to our study in which propofol was associated with a reduced acute Haemodynamic responses compared to Etomidate.[27],

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.

A comparative study between propofol and thiopentone for electroconvulsive therapy was done by Boey and Lai.[24] 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 conducted by Gazdag et al propofol and etomidate were compared during the ECT of patients with schizophrenia on the basis of their impact on seizure activity and on seizure-induced hemodynamic reactions. When using propofol, the increase in MAP was significantly lower than when etomidate was used. They concluded that propofol was more effective in attenuating the seizure-induced increase in MAP than etomidate, and supported the use of propofol in patients with greater cardiovascular risk[37].

This is in contrast with the review by Folk et al, who recommended that etomidate may be considered in patients with decreased cardiac output[39].

Villalong 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[22].

Geretsegger C et al comparing Propofol and methohexital as anesthetic agents for electroconvulsive therapy on seizure quality, therapeutic efficacy, and cognitive

performance came to a conclusion that patients on propofol showed a significantly lower increase in blood pressure post-ECT[49]

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.[50-] 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.

The choice of anesthetic for electroconvulsive therapy is based on the anesthetic requirements to be met and on the agent's impact on the seizure threshold. Thus, the non-barbiturate anesthesia etomidate revealed properties to enhance the seizure duration.

During the application of ECT, complications can occur at the induction and recovery stages. We did not encounter any complaints of pain on injection, myoclonus or increased tonus-related complications. In the recovery period, complications such as headache, dizziness, emesis and cough can be observed. Cough, which is probably due to increased secretions, can be overcome by the use of glycopyrrolate because of its peripheral effects.

CONCLUSION

In conclusion, propofol appears to be a safe anesthetic for ECT. In our study, it was superior to Etomidate in attenuating the haemodynamic responses to ECT. Compared with propofol, Etomidate was associated with longer seizure duration and may be helpful in patients with short seizure times (<20 s) despite a maximal electrical stimulus.

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. Etomidate when compared to propofol prolongs seizure duration. Hence in this study we compared Etomidate and propofol as induction agents for ECT. Forty patients undergoing ECT were divided into two groups to receive the induction agent either Etomidate or propofol. Motor Seizure duration was noted. 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. The seizure duration was significantly prolonged in Etomidate group when compared to propofol. All the haemodynamic parameters increased after electrical stimulus in both the groups. The rise was for a shorter duration in the propofol group when compared to patients induced with Etomidate. Propofol offers superior haemodynamic stability during the procedure. In conclusion, Etomidate prolongs seizure duration significantly and propofol is found to be a better induction agent for ECT with respect to haemodynamic stability compared to Etomidate.

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INFORMED CONSENT FORM

A study, **"COMPARISON OF EFFCT OF INTRAVENOUS ANAESTHTIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURING MODIFIED ELECTROCONVULSIVE THERAPY : A ONE YEAR RANDOMIZED CLINICAL TRIAL"** is being conducted by Dr. vishwas.G.K, post graduate in anaesthesiology at J. N. Medical College Belgaum, Karnataka. Under guidance of

Dr. C.S. Sanikop Prof & Head Dept. of Anaesthesiology, J. N. Medical College, Belgaum, under K.L.E.'s academy of Higher Education, Belgaum.

Respected _____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.

RESEARCH BEING DONE

To compare the effect of Etomidate and propofol on Seizure duration and haemodynamic responses during ECT.

The purpose of the study

You have been advised to undergo ECT by your treating psychiatrist. During the procedure we have been commonly using induction agents such as Thiopentone, Propofol. Now I am studying the effect of new drug Etomidate which when used

as an induction agent is known to prolong the seizure duration does not bring about changes in heart rate and blood pressure.

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. Etomidate, Inj. Propofol) during your ECT session.

Benefits and Risks:

Etomidate is associated with increased seizure duration and is haemodynamically stable compared to propofol.

Propofol is associated with shorter seizure duration and variable haemodynamic responses.

Alternatives:

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

Decline from participation

You have the option to decline from participation in the study without any discrimination and you will be treated as per the existing protocol for your condition.

New information

All information collected during the study from participant will be told as and when required.

Privacy and confidentiality

Privacy of individual will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Injury as a result of participation

There will neither be any compensation to or for the patient and his or her relatives nor there any monetary benefits for the damage incurred.

Costs of participation in this research

Participation is free of cost.

