Dissertation on

"COMPARISON OF ESMOLOL AND LABETALOL IN ATTENUATING HEMODYNAMIC RESPONSES AFTER ELECTROCONVULSIVE THERAPY"

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH - X (ANAESTHESIOLOGY)

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DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE FROM GUIDE

This is to certify that the dissertation entitled "COMPARISON OF ESMOLOL AND LABETALOL IN ATTENUATING HEMODYNAMIC RESPONSES AFTER ELECTROCONVULSIVE THERAPY"is a bonafide record work done by **Dr.M.Ranimariammal** under my direct supervision and guidance ,submitted to the Tamil Nadu Dr M.G.R Medical University in partial fulfillment of University regulations for M.D, Branch X Anaesthesiology.

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DECLARATION

I **Dr M.RANIMARIAMMAL**,solemnly declare that, this dissertation titled "COMPARISON OF ESMOLOL AND LABETALOL IN ATTENUATING HEMODYNAMIC RESPONSES AFTER ELECTROCONVULSIVE THERAPY" has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree or diploma to any other University or board either in India or abroad.This is submitted to The Tamilnadu Dr. M. G. R.Medical University,Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in April 2015.

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CONTENTS

ABSTRACT

Electroconvulsive therapy is used to treat the acute depression and chronic depression, resistant to pharmacological therapy .

Objective: This study was done to compare the effects of esmolol and labetalol in attenuation of hemodynamic responses after ECT.

Materials and methods:90 patients aged 18-60 years were randomly divided into three groups. Baseline parameters were recorded .Group C received 5 ml of normal saline ,group E received 1mg/kg esmolol and group L received 0.25mg/kg labetalol after induction. Heart rate, systolic BP and diastolic BP were recorded at 1min after test drug administration and 1,3,5,10 minutes after ECT .Hypertension and tachycardia occurred due to sympathetic nervous system activation after ECT.

Results: It was found that esmolol significantly attenuated the degree of tachycardia and hypertension, in the first three minutes compared to placebo whereas the rise in HR and blood pressure was significantly reduced in the labetalol group in comparison to placebo, from three minutes to ten minutes.

Conclusion: It was concluded that esmolol is effective in blunting the hemodynamic responses in the first three minutes after application of the electrical current, whereas Labetalol is effective from five minutes to ten minutes after ECT.

Key words: Electroconvulsive therapy, hemodynamic responses, esmolol, labetalol, sympathetic nervous system.

INTRODUCTION

Electroconvulsive therapy (ECT) was introduced in the 1930s to treat schizophrenia.Use of Electroconvulsivetherapy decreased through the 1970s because of negative publicity.Acceptance and use of ECT have again increased. Currently Electroconvulsive therapy is accepted due to the administration of general anesthesia to decrease the physical and psychological trauma associated with ECT.ECT consists of programmed electrical stimulation of the central nervous system to initiate seizure activity.The exact mechanism of the therapeutic effect of ECT remains unknown.ECT causes changes in chemistry of the brain, that will reverse the symptoms of the psychiatric disease.It is used in conditions where other modalities of treatment fails. Electroconvulsive therapy was developed in 1938.ECT is effective in treating many psychiatric illness,especially depression. Patients with severe depression resistant to pharmacological treatment and intolerable to the side effects of psychiatric drugs can also be treated with ECT.ECT is the treatment of choice for patients who need a rapid response.This includes those who are severely agitated,having delusion and suicidal tendency,refuse to take food and water,as well as catatonic condition.

ECT is also used as a mood stabilizer during the episodes of mania or depression in bipolar disease.Electroconvulsive therapy is useful in treating the psychotic episodes associated with schizophrenia.

In ECT,patients received high doses of electric current without anesthesia in older days,lead to vertebral or long bone fractures due to violent muscle contractures,short term memory loss, and other serious side effects.

ECT is performed under general anaesthesia now a days.People who have psychiatry illness can safely undergo ECT.Although ECT still causes some side effects,it now uses electrical currents given in a controlled setting to achieve the benefits with the fewer side effects.

Anaesthesiologist's aim is to provide safe and effective anaesthesia without interfering the beneficial effects of ECT in psychiatric patients.Activation of central nervous system during ECT leads to release of catecholamine which leads to increase in the blood pressure and heart rate.This physiological effects of ECT leads to infarction or ischemia or even stroke in patients with preexisting cardiac and cerebrovascular disease.Many drugs are used by various routes in attenuating the physiological responses during ECT.

In this study comparison of Esmolol and labetalol in attenuation of hemodynamic responses after ECT in the immediate period to ten minutes was done.Esmolol is an ultrashort acting beta1selective adrenergic blocker where as Labetalol is a combined alpha 1 and beta blocker.It has alpha 1and predominant beta adrenergic receptor blocking activity.In intravenous route alpha:beta action is 1:7 whereas in oral route is 1:3.There are studies to evaluate the efficacy of these drugs to attenuate the hemodynamic responses to ECT.

AIM & OBJECTIVES OF THE STUDY

To compare the effects of Esmolol and labetalol in attenuation of hemodynamic responses after ECT. The comparison of effects of these drugs was done by monitoring and comparing the following parameters

- Baseline heart rate, systolic and diastolic BP
- Heart rate, systolic and diastolic BP at 1 min after administration of the test drug.
- Heart rate, systolic and diastolic BP at 1,3,5,10 minutes after ECT

PRIMARY OBJECTIVE :

To study the effects of Esmolol and Labetalol in attenuation of hemodynamic responses after ECT.

SECONDARY OBJECTIVES :

1) To study the hemodynamic effects after ECT.

2) To compare the effects of Esmolol and Labetalol in attenuating the hemodynamic responses after ECT.

HISTORY

April 2013 saw the 75th anniversary of the first use of Electroconvulsive Therapy (ECT), making it the oldest surviving physical treatment in Psychiatry. In 16th century, the Swiss physician Paracelsus (Auroleus Phillipus Theostratus Bombastus von Hohenheim) treated psychiatry patients by inducing seizures by giving camphor orally where as in 1934, the Hungarian neuropathologist Ladislas Joseph von Meduna began the modern era of convulsive therapy by giving camphor intramuscularly (soon replaced with pentylenetetrazol) in treating catatonic schizophrenia. The electrical stimulation of a series of seizures in catatonic patient was first done by an Italian psychiatrist Lucio Bini and neurologist Ugo Cerletti in 1938 and produced a successful response.In United States ECT was introduced at 1939.

Fractures and dislocations are more in unmodified ECT .Curarae was used as a relaxant in ECT in 1940.In 1950s antipsychotic drugs were not developed.Insulin shock and lobotomy were used as an effective alternative for ECT.

Max Fink was the first to apply rigorous scientific research methods in 1950s. Suxamethonium as identified in 1951 and in 1958 controlled study on unilateral ECT was done. In 1960s,randomized control study was done to compare the effects of ECT in treating depression with pharmacological treatment.

It showed increased response rates in ECT.If the patients fear suffocation after giving muscle relaxants anaesthetists used to give some short acting anaesthetic drugs.In Britain most hospitals used unmodified ECT routinely by the mid 1950s.In 1957 at a London hospital, a patient had sustained fractures to both hips when undergoing unmodified ECT.He took legal action against hospital.The First Task Force Report was published by the American Psychiatric Association in 1978 on ECT,had the goal of establishing standards for consent and the technical and clinical aspects of the conduct of ECT.In 1985,the National Institutes of Health and National Institute of Mental Health Consensus Conference on ECT endorsed a role for the use of ECT and advocated research and national standards of practice.

MECHANISM OF ACTION OF ELECTROCONVULSIVE THERAPY

NEUROTRANSMITTER THEORY

NEUROENDOCRINE THEORY

ANTI CONVULSANT THEORY

BRAIN DAMAGE THERAPY

PSYCHOLOGICAL THEORY

Mechanism of action

The exact mechanism of action of ECT is not known fully. Electroconvulsive therapy affects all the components of central nervous system, including neuropeptides, neurotrophic factors, harmones and neurotransmitters.

Bilateral generalized seizure is needed for the beneficial and adverse effects of ECT.Seizure threshold raises during ECT by increasing GABA transmission and antagonism of receptors. Endogenous opioids are also increased during ECT. It also has the anticonvulsant properties. The neurophysiological effects of ECT is studied by Positron emission tomography. After ECT there will be reduction in glucose metabolism in bilateral anterior and posterior frontal areas represented the most consistent findings.

ECT affects all neurotransmitter system including serotonin, muscarinic, cholinergic,dopaminergic,beta-adrenergic systems. Brain-derived neurotrophic factor (BDNF), catechol-O-methyl transferase (COMT) second-messenger systems may play an important role in ECT.

Indications

ECT is used to treat the psychiatric disorder like schizophrenia, depressive disorder, bipolar disorder, and other psychiatric disorders.

Major depressive illness

In the acute phase of major depressive illness, patients have functional impairement, psychotic symptoms, high degree of severity of symptoms and catatonia.They are considered to undergo ECT.ECT may also useful in treating patients in whom response to the treatment is needed urgently, who are nutritionally compromised due to poor food intake or patients who have suicidal tendency.

Bipolar disorder

Patients with severe or treatment resistant mania or mixed episodes of bipolar disorder, or for patients who prefer this treatment modality(after consulting with the psychiatrist) may be considered to undergo ECT.Mania is charecterized by hyperactivity, intense euphoria and agitation that occurs as part of bipolar disorder. Other signs of mania include impulsive or risky

behavior, impaired decision making, psychosis and substance abuse.ECT is a potential treatment for pregnant patients having depression or severe mania.ECT is beneficial in treating the patients with rapid cycling bipolar disorder.Earely mania results from ECT.

ECT is also used as an alternative for the patients with life-threatening inanition (an exhausted condition due to poor intake of food and water), suicidal tendency or psychosis.ECT should also be considered in patients having depression with psychotic or catatonic features. Maintenance ECT is useful in patients who have acute episode of depression.

Schizophrenia

ECT is effective in treating the symptoms of acute schizophrenia but is not useful in treating chronic schizophrenia. Severe psychosis patients who have not responded to treatment with pharmacological agents like psychiatric medications may be considered to undergo ECT. When ECT is administered along with antipsychotic medications therapeutic beneficial is very good. ECT also should be considered for patients with prominent catatonic features like lack of speech, lack of movement, strange or fast movements and other symptoms.Schizophrenia is also associated with some other psychiatric disorders.In some cases,catatonia is caused by a medical illness.

Patients who have not responded to lorazepam can also undergo ECT.In depression patients ECT may be beneficial in patients having treatment resistant depressive symptoms or if features such as suicidal thoughts occur.

In the stable phase of schizophrenia, ECT may be beneficial in some patients who has response to ECT in the acute phase but not responded to pharmacological prophylaxis alone or who cannot tolerate that.ECT is also be effective when marked positive and affective symptoms are present.

Other psychotic disorders

ECT is effective in patients who have psychotic disorders related to schizophrenia, such as schizophreniform disorder and schizoaffective disorder. In combination with antipsychotics, ECT may also be considered for patients with schizoaffective disorder with severe psychosis that has not responded to treatment with antipsychotic medications.

Comorbid disorders

ECT is not usually recommended in treating obsessive-compulsive disorder(OCD) but may be considered in the treatment of comorbid disorders such as major depressive disorder, mania, and schizophrenia in patients with OCD.

Other disorders and indications

ECT will be effective in treating the patients with catatonia, neuroleptic malignant syndrome, depression associated with Parkinson disease,pain,and acute confusion psychosis.It is also used in the treatment of patients with intellectual disabilities who have treatment resistant mood or psychotic disorders.

ECT may be useful in patients with major depressive disorder . In some patients pharmacological treatment or psychotherapy has not been effective in maintaining stability during the continuation phase.In these patients we may consider ECT..

In some cases ECT is also used in special conditions like pregnancy, when medications can't be taken for the benefit of fetus, older patients who can't tolerate the side effects of drugs,in people who prefer ECT treatments over pharmacological treatment,when ECT has been successful in the past. Patients with melancholic and atypical depression can also be treated with ECT.

SIDE EFFECTS

ECT is generally safe,but it also has following risks and side effects

Confusion.

After treatment patients may have confusion for a short period even it may last from a few minutes to several hours.patients may not know where they are and why they are.Patients return to normal activities after some hours of rest after ECT,rarely confusion may last for several days or longer.Confusion is more in older patients than young adults.

Memory loss.

ECT will also cause memory loss in many way.Patients may not remember events that occurred before treatment began, a condition known as retrograde amnesia. It is very difficult to recall the events in the weeks or months leading up to treatment.Some people may have problems with memories from previous years,as well.Patients may not recall the events that occurred during the weeks of the treatment.And some people have trouble with memory of events that occur even after ECT has stopped. Usually these memory problems may be improved within 2 months.

Physical side effects

Patients may have headache,nausea,vomiting,pain in the jaw,myalgia and spasm of the muscles.They are treated by supportive medications.

Medical complications.

During ECT, heart rate and blood pressure raises due to sympathetic responses. Patients who have cardiac diseases like coronary artery disease, and people who have hypertension, diabetis mellitus ,sinus tachycardia are at risk. Potential arrhythmias like ventricular tachycardia, atrial fibrillation. Diabetic patients may have silent ischemia so they have more risk.

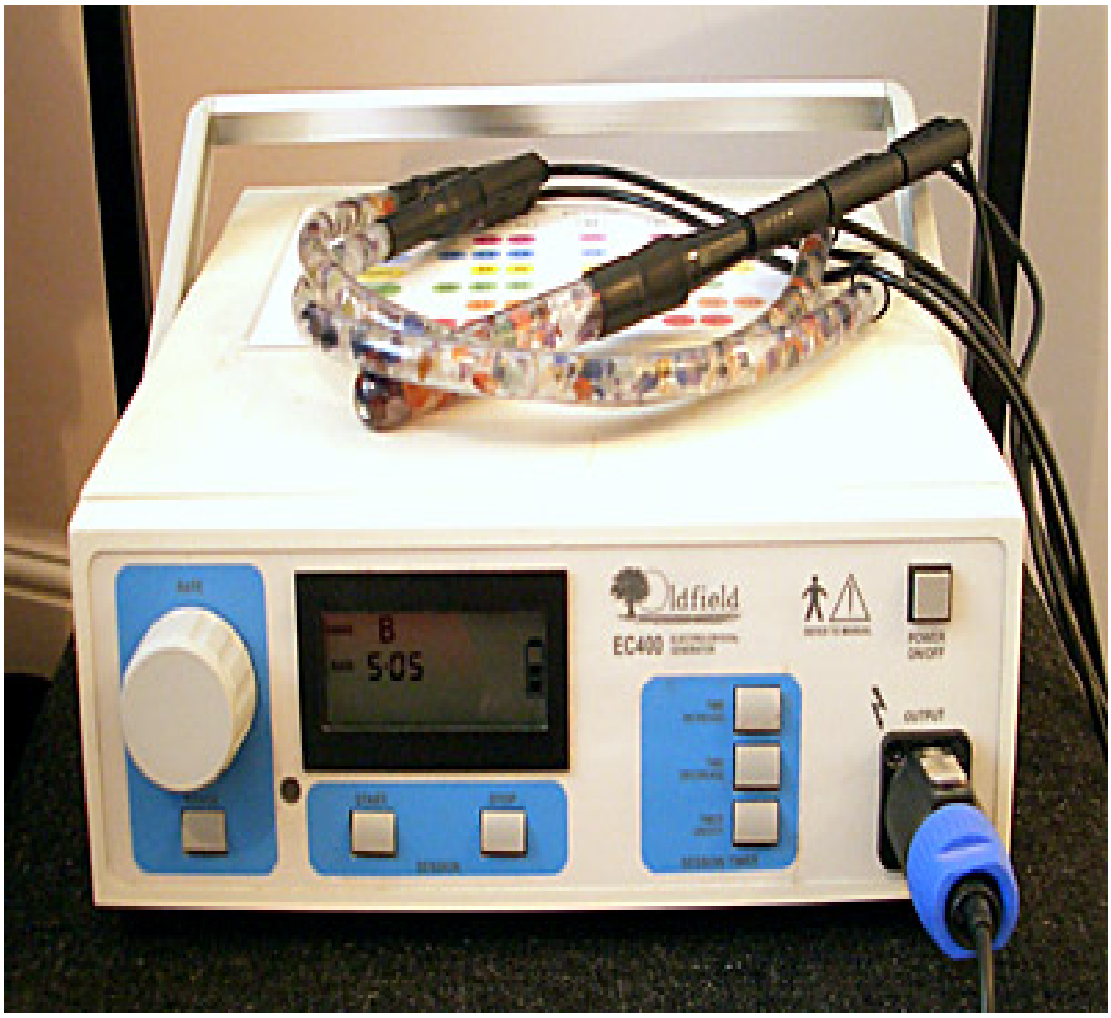
PROCEDURE

Preparation

Anesthesia

Initially ECT was performed without anaesthesia.After 1950 ECT was performed under anaesthesia.The goal is to achieve a light level of anaesthesia. Drugs used in

ECT are barbiturates like Methohexital and Thiopentone sodium,ketamine hydrochloride,Etomidate,Alfentanyl,Propofol.Methohexital is commonly used in ECT as it is safe and efficacy is good and it is cheap.Inhalational agents such as sevoflurane. The cognitive outcome after ECT depends upon the anaesthetic medication not the choice of agents but the dosage.Appropriate dose should be assessed and adjusted with that dose in subsequent treatments.



Equipment

The ECT treatment and recovery room should contain a monitor with pulseoxymetry, BP cuff, ECG electrodes, Oxygen delivering system.

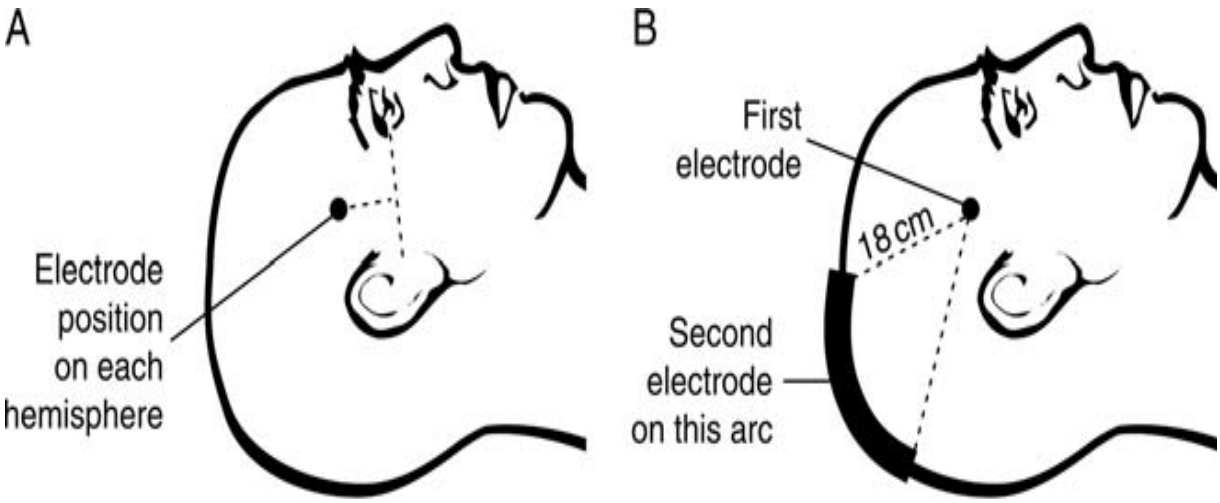
ECT room

Positioning

Common electrode positions in ECT electrodes are placed in right unilateral,bifrontotemporal, and bifrontal positions.Electrodes are placed bifrontotemporally, with the center of each electrode approximately 1 inch above the midpoint of an imaginary line drawn from the tragus to the external canthus in the bifronto temporal position(bilateral position). In case of right unilateral position, one electrode is placed on the nondominant fron to temporal area, and the other electrode is placed over the nondominant centroparietal scalp, just lateral to the midline vertex.

In most of the people, unilateral electrode placement is always over the right hemisphere,because of the left hemisphere dominance.

Electrode is placed more frontally on each side of the head in bifrontal position than in standard bifrontotemporal placement.In asymmetric bilateral position, the left electrode is moved about 6 cm anterior from the standard frontotemporal position, and its lateral edge is medial to the bony intersection ridge between the temple and the forehead. The right electrode is in frontotemporal position.



(A)Bilateral ECT(Bitemporal electrodes). (B) Unilateral ECT.