Reimbursement for any expenses for participation in research

No reimbursement for any of your expenditures

Withdrawal or be removed

To start with as the participation was voluntary so is the decision to withdraw. Such a step will not alter the participant's management by any staff in hospital. Researcher can remove you from the study if circumstances arise.

Whom to contact

If you have any queries, in future or in case of study related injury or illness, you may contact. Dr.Vishwas.G.K at Department of Anaesthesiology, KLES Prabhakar kore Hospital & MRC, Ph No. 9886119038

For any information about the study during the study or after that may be collected from Dr.C.S.Sanikop Prof & Head Department of Anaesthesiology, KLES Prabhakar kore 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,J.N. Medical College and Chairman.,Institutional Ethical Committee for Human Subjects Research, Ph. 0831-2473777.

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 Date

_____ _____
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

INFORMED CONSENT FORM

A study, **"COMPARISON OF EFFCT OF INTRAVENOUS ANAESTHTIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURING MODIFIED ELECTROCONVULSIVE THERAPY : A ONE YEAR RANDOMIZED CLINICAL TRIAL"** is being conducted by Dr.XXXXXX, post graduate in anaesthesiology at J. N. Medical College Belgaum, Karnataka. Under guidance of

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Benefits and Risks:

Etomidate is associated with increased seizure duration and is haemodynamically stable compared to propofol.

Propofol is associated with shorter seizure duration and variable haemodynamic responses.

Alternatives:

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

Decline from participation

You have the option to decline from participation in the study without any discrimination and you will be treated as per the existing protocol for your condition.

New information

All information collected during the study from participant will be told as and when required.

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Injury as a result of participation

There will neither be any compensation to or for the patient and his or her relatives nor there any monetary benefits for the damage incurred.

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Reimbursement for any expenses for participation in research

No reimbursement for any of your expenditures

Withdrawal or be removed

To start with as the participation was voluntary so is the decision to withdraw. Such a step will not alter the participant's management by any staff in hospital. Researcher can remove you from the study if circumstances arise.

Whom to contact

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

For any information about the study during the study or after that may be collected from Dr.XXXXXX Professor, Department of Anaesthesiology, KLES Prabhakar kore Hospital & MRC, Ph No. 0831-2473777.

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

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 Date

_____ _____
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

PROPOFOL																										
Sl no	**IP No**	**Age**	**Sex**	**Weight**	**Diagnosis**	**SEIZURE DURATIO**	**HR PI**	**PO I**	**0**	**1**	**2**	**3**	**4**	**5**	**10**	**SBP PI**	**PO**	**0**	**1**	**2**	**3**	**4**	**5**	**10**	**DBP PI**	**PO**
1	3E+05	25	M	48	PSYCHOSIS	55	96	90	119	121	111	103	108	106	101	120	110	143	144	140	118	114	108	116	90	84
2	3E+05	18	F	38	DEPRESSION	30	90	92	104	115	118	100	99	116	115	144	120	143	131	129	125	135	123	125	90	84
3	3E+05	17	F	42	SCHIZOPHRENIA	38	84	86	91	128	148	117	148	133	139	121	118	115	121	133	115	138	129	120	84	76
4	3E+05	32	F	52	PSYCHOSIS	30	68	66	69	64	65	81	144	135	118	120	118	119	119	145	117	127	131	123	72	64
5	3E+05	19	F	38	SCHIZOPHRENIA	42	81	80	82	84	82	90	86	86	86	116	112	108	106	106	122	118	116	114	75	70
6	3E+05	26	M	40	MANIA	61	101	102	104	108	108	110	120	128	128	127	122	126	124	126	126	127	127	126	74	70
7	3E+05	28	M	60	PSYCHOSIS	34	100	98	102	108	106	104	102	102	102	108	106	100	94	96	98	98	102	100	67	65
8	3E+05	18	F	41	PSYCHOSIS	26	100	116	113	112	117	114	112	114	109	109	116	113	113	116	109	107	107	114	70	64
9	3E+05	50	F	40	SCHIZOPHRENIA	42	80	82	84	79	74	70	68	68	68	134	120	112	116	114	110	106	97	96	77	68
10	3E+05	50	F	42	PSYCHOSIS	52	72	74	132	108	96	86	82	82	84	120	128	136	140	192	170	163	150	148	74	72
11	3E+05	47	M	58	PSYCHOSIS	30	77	69	79	102	104	106	102	90	86	120	118	120	142	140	136	132	132	130	80	72
12	3E+05	52	M	75	SCHIZOPHRENIA	52	60	60	72	70	68	64	64	62	62	152	152	172	162	160	158	158	156	154	96	96
13	3E+05	39	F	70	SCHIZOPHRENIA	32	110	122	140	161	162	150	144	140	112	157	158	243	196	178	164	166	166	164	110	117
14	3E+05	43	F	43	CATATONIA	30	75	78	88	82	99	94	92	92	92	118	98	129	133	130	125	122	120	122	70	59
15	3E+05	35	F	56	DEPRESSION	30	94	98	99	104	94	95	93	98	96	107	107	105	116	120	119	112	113	112	76	70
16	3E+05	58	M	75	DEPRESSION	41	67	66	66	67	71	74	74	74	72	153	150	152	150	144	119	113	112	112	106	100
17	3E+05	20	M	44	SCHIZOPHRENIA	31	90	92	87	83	91	90	88	88	88	88	93	112	114	91	90	90	92	90	54	71
18	3E+05	22	M	46	SCHIZOPHRENIA	32	68	70	72	74	76	72	72	70	70	112	118	124	130	132	120	118	120	114	72	76
19	3E+05	56	M	70	SCHIZOPHRENIA	42	90	88	86	82	80	78	76	76	72	144	140	140	144	144	136	132	134	134	90	82
20	3E+05	30	M	50	PSYCHOSIS	36	78	76	78	82	84	82	80	80	72	122	120	118	118	118	118	120	120	122	80	84

Sl no	IP No	Age	Sex	Weight	Diagnosis	SEIZURE DURATIO	HR PI	PO I	0	1	2	3	4	5	10	SBP PI	PO	0	1	2	3	4	5	10	DBP PI	PO
sl no	IP No	Age	Sex	Weight	Diagnosis	SEIZURE DURATION	HR PI	HR PO	0	1	2	3	4	5	10	SBP PI	SBP P0	0	1	2	3	4	5	10	DBP PI	DBP P0
1	310817	19	M	56	MANIA	68	72	72	76	84	102	90	88	84	78	118	116	116	118	146	142	128	124	118	72	68
2	309821	18	F	53	DEPRESSION	69	90	120	113	133	126	120	110	96	90	124	136	130	160	168	150	144	136	130	76	92
3	314883	20	F	38	PSYCHOSIS	58	72	94	72	96	97	96	99	98	98	90	103	98	110	109	108	87	88	88	60	65
4	316743	54	M	52	SCHIZOPHRENIA	47	71	80	105	133	85	90	90	86	88	106	110	147	133	133	117	118	116	114	66	68
5	315201	34	F	55	SCHIZOPHRENIA	27	86	103	110	88	90	86	88	88	90	137	115	145	145	144	140	136	134	132	88	70
6	321421	45	M	52	SCHIZOPHRENIA	52	78	80	90	92	88	80	82	80	82	140	140	142	144	146	140	142	142	142	80	80
7	315571	20	F	48	SCHIZOPHRENIA	52	72	72	74	76	76	72	74	74	74	118	118	116	114	116	114	112	116	116	68	70
8	316903	36	F	52	DEPRESSION	50	80	80	82	84	86	84	82	82	82	118	120	122	120	120	118	120	124	122	72	80
9	321991	40	F	51	SCHIZOPHRENIA	61	92	96	98	92	96	94	92	92	94	136	134	132	134	136	144	144	132	132	86	86
10	323061	22	F	48	SCHIZOPHRENIA	48	72	74	76	78	74	74	76	72	74	136	138	140	132	132	136	134	132	132	80	80
11	320485	25	M	46	MANIA	46	79	80	81	84	86	81	80	82	84	116	116	118	120	118	118	120	116	114	76	78
12	320587	20	M	54	CATATONIA	53	68	70	72	74	76	72	70	72	73	118	118	118	120	122	124	124	118	118	68	70
13	321861	21	F	39	SCHIZOPHRENIA	53	82	84	86	86	88	84	82	82	82	144	142	148	146	142	142	142	144	138	82	84
14	322683	22	F	40	CATATONIA	52	80	82	82	84	80	82	82	84	84	132	132	130	134	134	132	132	128	126	82	78
15	323389	30	M	52	DEPRESSION	45	76	78	78	84	82	80	82	82	82	126	124	126	130	128	126	128	129	132	78	80
16	321991	40	F	51	PSYCHOSIS	54	88	86	90	92	88	86	86	88	86	128	128	130	122	128	126	128	130	130	82	86
17	320589	20	M	54	CATATONIA	48	72	76	78	76	72	72	74	72	70	114	118	120	122	120	122	122	118	118	76	74
18	321861	21	F	40	SCHIZOPHRENIA	52	76	78	78	82	84	82	82	82	80	138	138	140	142	140	138	138	136	138	82	88
19	323691	40	M	51	SCHIZOPHRENIA	42	86	90	90	92	92	94	92	96	94	118	120	120	122	124	126	128	122	124	72	82
20	325721	25	M	46	SCHIZOPHRENIA	48	76	76	78	76	76	78	80	72	74	130	130	132	130	124	128	118	122	134	82	82