Pre-treatment Evaluation

Pre ECT evaluation must include:

History, cardiovascular and respiratory system examination, cognitive assessment and other systems examination. Laboratory investigstions includes complete hemogram, Serum biochemistry, renal function tests ,ECG,X-ray chest. Consultation with cardiologist, neurologist, neurosurgeon, or endocrinologist as needed by special conditions.

Informed Consent

In ECT written informed consent is an important part. This should be documented in the patient's medical record and should include a discussion of the disease,course,and the option of receiving treatment.The family members should participate in that discussion and consent should be obtained from the family members.

Electroconvulsive Therapy with Comorbidity

Assosciated comorbid conditions and their treatments may affect the response to and risks associated with electroconvulsive therapy.

Neurological diseases

Should be cautious with the patients having space occupying intra cranial tumors.ECT treatment may result in brain edema and herniation.Patients with intracranial pathology without mass effect can undergo ECT safely.As ECT increases the blood flow to the brain it increases intracranial pressure.Risk during ECT increased in patients with increased intracranial pressure or with cerebrovascular disease and cerebral aneurysms.

Cardiac diseases

Patients who have cardiac disease should undergo thorough evaluation before ECT.Patients who have unstable angina,uncompensated congestive heart failure, uncontrolled hypertension, atrioventricular block more than second degree and symptomatic ventricular arrhythmias are at risk.Hypertension should be controlled with antihypertensives before going to ECT. Patients with a recent myocardial infarction (MI) are at high risk of cardiac complications failure,after 2 weeks of MI risk is reduced and after 3 months of MI risk is further reduced.Patients with cardiac pacemakers and implantable cardioverter defibrillators can safely undergo ECT with a proper pre-ECT cardiac and pacemaker/defibrillator assessment.ECT can also be used in the presence of severe aortic stenosis.

Other comorbidities

Patients who require more work up and close monitoring during ECT are patients with diseases such as pheochromocytoma, hyperthyroidism, or with sensitivity to anesthesia like pseudo cholinesterase deficiency, amyotrophic lateral sclerosis, porphyria,or with cognitive sensitivity as traumatic brain injury. Due to the stimulation of vagus nerve gastro esophageal reflux disease may worsen during ECT. Other patients require close monitoring are patients with diabetes, metabolic disorders such as hyponatremia, hyperkalemia, hypokalemia, COPD, hypercoagulable states, renal disease and glaucoma.

Electroconvulsive Therapy and drugs

Drugs like antiarrythmics, antihypertensives, antianginals, bronchodilators, glaucoma drugs, and steroids can be given prior to ECT safely.Proton pump inhibitors and H2 blockers can also be used.

Hypoglycemics and diuretics must be withheld until ECT treatment. If possible patient should discontinue theophylline.As antiepileptics may raise the seizure threshold, may affect the clinical efficacy of ECT.Anticonvulsant dose should be reduced during ECT.

Monoamine oxidase inhibitors (MAOIs) can also be used safely. Before 7-14 days some clinicians may withhold MAOIs.When ECT is more effective when combined with antipsychotic drugs in schizophrenia than either treatment alone.Combination of ECT and antipsychotic drugs is safe and effective in refractory schizophrenia.

Use of lithium during ECT usually has no problems but some patients will have the risk for delirium or duration of seizures may be prolonged. Benzodiazepines dose should be reduced or if possible discontinued.ECT can also be given in combination with antidepressants safely.High doses of Bupropion can be used with caution.

Electroconvulsive Therapy in the Elderly

More number of patients who receive ECT belongs to the geriatric age group. ECT is useful in treating catatonia in geriatric patients,and also in psychotic disorders and mania in bipolar disorder.Usually, geriatric patients with depression responds well to ECT than young adults. ECT is indicated in patients with depression associated with psychosis,suicidal tendency, or severely malnourished,it is also helpful in treating treatment resistant nonpsychotic major depression.

Seizure threshold also rise in geriatric patients,and difficult to induce effective seizures. During and after ECT geriatric patients are at higher risk for persistant confusion and greater memory deficits.A 2003 Cochrane Database review of ECT for elderly patients with depression found that solid conclusions could not be drawn as to whether ECT was more effective than antidepressants or regarding the safety and adverse effects of ECT in these patients.

Electroconvulsive Therapy in Pregnancy

During pregnancy ECT is safe and its efficacy is good for the mother in treating the major depressive illness during pregnancy.ECT is also more potent in treating severe manic episodes of bipolar and also in severe depression.It is also used in pregnancy in patients who do not want to take the pharmacological treatment to avoid the exposure of psychiatric drugs or those who are resistant to standard drug therapy.Before going to ECT patient consult the obstretician and monitoring of the fetus should be done as needed.Patients in the third trimester should not lie in the supine position.They should turn to left during ECT.It avoids the compression of the great veins and allows more blood to the fetus otherwise fetal hypoxia may occur.Avoidence of hyperventilation is necessary.

Anesthesia drugs minimally crosses the maternal fetal barrier.As ECT does not cause teratogenicity and neonatal toxicity it is considered as a safe procedure.Pregnancy should be considered as full stomach always.So pregnant women have the increase risk of aspiration due to increased gastroesophageal reflux.So they are premedicated with sodium citrate which is called non particulate antacid.ECT is also relatively safe in breast feeding mother.Anesthetic drugs have minimal risk to the nursing infant.If the nursing mother delays feeding for few hours after an ECT treatment the drug exposure is minimal.Lactating women can use the expressed breast milk after ECT and it can be collected in the bottle before ECT.

Conduct of anaesthesia

Check the consent and ask for starvation and administration of regular medicines before ECT.Emergence may delay when sedatives are used and duration of seizure may be altered.As the ECT may cause urinary incontinence ask the patient to empty the bladder before ECT.Many of the anaesthetic drugs have anticonvulsant properties.The choice of anaesthetic agents should provide anaesthesia without affecting the efficacy of ECT.

Pretreatment sedation

Pre ECT sedation is given to relieve the anxiety.Sedative drugs are given in some patients before first ECT to reduce the awarness and make the patient calm. The sedatives can be given intramuscularly as oral is not allowed.Drugs having anti convulsant properties should be avoided.As drugs like barbiturates and benzodiazepines have anticonvulsive effects they are counter productive.It is difficult to judge the efficacy of ECT in patients who are taking potent neuroleptics as it may obscure the clinical signs.In patients with depression or mania,clinical signs and symptoms may be masked by potent neuroleptics.So it is difficult to judge the effectiveness of the course of the ECT.Therefore 25-30 mg of promethazine or 2.5-5 mg of droperidol or hydroxyzine given intramuscularly, are useful because these sedatives enhances seizure activity without affecting the seizures.

Anticholinergics

Bradycardia occurs for a short period after the application of electric current in ECT,which is followed by tachycardia.It corresponds to the seizure activity.Before induction administration of the anticholinergics like glycopyrrolate or atropine will reduce the incidence of bradyarrythmias and asystole.It is also used to reduce the airway secretion and it dries the secretions there by it reduces the risk of bronchospasm.

In patients taking beta-adrenergic receptor blockers anticholinergics may be useful.Due to lack of an evidence base in altering the cardiovascular effects of ECT, anticholinergics were not used by all physicians. Anticholinergics may increase preexisting tachycardia and it may cause urinary retention, constipation, fecal impaction.

Induction agents

Many intravenous anesthetics have been used to induce anesthesia for ECT, including methohexital, thiopental, propofol, and ketamine.Dosage of inducing drugs is titrated according to the patient weight it can be modified as needed depending on any changing seizure thresholds and previous response to ECT. Compared with other barbiturates.Methohexital has minimal anticonvulsant properties.Previously the drug was not available.So other hypnotic drugs were used.Now it is used as a gold standard drug.Etomidate dose of 0.15-0.3mg/kg produces seizures,but others don't.It has disadvantages like nausea and vomiting,more hemodynamic changes and recovery may be slow.It may also cause adreno cortical suppression.Propofol can be used as it will not affect the seizure quality.It will be used in the dosage of 1-2mg/kg.Thiopentone is also used because of its availability.Usually ketamine is not used because it increases intracranial hypertension and emergence.

Etomidate can also be used as i.v. inducing drug that may decrease the threshold of seizures.Opioids such as remifentanil (1 mg/kg over 30–60 seconds) or alfentanil (10–25 mg/kg) can be given in combination with inducing agents other than etomidate.Whatever drug is used, It is adviceable to use the same drug used in the initial treatment throughout course of treatment to avoid interfering with the seizure threshold (which generally increases over a course of ECT). For induction Sevoflurane 6–8% inspired concentration can also be used.It reduces the duration of seizures when compared with methohexitol. It can be used as an inducing agent when venous access is difficult.It reduces the contraction of uterus in pregnancy.Disadvantages are more time consuming and equipment needed.

Neuromuscular blocking agents

Because of the impedence of the monitoring of peripheral seizure duration,it is not necessary to block neuromuscular junction completely it is also not desirable.Partial neuromuscular blockade is necessary,to reduce the peripheral manifestations of the seizure and to prevent musculoskeletal trauma to the patient. Neuromuscular junction blocking agents reduces the muscular contractures. There by it reduces the risk of serious injuries.Complete blockade of neuromuscular system is needed in high risk patients having osteoporosis which may produces fractures of long bones or vertebra during ECT,or a history of injury to the spine. EEG monitoring is

very useful in monitoring the seizure activity and also visible muscle activity more accurately,when complete relaxation needed.Most commonly used drug to produce neuromuscular blockade is Succinylcholine in the dosage of 0.5 mg/kg.In cases of preexisting skeletal injury,severe osteoporosis and severe cachexia large dose up to 1.5 mg/kg may be needed.Non depolarizing neuromuscular blocker can be used if suxamethonium is contraindicated.Mivacurium is a short acting neuromuscular blocking agent.But ,modification of the seizures is not sufficient with low doses (0.08 mg/ kg) of Mivacurium,so lowest dose should be 0.15 mg/kg.Vecuronium and rocuronium is used as precurarizing agents but these drugs can be used with the advent of sugammadex. Nondepolarizing neuromuscular blocker is indicated in patients with severe hypercalcemia, severe osteoporosis, severe neuromuscular disease, pseudocholinesterase enzyme deficiency, and patients having previous history of malignant hyperthermia or in the family members.