0	**1**	**2**	**3**	**4**	**5**	**10**	**MAP PI**	**PO**	**0**	**1**	**2**	**3**	**4**	**5**	**10**
104	97	100	78	73	72	64	100	92	110	111	110	98	82	79	76
102	84	96	85	90	88	80	92	90	116	101	106	97	104	98	96
80	76	97	79	95	92	75	96	90	91	92	114	90	109	103	87
74	92	101	64	77	84	80	86	84	86	101	83	79	88	101	82
62	68	74	68	64	60	62	84	84	82	82	80	78	80	72	76
74	72	80	78	73	68	70	87	86	78	80	82	82	89	80	78
50	51	54	48	48	50	52	78	84	72	68	68	66	66	68	72
79	68	70	62	59	59	65	83	88	90	84	81	76	74	73	79
69	70	62	54	51	50	92	82	84	79	74	74	74	68	66	68
88	90	112	106	90	88	88	86	80	110	102	156	130	120	110	108
78	94	92	88	86	84	82	92	86	90	106	102	98	100	98	98
108	110	104	100	96	98	92	126	120	144	120	118	108	104	102	104
168	159	148	120	110	120	114	124	120	140	172	168	142	138	145	144
83	80	86	73	71	73	71	86	70	74	92	99	99	96	90	88
76	83	82	85	75	77	78	86	82	86	95	98	82	103	89	90
107	100	88	76	71	70	68	122	120	124	120	116	88	82	80	78
63	64	56	46	48	46	48	66	79	82	80	72	58	60	58	60
78	76	76	74	76	72	72	84	84	90	96	92	82	80	78	76
96	96	84	72	74	72	70	96	90	98	94	94	90	88	86	84
86	88	82	78	86	84	90	96	90	98	96	98	92	88	92	100

0	1	2	3	4	5	10	MAP PI	PO	0	1	2	3	4	5	10
0	1	2	3	4	5	10	MAP PI	MAP PO	0	1	2	3	4	5	10
76	72	82	92	88	76	72	85	78	98	96	94	108	88	86	82
88	114	98	90	86	84	80	90	106	100	108	108	118	114	110	108
55	70	73	72	68	48	55	48	78	68	84	84	84	63	60	63
101	70	70	76	74	68	68	77	80	115	86	86	90	92	88	86
90	90	88	80	86	82	82	103	84	108	106	106	108	102	98	98
82	82	80	76	82	68	72	98	98	100	98	98	88	100	96	98
72	70	72	72	72	78	74	84	86	82	80	80	82	84	82	80
82	84	82	84	86	84	82	86	90	92	94	94	90	90	88	92
88	90	82	80	76	78	70	104	104	102	106	106	96	106	94	96
82	76	76	75	78	72	76	98	98	100	96	96	94	94	94	96
80	84	80	80	78	76	68	96	94	96	92	92	96	98	92	90
70	80	78	76	74	76	75	84	86	86	92	92	88	86	84	80
84	88	82	80	82	80	76	106	104	114	114	114	104	104	104	98
86	82	76	78	76	74	76	98	96	96	100	104	92	90	88	88
82	80	68	76	76	78	74	90	90	88	104	100	92	90	90	92
84	86	88	86	84	84	80	98	102	104	110	106	98	98	100	98
72	74	80	80	78	74	72	90	92	94	100	98	96	94	92	92
90	96	82	84	84	80	84	102	104	110	108	108	100	98	96	98
76	76	74	76	78	76	72	96	98	108	104	104	102	100	96	94
80	86	80	78	76	72	76	100	98	100	108	106	100	100	94	98