Prior to electrical current stimulation, the reduction or loss of knee, ankle, and plantar withdrawal reflexes shows the adequacy of muscle relaxation. Loss of muscular tone, the decreased response to a nerve stimulator or any combination of these factors can also shows the adequacy of muscle relaxation.

Adjuncts

Some drugs can be added in high risk patients to lower the dose of inducing agent or commonly to attenuate the hemodynamic responses.Parasympathetic side effects may be dimnished with the use of atropine or glycopyrrolate.As glycopyrrolate lacks the adverse effects of central nervous system it can be used as an anti-sialogogue and it reduces the tachycardia after ECT.Atropine is avoided as premedicating agent as it increases myocardial work and oxygen demand.Atenolol given before ECTor short acting beta blockers like esmolol used intra procedurally prevents adverse sympathetic effects.Calcium channel blockers is also used to control blood pressure effectively.Nifedipine is used sublingually and nicardipine used IV to reduce the BP,but it causes reflex tachycardia.Diltiazem is also used to decrease BP.Alpha2 agonists like dexmedetomidine is also used to attenuate the hemodynamic responses. Glyceryl trinitrate should be used to reduce the risk of myocardial ischemia and infarction in patients at high risk.There is no role in the use of intravenous lignocaine.

Airway management

Patient should be pre oxygenated with 100% oxygen.Endotracheal intubation is not routinely needed unless patient has the risk of aspiration as in pregnancy and obesity.Ventilation can be assisted with face and mask.

After induction, face and mask ventilation can be continued to assist the respiration.As hyperventilation reduces seizure threshold and may prolong duration of seizures it should be avoided.Patient's tongue,lips and teeth should be protected by inserting the bite block.Ventilation should be assisted gently during the procedure until breathing resume.Magnitude of the stimulus will be titrated during initial sessions until an adequate seizure is generated.In this situation further doses of inducing agent are needed for the maintenance of anaesthesia.

Postoperative considerations

Standard monitors are attached during recovery and should supply oxygen untill saturation maintains in room air.Early recovery makes discharge faster according to the standard criteria.Reassurance is more important. Commonly facing side effects are violent behaviour, agitation, confusion,amnesia, headache, nausea and vomiting myalgia,heamodynamic complications may exist at this stage.The most difficult problem to face is emergence agitation.Minimal dose of midazolam can be used as simple measure.

Physical and psychological needs of the patient

Routine follow up in electroconvulsive therapy is mandatory to conclude both hemodynamic responses to ECT and to note down the side effects scheduled above in order to prevent, reduce,and treat the problem.Some patients may elicit an intense fear of treatment,as a rare psychological effect. Reassurance is mainstay to reduce the adverse effects of treatment.

Special considerations

Cerebral aneurysm

An increase in the wall stress of aneurysm may lead to rupture or enlargement of aneurysm.During ECT thiopentone increases the cerebral blood flow more when compared to propofol.So propofol can be used safely.Beta blockers and Sodium nitroprusside can inhibit the increase of aneurysm.

Intracranial mass lesions

Admininistration of steroids and diuretics before ECT reduces the intracranial pressure.Hyperventilation may be beneficial when applied before ECT.

Pacemakers or implantable defibrillators .

Due to high tissue resistance only small amout of electric current reaches the device.so,risk is low.Pacemaker activity may be triggered by skeletal muscle contractions during tonic clonic seizures.Temporary conversion to fixed rate pacing is usually recommended prior to ECT.Internal cardioverter defibrillators should be deactivated prior to ECTand reactivated in the early recovery period.

Neuroleptic malignant syndrome

Some antipsychotic medicines produce very serious side effects like neuroleptic malignant syndrome as similar with malignant hyperthermia.It is presented with fever,muscle rigidity,elevated creatinine levels,delirium and autonomic instability.

As halothane and succinylcholine trigger Malignant Hyperthermia they should be avoided.

Pregnancy

As pharmacotherapy may produce teratogenicity ECT is to be considered as a safe and effective form of treatment in pregnancy.It may increases the risk of aspiration in the mother and also spontaneous abortion and preterm labour.

If patient has history of preterm labour tocolytic drugs should be given before ECT.Sevoflurane used for the maintenance in third trimester pregnancy will decrease the risk of uterine contractions.

Consent

The consent should be taken in writing from the patient, or their relatives as the case may be ,before the start of the treatment.Some centres believe in renewal of consent after every treatment.The following points must be considered while obtaining the consent.

I. Adequate information must be given regarding the procedure, the expected benefits, side effects and complications. Discussion must be at this stageso as to allow clarifications of any doubts or apprehensions that the patients or the family members have.

II.The patient should be aware of his/her right to refuse treatment before or at any time during the ECT course.

III.Patient should be aware of the balance of advantages and disadvantages of the available treatment options.

TECHNIQUE

Overview

The electrical current stimulus must be sufficient to induce a seizure. In modern electroconvulsive therapy machines a brief pulse wave form is used.The dose of discharged charge can be measured in millicoulombs. Three methods are used to determine Stimulus intensity and dosing can be determined by Empirical titration, Formula based titration,and Fixed dosages.Progressively higher doses of electric current are given in empirical titration,until seizure threshold is reached during the first session of ECT.Seizure threshold is determined by this method accurately. The dose is determined by some factors like age,sex, and placement of electrodes in formula based titration.Independent of patient or other factors,a fixed dose is given in the third method. A fourth method, in which intensity of the stimulus is increased progressively during delivery from a subconvulsive to a convulsive level,called the glissando technique,is not used. When determining intensity of stimulus, changes in threshold of seizures and dosing during the treatment course should also be considered. Threshold of seizure may increase in ECT.

Quality of the Seizures

Duration of seizures has minimal effect on the efficacy of electroconvulsive therapy, and seizure duration is associated with intensity of the stimulus. When the electrical stimulation is inadequate it may result in limited seizures. It is manifested by duration of seizure less than 15 seconds in EEG.

Confirmation of seizure activity and documentation of seizure duration can be done with the use of EEG. The "cuff" procedure is used to monitor seizures motor activity, in which distribution of a muscle relaxant is blocked to the hand or foot by using a tourniquet to maintain the potential for muscle contraction.

Treatment Frequency

ECT is given 3 times per week in the United States regardless of the placement of electrode. Usually frequent regimens of ECT is not recommended. Memory impairment is less when treatment is given two times per week compared with treatments three sessions per week. Same degree of the final clinical improvement is seen in patients receiving ECT three times a week when compared with patients receiveing ECT two times a week, although possibly at a slow response rate.

More than one adequate seizure is induced under anaesthesia, in the same session in Multiple monitored ECT(MMECT).Neuroleptic malignant syndrome, an urgent clinical condition may need MMECT,it is not recommended usually.

Number of ECT

The number of treatments needed to achieve a full clinical response in patient varies widely.Usually 6-12 treatments is enough to show the response.After a few treatments some patients show response,and some may not show response even after ten sessions of ECT.The number of treatments depends upon the function of the degree of the illness,and the rate of improvement of the clinical symptoms and signs,as well as the degree of cognitive side effects.

Treatment Complications

The main complications of electroconvulsive therapy are cognitive adverse effects and mortality.

Cognitive side effects

Major side effects during ECT are cognitive side effects.The severe side effects occurs postictally after ECT,with impairement of memory,praxis and attention and a brief period of disorientation.

These effects may be reversed.Severity and extent of cognitive side effects may vary significantly in individuals after ECT.Various electrophysiological studies,neuroimaging,and biochemical studies,correlates the adverse effects of ECT on cognitive function may exist.

Occurance of Cognitive deficits depends on the ECT technique.In this situation the technique of ECT can be modified and can switch over to unilateral technique.Cognitive side effects may be increased when lower the stimulus dose, stopping medications and increasing the time interval between treatments.

After ECT anterograde and retrograde amnesia may occur. Rapid recovery is seen in antegrade amnesia.Deficits for events closest to the treatment time occurs in retrograde amnesia. In some patients delirium occurs postictally.

A prospective,longitudinal study of clinical and cognitive outcomes in patients treated with ECT for major depression was done. Patients were treated at 7 facilities and study was done.It was found that outcome of cognitive and clinical functions varied across facilities. These differences mainly dependant on the ECT technique. A recent review in older patients it was found that older adults show mixed responses regarding the impact of ECT on cognitive function.

Mortality

Most common causes of the mortality during ECT are Cardiovascular complications and pulmonary complications.Patients undergoing ECT have the mortality rate of 1 in 10,000 patients and it is 1 in 80,000 in patients undergoing treatments.This mortality rate is about the same as that associated with minor surgeries.Patients with severe medical disorders may have the higher mortality rate when compared to patients with,tricyclic antidepressant therapy.

Other adverse effects

Soon after the administration of ECT the patient may go for asystole.Patients receiveing medications that lower seizure threshold may have prolongation of seizure duration and also status epilepticus.Patients who metabolize succinylcholine slowly due to decreased level of pseudocholinesterases may go for prolonged apnea.Headache occurs commonly.It can be treated with drugs such as NSAIDS,acetaminophen,aspirin, sumatriptan, and analgesics like codeine can be used rarely.Myalgia and nausea can occur. Mania after ECT is rare.

PHYSIOLOGICAL RESPONSES TO ECT

Cardiovascular effects

The effects of ECT in the cardiovascular system occurs as a result of autonomic system.Starting with the electrical current stimulus,initially stimulates parasympathetic system which causes parasympathetic discharge primarily by stimulating the neurons of the hypothalamus to the vagal nerve resulting in bradycardia,hypotension or even asystole lasts for a transient period of 10-15 seconds.This is followed by sympathetic nervous system activation,which releases adrenaline and noradrenaline which cardiac arrhythmias.Systolic blood pressure increases up to 30–40% of baseline and heart rate increases by 20% of baseline.The blood pressure and heart rate changes maximizes when increase in plasma adrenaline level increases 10 fold and noradrenaline level increases 3 fold.This corresponds to the 1 minute of ECT.The plasma adrenaline level reaches the control level 10 minutes after ECT but noradrenaline level remained high even after 10 minutes of ECT.

Myocardial oxygen consumption will increase in ECT.It increases more in 1.Bilateral ECT,2.Elderly,3.During hyperventilation which causes hypocapnia Myocardial oxygen consumption increases during seizure activity and oxygen supply to myocardium will be reduced.So patients with

preexisting disease have increase risk of Myocardial ischaemia and infarction.

Decrease in systolic and diastolic function of left ventricle may occur and remains up to six hours after Electroconvulsivetherapy.And also cardiac rupture can occur.

Cerebral effects

Blood flow to the brain increases during ECT. This leads to increase in intracranial pressure.Cerebral oxygen consumption is also increases during ECT.Transient ischaemic attacks,intracerebral haemorrhage, and cortical blindness can also occur.Other complications include,prolonged seizures or status epilepticus.Cognitive side effects occurs commonly.Patients with pre-existing dementia are more prone for cognitive side effects.Impairment of orientation, impaired attention, and memory loss are frequent problems after ECT.

Continuation Electroconvulsive Therapy

Relapse of the psychiatric illness can be prevented by continuation ECT.After the first few months of ECT the risk of relapse is increased.so continuation of ECT is needed.Indications of continuation electroconvulsivetherapy includes patient's preference,resistance and intolerance to the medicines, Pharmacotherapy resistant schizophrenia is

effectively treated with continuation ECT combined with neuroleptics.It can also prevents the relapse of schizophrenia after responding to the ECT.

A comparative study of effects of lithium and nortriptyline in combination with ECT was done in patients underwent continuation ECT.In that study both of the drugs given with ECT reduces the relapse when compared to the placebo.When lithium and nortriptylin was given combined with ECT it prevents the relapse more when compared to placebo.

Maintenance Electroconvulsive Therapy

Recurrence of the psychiatry illness is prevented by the maintenance of ECT.Studies concluded that geriatric patients with unipolar major depression undergoes maintenence ECT in addition with the administration of nortriptyline significantly increases the mean survival time than administration of nortryptyline alone.

Pharmacological Therapy

Pharmacological treatment given to patients after ECT may vary with the clinical diagnosis of the patient. Prophylactically given medication after ECT is beneficial to the patients who are resistant to the pharmacological treatment and who have major depressive illness.Outcome of the patients after ECT depends upon the pre ECT condition.Remission rate is seen in patient who does not respond to the drug therapy and have chronic

psychiatric illness especially depression,but is not depends on age and physical illness.Melancholic features has no role in the prediction of response to ECT.

Psychotherapy

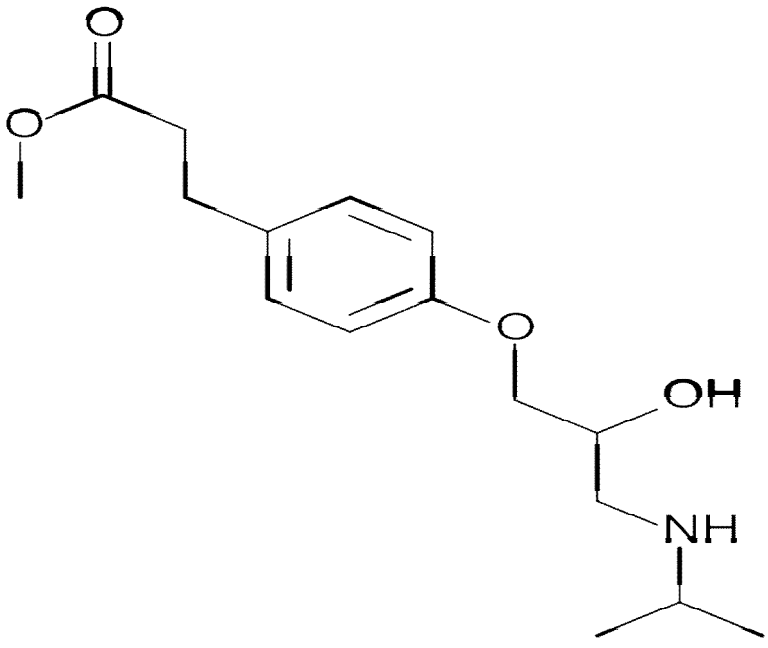
Some patients may need psychotherapy after ECT.It is very useful in treating the residual symptoms and it encourages the patients to return to routine life.Efficacy of antidepressant action of ECT may be prolonged by cognitive behavioral therapy.

PHARMACOLOGY OF ESMOLOL

Esmolol hydrochloride is a cardio selective,competitive ultra short acting and intra venously acting beta blocker.It has faster onset of action.Esmolol has minimal partial agonistic activity or no direct effect on membrane potential at normal treatment doses.It blocks the stimulatory effects of norepinephrine on the sinus and AV node.It comes under classification of antiarrhythmic drugs,class II.Esmolol is rapidly eliminated from the plasma,with the elimination half life of 9-10 minutes.

CHEMISTRY

Chemical formula of Esmolol hydrochloride is (C16H25NO4.HCL) ,(R,S)-4-[2 hydroxy-3-1[(1-methylethyl)amino]propoxy]benzenepropanoic acid methyl ester hydrochloride.and consists of following structure



Molecular weight of Esmolol hydrochloride is 331.8.It has the pka value of 9.5.It poses the chiral centre and racemate is used clinically.Esmolol is a crystalline powder which is white to off-white in colour.It is very soluble in alcohol and freely soluble in water.It is available with octanol/water partition coefficient of 0.42.

Esmolol hydrochloride intended to provide a source of drug for use as a loading dose contains as a 100mg in 10 ml vial.It is prepared as a sterile,colorless,clear and a nonpyrogenic solution.To balance the ph from 4.5 to 5.5 it is necessary to add Sodium Hydroxide or Hydrochloric Acid,1.688 mg Sodium Acetate Anhydrous (equivalent to 2.8 mg Sodium Acetate Trihydrate) and 0.546 mg Glacial Acetic Acid.

Esmolol beta 1 adrenergic receptor blocker and is the most cardioselective agent with relatively little beta 2 blockade activity,at doses commonly used clinical settings.It is available only for intravenous infusion with the elimination half life of esmolol from the plasma is nearly 9.2 minutes.It is best described by a two compartment open model.It blocks the beta 1 receptors present in the cardiac muscle at therapeutic doses and blocks the beta 2 receptors present in the bronchial smooth muscles.

Pharmacokinetics and Metabolism

Plasma levels of Esmolol can be determined by high performance liquid chromatography or gas chromatography-mass spectrometry.Esmolol not suitable for oral administration due to its rapid hydrolysis and is available only for intravenous use distribution is very rapid with an alpha phase half life of only two minutes.Esmolol is extensively and rapidly metabolized by erythrocyte cytosolic esterases to yield 3-[4-(2-hydroxy-3-{isopropylamino}-propoxy)phenyl]propionic acid and methanol.These metabolite has very weak beta adrenergic blocking activity.Elimination half life of these metabolite is 4 hrs and it is cleared at glomerular filtration rate.Esmolol is not a substrate for erythrocyte membrane or plasma esterases.Less than 1% of Esmolol is excreated unchanged in urine.Esmolol Hydrochloride is cleared from the body at a rate of 285ml/kg/min,which is greater than cardiac output.Hepatic disease has no effect on,volume of distribution,total body clearance,elimination half life of esmolol.Pharmacokinetics of esmolol is not affected by renal failure,with the half life,volume of distribution and clearance are very similar in patients maintained on hemodialysis as in healthy individuals.Esmolol Hydrochloride is rapidly distributed in our body.Esmolol Hydrochloride is rapidly distributed within two minutes of administration.

Methanol levels monitored in subjects getting Esmolol for 6 hrs at 300microgram/kg/min ranged from 2.8 to 5.9 mg/lit and when administered for 24 hrs at 150mic/kg/min methanol level ranges from 2.9 to 13.2 mg/lit.In either case methanol level is less than two percentage of that normally associated with toxicity.55% of Esmolol has been bound to human plasma protein, and has extensive presystemic metabolism.

Pharmacodynamics

Esmolol given as an infusion of 50-200 mic/kg/min inhibits isoproterenol associated rise up in heart rate in healthy volunteers.Exercise induced tachycardia and hypertension were reduced by esmolol at a dose dependent manner over the range of 100-500 mic/kg/min with estimated EC50 values of 113 and 134mic/kg/min respectively.Single intravenous bolus dose of 100mg and above have been noted to prolong PR interval on ECG but not on QRS duration or the QT interval. More detailed electrophysiological studies in patient receiving 300mic/kg/min have shown no direct effect on intrinsic sinus automaticity, AV nodal refractoriness or his purkinjie system. negative inotropic effect have been observed at doses of 16mg/min.,in patients with severe left ventricular function. as suggested by its pharmacology.

Esmolol is relatively bronchial sparing. for example ,esmolol 8-24 mg/min given to cardiac patients with copd and chrnic obstructive pulmonary disease demonstrated large decreases in the heart rate (84± to 69± to beats /min.systolic blood pressure (124±3 to 106±3 mmhg)with out reducing fev1/fvc or PEFR.A mild asymptomttic decrease was recorded in 3 of 50 patients studied.

When esmolol is administerded at a bolus followed by a continous infusion ,with a onset of b blockade activity occurs within two minutes with 90% of steady state b blockade occurring within five minutes,The fall in plasma renin activity is gradual.Full recovery from the cardiac effects of esmolol is observed 18 to 30 minutes after terminating the infusion.

THERAPEUTIC USE

1.To control the heart rate in supraventricular tachycardia

2.Intra and post operative tachycardia and hypertension.

Mode of use

Esmolol injection is administered a continuous intravenous infusion using a controlled rate electric control pump.It is recommended that to reduce hyperosmolarity,esmolol be administered in a single entity soloution such as 5%dextrose or normal saline.Dilution to a contration of 10g/l and administration into a large vein will help minimize phlebitis.

Esmolol is also available as a 100mg vial which intended to provide a premixed source of drug for use as a loading dose while the infusion is being prepared. Single dose vial may also be appropriate for transient situations such as tracheal intubation,which only require a single,one time injection.

INDICATIONS

Supraventricular Tachycardia

Esmolol is used to control the ventricular rate rapidly in atrial fibrillation and atrial flutter.It is also in the setting of noncompensatory sinus tachycardia when it is deemed necessary to intervine.A placebo controlled trial of esmolol in patients with supraventricular tachyarrythmias demonstrated a 72% response rate,defined as a 20 bpm reduction in rate or a rate under100bpm.The average dose producing this response was 97.4mic/kg/min.

Esmolol has been used combined with digoxin in the acute treatment of atrial fibrillation and flutter.After a dose of 0.25 or 0.5 mg diogoxin,esmolol was administered in doses of 2mg/min.In another study in patients with atrial flutter or fibrillation,esmolol was compared with verapamil.Both drugs were effective in controlling heart rate but a greater propotion reverted to sinus rhythm with esmolol,particularly when the onset of arrhythmia was recent.