		PROPOFOL		ETOMIDITE	
		Frequency	Percent	Frequency	Percent
Valid	CATATONIA	1	5	3	15
	DEPRESSION	3	15	3	15
	MANIA	1	5	2	10
	PSYCHOSIS	7	35	2	10
	SCHIZOPHRENI	8	40	10	50
	Total	20	100	20	100

p VALUE BY CHI-SQUARE TEST IS 0.3628

PROFORMA

"COMPARISON OF EFFCT OF INTRAVENOUS ANAESTHTIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURIMG MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CLINICAL 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:

DIAGNOSIS:

ANAESTHETIC PROCEDURE:

Intravenous line will be secured using appropriate IV cannula and fluids will be started. All patients were pre medicated with inj. Glycopyrrolate 0.2 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. Etomidate 0.2 mg./kg or inj. Propofol 1 mg./kg.

After noticing of loss of eyelash reflex, blood pressure cuff applied to the lower limb was inflated to isolate the foot & permit accurate measurement of motor seizure duration.

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.

Electrical stimulus 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. The seizure duration was noted.

Any adverse effects were also noted.

INDUCTION:

Premedication: Inj glycopyrrolate 0.2 mg iv

Group P: inj etomidate ___ mg(0.2mg/kg)

Inj suxamethonium ___ mg(1mg/kg)

Group T: inj propofol ___ mg (1mg/kg)

Inj suxamethonium ___ mg(1mg/kg)

Readings were recorded in the following manner:

Strength of current:

	Etomidate group	Propofol group
Seizure duration in Sec		

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:

"COMPARISON OF EFFECT OF INTRAVENOUS ANAESTHETIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURING MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CLINICAL TRIAL"

BA0108002

DISSERTATION

SUBMITTED TO

KLE UNIVERSITY, BELGAUM KARNATAKA

IN PARTIAL FULFILLMENT

OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER DEGREE

IN

ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELGAUM – 10, KARNATAKA

MAY – 2011

KLE UNIVERSITY, BELGAUM, KARNATAKA

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"COMPARISON OF EFFECT OF INTRAVENOUS ANAESTHETIC AGENTS ETOMIDATE AND PROPOFOL ON SEIZURE DURATION AND HAEMODYNAMIC RESPONSES DURING MODIFIED ELECTROCONVULSIVE THERAPY: A RANDOMIZED CLINICAL TRIAL"** *is a bonafide research work done by* **BA0108002** *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
SD	Seizure duration
Sl. No.	Serial Number
Wt	Weight in kilograms

ABSTRACT

BACKGROUND: With administration of ECT, blood pressure & heart rate steeply increase secondary to rise in plasma adrenaline and nor adrenaline levels. 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 Etomidate and Propofol on Seizure duration and haemodynamic parameters.

TYPE OF STUDY: Randomized clinical trial

METHODS AND MATERIALS: 40 patients between age the of 18 and 58 years of either gender, belonging to ASA Grade-I and II scheduled for modified ECT were included. Patients were allocated into two groups. Anaesthetic technique was standardized for all patients.

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

Patients were induced with one of the study drugs , i.e Inj. Etomidate 0.2 mg/kg (group E) or inj. propofol 1 mg/kg (group P). Blood pressure cuff applied to the lower limb was inflated to isolate the foot & permit accurate measurement of motor seizure duration.

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

Electrical stimulus was applied by bilateral electrodes to the temporal regions. Motor seizure duration was noted. HR, SBP, DBP and MAP 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 and the heart rate did not reach the baseline even after 10 min .There was a rise in the mean systolic blood pressure by approximately 7 mm of Hg in the group P compared to

4 mm of Hg in the group E. The mean diastolic blood pressure rise in the propofol group was 6 mm of Hg as compared to 5 mm of Hg in the group E. The mean arterial pressure in the both the groups increased by 7 mm of Hg. The parameters reached the baseline earlier with group P when compared to group E.

CONCLUSION: From our study we conclude that, the induction agent propofol could blunt the sympathetic response to electro-convulsive therapy more effectively than Etomidate whereas Etomidate significantly prolongs seizure duration when compared to propofol.

KEYWORDS: *Electroconvulsive therapy, Etomidate, propofol, seizure duration haemodynamic responses.*

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