Intraoperative and postoperative tachycardia and/or hypertension

Postoperative hypertension is often a transient phenomena and is thought to be due to excessive catecholamine release.The patients frequently release exhibit tachycardia as well as hypertension.Beta blockade with esmolol is under investigation as an alternative to commonly used intravenous vasodilator therapy,typically the use of nitroprusside.

Tracheal intubation produces a hemodynamic response of hypertension of hypertension and tachycardia.This action is undesirable in patients with ischemic heart disease and limited coronary blood flow reserve.The administration of a single bolus of esmolol prior to induction of anaesthesia is effective in attenuating this response.

Other uses

Other possible use under investigation include acute hypertensive crisis,acute myocardial ischemia,medical therapy for aortic dissection.management of thyrotoxicosis,induction of bradycardia ,for performance of coronary bypass without the use of cardio pulmonary bypass,and treatment of the hyperdynamic effects of drug over dosage such as that of cocaine and theophylline.

CONTRAINDICATIONS

Esmolol is contraindicated in patients with sinus bradycardia, cardiogenic shock, heart block greater than first degree,or overt heart failure.

CAUTION

Hypotension:

Hypotension is defined as systolic pressure less than 90 mmHg and/or diastolic pressure less than 50 mmHg.In clinical studies 20-50% of patients treated with esmolol have experienced hypotension.About twelve percentage of the patients had symptoms mainly diaphoresis and dizziness. Patients with low BP should be closely monitored. To reverse the hypotension, decrease the dose or termination of infusion,usually it will take 30 minutes.

Congestive heart Failure

The decrease in contractility with beta blocker therapy can cause an exacerbation of congestive heart failure.This is especially true of acute heart failure.In chronic heart failure states,β-blockers are better tolerated,at least in small doses.

Sinus bradycardia

Esmolol may lead to exacerbation of pre-existing sinus bradycardia with resultant hemodynamic compromise.

Heart block greater than first degree

In the presence of second degree heart block,AV nodal conduction can be further compromised.It could potentially lead to a higher degree of heart block and worsening bradycardia with more serious hemodynamic disturbances.

Cardiogenic shock

Esmolol,as is the case with any beta blocker,has a negative ionotropic effect by decreasing the endogenous beta adrenergic stimulation of cadiac contractility.In a patient with a low cardiac output this may cause,or worsen,cardiogenic shock.

ADVERSE EFFECTS

Potentially life threatening effects

Sudden death has been reported following use of esmolol.Esmolol may cause profund bradycardia and hypertension in patients with severe impairment of myocardial function who are dependent on sympathetic drive to maintain their cardiac output.Esmolol should be discontinued at the first sign of deteriorating myocardial function.Although esmolol is short acting,immediate intervention may require dopamine or dobutamine.Verapamil administered concurrently with esmolol has resulted in cardiac arrest.

Acute overdose

Accidental overdosage of esmolol has generally occurred as an error in dilution.Known doses of 5000 to 6000mic/kg being administered over 1-2 minutes have been reported.Toxic effects are bradycardia, hypotension,drowsiness and loss of consciousness.These effects generally resolves within 10 minutes of stopping the infusion,although in some cases pressor agent was given.Bradycardia could not be treated with atropine.Bronchospasm may respond to a beta2 stimulating agent.Cardiac failure may respond to administration of glucagon.Cardogenic shock may require the administration of dopamine or dobutamine initially high doses.

Symptomatic hypotension will usually respond to the administration of fluids and/or pressure agents,although the majority of cases of hypotension are asymptomatic and require no therapy apart from reduction in esmolol usage.

Severe irreversible adverse effects

Hypotension is the most common side effected with esmolol.No other serious or irreversible side effects have been described.

Symptomatic adverse effects

Symptomatic adverse effects include hypotension, bradycardia, dizziness, diaphoresis, other CNS side effects include weakness and irritability and intravenous site inflammation.Approximately 1% of patients had peripheral ischemia.

Interferance with clinical pathology tests

There is no reports of esmolol affecting the results of any blood tests.

High risk groups

No information is **available** on the use of esmolol in neonates.

Breast milk

No information available regarding the passage of esmolol or its metabolites through breast milk.

Pregnant women

Administration of esmolol in pregnant women can lead to dose related beta blockade of the fetus as well as a decrease in fetal arterial po2.Fetal bradycardia has been repoted when a mother was treated with esmolol to reduce blood pressure in the face of an intracranial arterial venous malformation.Based upon this esmolol should not be used in pregnancy.

Children

One study was performed in children aged 2-16 yrs suggests that the dosage needed to cause the beta blockade is larger than in adults.The study recommended a dose of 600mic/kg infused over 2 min followed by infusion 200mic/kg/min.However controlled trials have not been performed in this population.Therefore true risk/benefit cannot be assessed.

The elderly

No information is available regarding the safety and efficacy of esmolol in the elderly.

CONCURRENT DISEASE

Heart disease

Patients with AV heart block other than first degree heart block,cardiogenic shock,bradycardia or cardiac failure should not receive esmolol.

Chronic obstructive pulmonary disease or asthma

Patients with these diseases should be closely monitored during the administration of esmolol.

Diabetes

Esmolol should be used with caution in patients with diabetes since beta blockade may mask the symptoms of hypoglycemia.

Renal disease

In renal failure the metabolite AS-8123 may accumulate with the potential for causing undesirable bradycardia and hypotension.

DRUG INTERACTIONS

Potentially hazardous interactions

Verapamil

It has a marked cardiac depression properties as well the potiential for supreesion of AV conduction.Use esmolol,which has similar effects,has situated in cardiac arrest in patients who have received both medications simultaneously.

Digoxin

Esmolol when concurrently administered with digoxin under steady state conditions,caused a 10% increase in digoxin levels in healthy males.This increase in serum digoxin levels are not associated with an increase in PR interval or with significant changes in heart rate and blood pressure.

Warfarin

When esmolol and warfarin are administered concurrently,there are no changes in the plasma warfarin concentration.However there is an increase in serum levels of esmolol.These changes are small does not result in marked hamodynamic changes.

Morphine

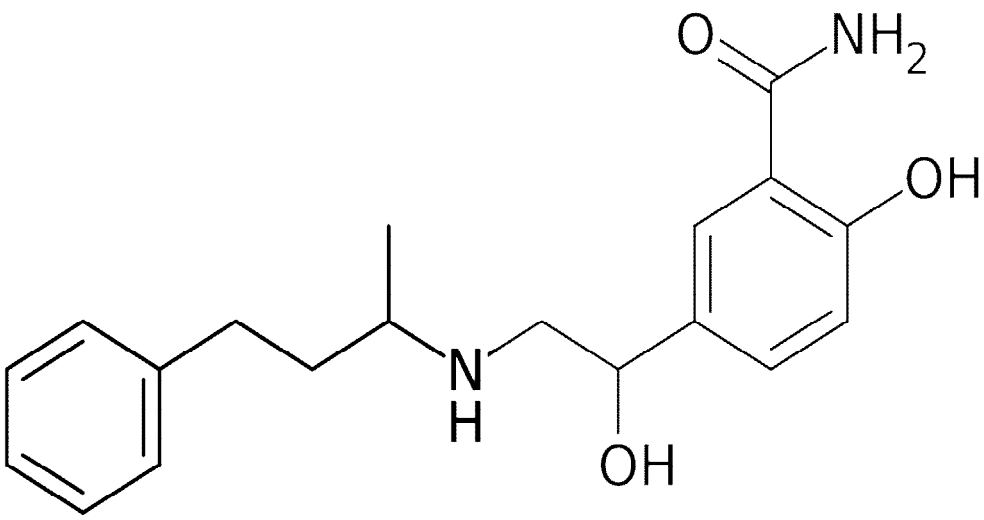
Morphine has been noted to cause an increase in steady state blood levels of esmolol when administered concurrently.

Succinylcholine

Succinylcholine has been shown to cause an increase in neuromuscular blockade in patients receiving esmolol.

PHARMACOLOGY OF LABETALOL

Labetalol hydrochloride is a competitive antagonist at beta 1 and beta 2 adrenoreceptors.,with some intrinsic activity at beta 2 receptor.Labetalol in addition to beta adrenoreceptor blocking property has competitive alpha receptor antagonistic properties at post synaptic region.Labetalol designed as 5-{(r,s)-1-hydroxy-2-{(1-methyl-3-phenylpropyl)aminoethyl}-salicylamide hydrochloride and it contains following structure:



Molecular formulae of labetalol is C19 H24 N 2O3. HCl and it has molecular weight of 364.9.It consists of two optical centers and so clinical preparation consists of equal proportion of four isomers.Dilevalol, the R,R' stereoisomer, makes up 25% of racemic labetalol.It is a crystalline powder which is white or off white in colour.Labetalol is odorless and it is soluble in water.

Labetalol hydrochloride injection is a clear, sterile colorless to light yellow, isotonic aqueous solution for intravenous (IV) injection with a pH range of 3.0 to 4.5. ,containing labetalol hydrochloride 5 mg /ml in 20 ml or 40 ml vials.excipients include dextrose,methylparaben,and propylparaben.The injection is intended for slow intra venous injection or suitably diluted intra venous infusion.

CLINICAL PHARMACOLOGY

Competitive beta adrenergic blockade has been demonstrated in humans by parallel shift in the log dose-heart rate response curve for isoproterenol. Competetive alpha adrenergic blockade has been demonstrated in humans by the parallel shift in the log –dose pressor respone curve to phenylephrine.

Pharmacodynamics

The potency ratio of alpha:beta adrenoreceptor antagonism is approximately 1:7 when given intravenously and 1:3 when given orally.After administering the intravenous dose of 0.5 to 2.0mg /kg ,labetalol may produce an immediate fall in blood pressure associated reduction in the heart rate.Cardiac output may not be affected much.Peripheral vascular resistance may be reduced.Labetalol is very useful in blunting heart rate and blood pressure response to exercise.It also blocks the pressor and heart rate

response to parentral epinephrine.Isoproterenol induced fall in diastolic blood pressure.Orally administered Labetalol decreases the blood pressure as well as heart rate.Single oral dose of labetalol given to patients with ischemic heart disease has no significant effect on intraventricular conduction, sinus rate, or QRS duration.It prolongs the atrioventricular (A-V) conduction time and effective refractory period.

The effects on A-V nodal refractoriness were inconsistent.Through a mixture of its alpha- and beta-blocking effect,it can produce dose related fall in blood pressure with out causing tachycardia or bradycardia.Elevated plasma renins are reduced.Doses of labetalol that controlled hypertension may not affect renal function in mildly to severely hypertensive patients with normal renal function.Blood pressure is lowered more in the standing person than in the supine person due to alpha receptor blockade with symptoms of postural hypotension.

Pharmacokinetics and Metabolism

Labetalol is absorbed rapidly after oral administration(well absorbed orally).In fasting individuals the peak plasma concentration occurred 20-60 minutes after a dose of 100mg where as 40-90 minutes after a dose of 200 mg.Systemic bioavailability ranged from 11-86% after a dose of 100 mg.The wide variation among individuals in total labetalol plasma concentration is due to extensive pre systemic metabolism(14-89%) plasma half life range

from 1.7-6.1 hr with a mean of 3.3 hr.Plasma protein binding capacity of Labetalol is 50%.Labetalol undergoes hepatic biotransformation,and less than 5% of the drug is recoverd unchanged in the urine.The bioavailability considerably incresed in hepatic cirrhosis.Volume of distribution in humans is 3.4-10.7l/kg/l.Less than 5 percentage of labetalol is excreted unchanged in urine.

Metabolites of labetalol are mainly excreted in urine but 12-27% excreted in feces.Smaller amounts of o-phenyl glucoronide has been identified.

INDICATIONS AND USAGE

Inj.Labetalol is mainly used in hypertension,angina pectoris,where a hypotensive technique is indicated in anaesthesia,and pheochromocytoma.

DOSAGE AND ADMINISTRATION

Inj.Labetalol hydrochloride is mainly used intravenously in emergencies where rapid control of BP is needed,because the intravenous route avoids presystemic metabolism the dose should be proportionately lower than oral dosage.It is administered either by repeated intravenous injection or slow intravenous injection.

Repeated Intravenous Injection:

Inj.Labetalol hydrochloride can be given for the intravenous treatment of severe hypertension ,with an starting dose of 20 mg administered over one to two minutes :additional doses of 40 mg and 80 mg at 10 minutes time interval until a satisfactory response has been obtained or a total of 300 mg has been administered.heamodynamic response usually occur within five minutes.

Slow Continuous Infusion

Alternative to repeated intravenous infusion ,slow continuous infusion at at rate of a starting dose 2mg/min and continued until satisfactory response has been obtained.Effective dosages range from 50-300 mg.for hypertensions of pregnancy and for hypertensions after acute myocardial infarction;for the former an initial rate of 20mg/hr doubled every 30 minute until a satisfactory response has been obtained.In the latter ,an initial dose of 15 mg/hr gradually increased until a satisfactory response has been observed.

CONTRAINDICATIONS

Labetalol is absolutely contraindicated in bronchospasm,untreated heart failure,low cardiac output status,bradycardia,severe hemorrhage and hypoglycemia.

CONDITIONS TO BE USED WITH CAUTION

Severe hepatocellular injury may rarely occur with Labetalol therapy.Usually it is reversible,and even hepatic necrosis and death may occur.Patients on Labetalol should undergo periodic hepatic laboratory tests.Laboratory testing should be done at the very first symptom or sign of liver dysfunction like persistent anorexia, pruritus, unexplained “flu like” symptoms, jaundice, right upper quadrant tenderness dark urine and jaundice.If there is evidence of liver injury or jaundice, labetalol should be stopped and not restarted.

Heart Failure

The adverse effects of beta adrenoreceptor blockade on myocardial contractility are counteracted by the alpha adreno blocking action of labetalol which causes a reduction in after load.labetalol causes a reduction in myocardial contractility and in patients with impared left ventricular function ,may cause a reduction in cardiac output.

In Patients without a History of Cardiac Failure

Labetalol has a variable effect on the heart rate and can depress the conduction in A-V node. In patients with high grade atrioventricular block or sever sinus bradycardia its use may be hazardous.

Ischemic Heart Disease

Labetalol dosage shold be tappered slowly mainly in patients with coronary artey disease, in order to avoid exacerbations of angina pectoris and myocardial infarction.In such situations,labetalol should be readministered absolutely,for a period of time and further measures for managing unstable angina should be taken.

Nonallergic Bronchospasm (e.g., Chronic Bronchitis and Emphys ema)

Labetalol has got a lesser tendency to cause bronchoconstriction than propranolol but has been reported to cause severe bronchospasm in patients with asthma.It may render such patients unresponsive to normal doses of bronchodilators such as albuterol.

Pheochromocytoma

Labetalol inhibits both the chronotropic and pressor effects of circulating catecholamines.It has been found to be effective both pre and perioperatively in the management of patients with pheochromocytoma .Satisfactory blood pressure control was reported in patients having adrenal tumors provided with labetalol.However some patients could not tolerate high dose of labetalol and was treated with a combination of propranolol and phenoxybenzamine.

Diabetes Mellitus and Hypoglycemia

The metabolic response to hypoglycemia is achieved,in part through stimulation of beta-adrenoreceptors.Thus labetalol may enhance any tendency to hypoglycemia and will mask some of the symptomatic responses such as tremor.

Major Surgery

Discontinuing long term treatment of beta blocker therapy prior to surgery should be avoided.

PRECAUTIONS

Intraoperative Floppy Iris Syndrome (IFIS) which is recorded while doing cataract surgery in some patients getting treatment with alpha -1 blocker.This is a type of small pupil syndrome which has combined flaccid iris that shows no good response during intraoperative irrigation currents,inspite of preoperative standard application of mydriatic drugs,there is an increase in intraoperative miosis and effective prolapse of the iris directed on the side of phacoemulsification incisions.Ophthalmologist mandatorily should be aware and be ready for modification of surgical techniques like way of using iris hooks,viscoelastic substances or iris dilators.No marked beneficial effects recorded ,stopping alpha one blocker therapy before cataract surgery.

After Coronary Artery Bypass Surgery:

Patient group having low cardiac indices and increased systemic vascular resistance following intravenous Labetalol noted to have significant reduction in cardiac output and very smaller change in systemic vascular resistance.These patients are more prone for hypotension following labetalol treatment.So labetalol is not recommended in that patients.

Drug Interactions

Potentially hazardous interaction .The heart rate may fall during general anaesthesia in patients treated with labetalol.The hypotensive effect of halothane enhanced by labetalol.Care should be taken if labetalol is used concomitantly with drugs like verapamil.The bioavailability of labetalol can be increased by concurrent administration of cimetidine.It has been suggested that there may be an increased incidence of tremor during therapy with a combination of labetalol and tricyclic antidepressants. The bioavailability of labetalol is increased when it is administered with food.

Pregnancy

Teratogenic Effects - Pregnancy Category C

Although no tertogenic effects have been demonstrated ,the routine use of labetalol during first trimester is not recommended.

Nonteratogenic Effects

Labetalol crosses placenta and adverse effect on fetus is possible.however in practice bradycardia,hypotension,and hypoglycemia are uncommon**.**

Nursing Mothers

Labetalol excreted in breast milk with an average milk to plasma ratio of 1.5.however the small amount of drug ingested by the nursing infant prouduce any adverse effects.

ADVERSE REACTIONS:

Acute over dosage may result in bradycardia and cardiogenic shock.Labetalol may cause postural hypotension,precipitate heart failure,it has been reported to cause bronchospasm,licheniform skin rashes,retention of urine,systemic lupus erythamatosus.Distrurbances of liver function including frank jaundice and liver necrosis have also been recorded.Labetalol in generally well tolerated but may cause headache,nasal stuffiness,scalp tingling ejaculatory failure,and worsening of intermittent claudication.Other unwanted effects include dyspepsia,nausea,vomiting and night mare.

MATERIALS AND METHODS

This was a prospective randomized controlled double blinded study.After ethical committee approval and informed written consent obtained from the family members of the patients,the study was conducted in 90 eligible patients after explaining the procedure details to family members of the patients.This study was conducted at Government Rajaji Hospital attached to Madurai Medical College.

INCLUSION CRITERIA :

1.Psychiatric patients undergoing Electro convulsive therapy

2.ASA I and II patient

3.Either sex

4.Age between18-60 years

EXCLUSION CRITERIA :

1. Patients with II degree AV conduction block or greater,
2. Bradycardia Heart rate less than 50/min
3. Systolic Blood pressure less than 90mmhg
4. Asthmatic patients
5. patients with history of drug allergy
6. Recent Myocardial infarction (with in 3 months)

METHODOLOGY

90 ASA I and II patients undergoing Electro convulsive therapy were randomly divided into three groups.Each group contains thirty patients. Patient was premedicated with Inj.Glycopyrrolate 0.2 mg im 30 minutes before ECT.Patient shifted to ECT room and IV line secured with wide bore IV cannula.

Group C-Control group received normal saline 5ml,

Group E-Esmolol group received 1mg/kg of esmolol,

Group L-Labetalol group received 0.25mg/kg of labetalol.

PREOPERATIVE EVALUATION

A routine pre anaesthetic assessment of the patient included history regarding the severity and duration of symptoms, history of any other systemic illness, history of any other previous surgeries. A detailed examination was done by assessing the general condition, airway , nutritional status, weight and height of the patient. A thorough systemic examination of cardiovascular and respiratory system was made. The following basic investigations like haemoglobin, urine examination for sugar ,albumin and microscopy, blood sugar, blood urea, serum creatinine, standard 12 lead

ECG, echocardiography, serum electrolytes and X ray chest were done for all patients.

MONITORS:

Pulse oxymetry,Blood pressure cuff,ECG leads,Capnography was attached

MONITORING OF BASELINE PARAMETERS:

Baseline Pulse rate,Systolic and Diastolic Blood pressure,SPO2 were recorded and marked as “o”

PROCEDURE:

Patient was preoxygenated with 100% Oxygen and patient was induced with Inj.Propofol 1-2 mg/kg.Immediately after induction patients in control group received normal saline 5ml,and group E and L received Inj.Esmolol 1 mg/kg and Inj.Labetalol 0.25 mg/kg respectively as bolus.Parameters monitored and to be recorded after 1 min of test drug and noted as X.After that BP cuff was inflated above the systolic BP to isolate the another limb then Inj.Succinylcholine 1mg/kg was given. ECT current was given after two minutes of administration of test drug after applying an oral soft bite block.Electric shock current applied to the patients were same.

In Government Rajaji Hospital ECT electrodes were placed bitemporally.A Monitored Electroconvulsive Therapy Apparatus (MECTA) was used to deliver the electrical stimulus.Assesement of the effectiveness of the electric current applied in ECT was made by seeing the tonic-clonic seizures in the isolated arm.Patient was ventilated with 100% oxygen by controlled and assisted method until spontaneous respiration returned.Baseline pulse rate,systolic BP and diastolic BP were recorded and marked as “o”.After 1 minute of administration of test drug these parameters monitored and recorded as “X”.After 1 minute,3 minutes,5 minutes and 10 minutes of ECT pulse rate,systolic BP and diastolic BP were recorded and marked as A,B,C,D accordingly. Fall in blood pressure more than 25% from baseline was considered as hypotension and treated IV fluids and fall in pulse rate less than 50/min was considered as bradycardia and treated with Inj.Atropine 0.3 mg.By using the statistical analysis system all statistical analysis was done.The relation among the treatments was determined by T test. P value <0.05 is statistically significant.

STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2010)** developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square ‘t’ value and 'p' values were calculated. ‘t’ test was used to test the significance of difference between quantitative variables and Yate’s and Fisher’s chi square tests for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship

OBSERVATIONS AND RESULTS

Group C :Control cases – 30 cases

Group E : Patients given IV Esmolol – 30 cases

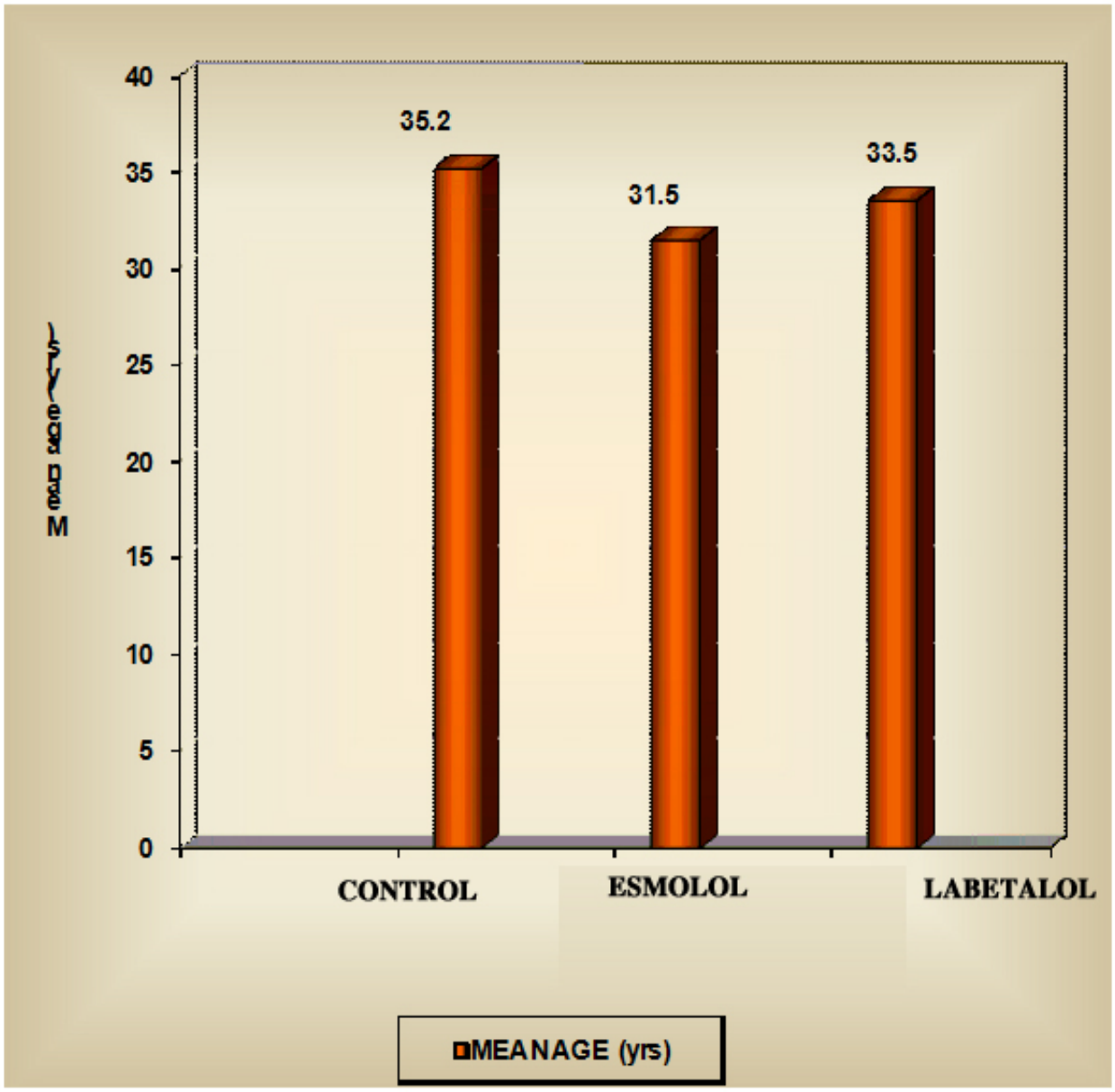
Group L :Patients given IV Labetalol – 30 cases

A : PROFILE OF CASES STUDIED

A : Age Distribution

Group	**Age in years**	
	Mean	**SD**
Control Group	35.2	8.0
Esmolol Group	31.5	9.2
Labetolol Group	33.5	8.0
'p' value between		
Control & Esmolol Group	0.1078	
Control & Labetolol Group	0.4317	
Esmolol & Labetolol Group	0.374	

Mean age of group C was 35.2 years and group E was 31.5 years & Mean age of group L was 33.5 years.There is no statistical difference between these groups.

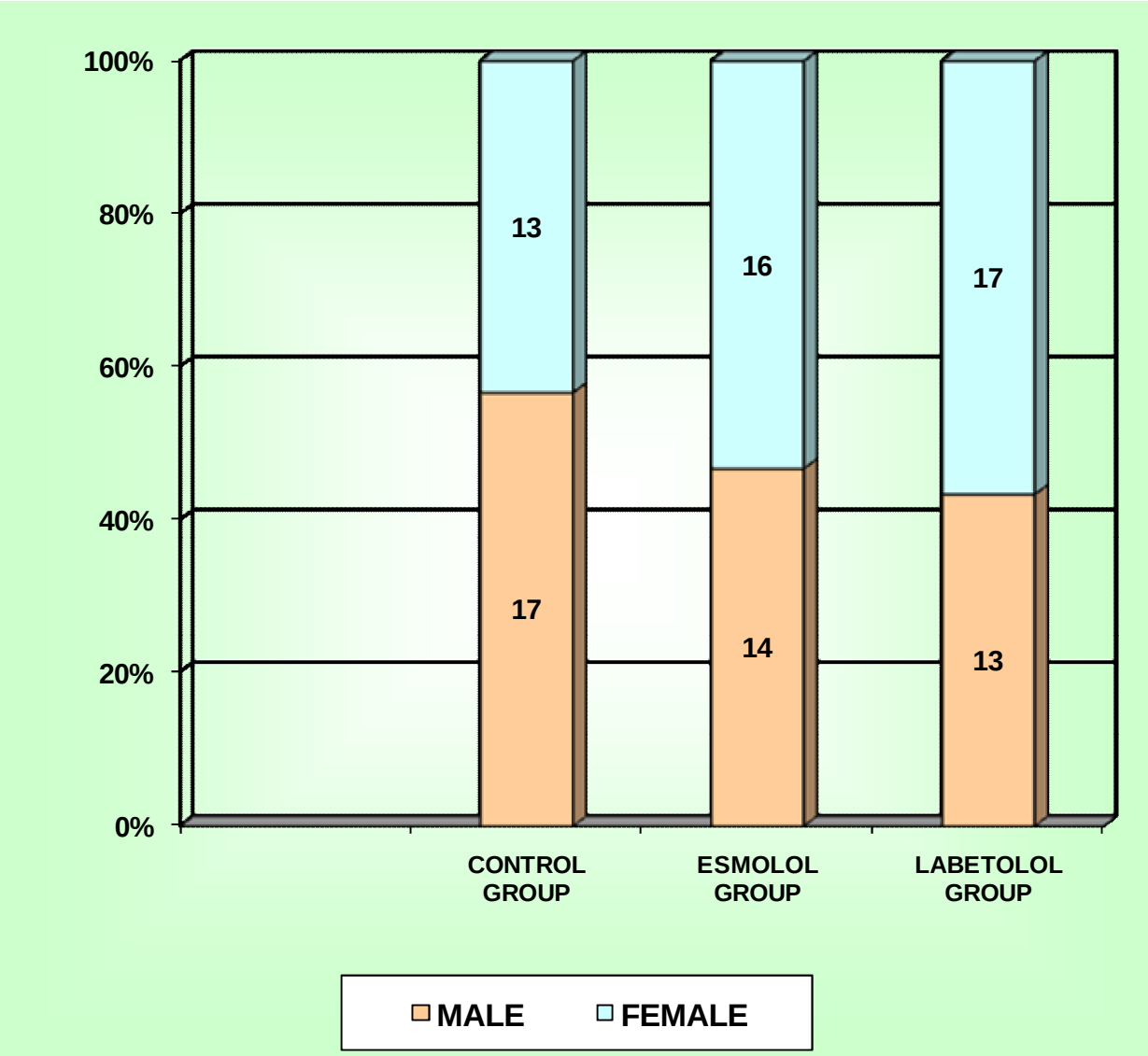


This is the graphical representation of mean age of all the three group.There is no significant difference in all three groups

Table A2 : Sex Distribution

Group	Sex			
	Male		Female	
	No	%	No	%
Control Group	17	56.7	13	43.3
Esmolol Group	14	46.7	16	53.3
Labetolol Group	13	43.3	17	56.7
'p' value between				
Control & Esmolol Group	0.3029			
Control & Labetolol Group	0.2195			
Esmolol & Labetolol Group	0.5			

56.7% in Group C and 46.7% in Group E &43.3% in group L were male. 43.3% in Group C& 53.3 in Group E & 56.7 % in group L were female. The sex distribution did not have any statistical significance.

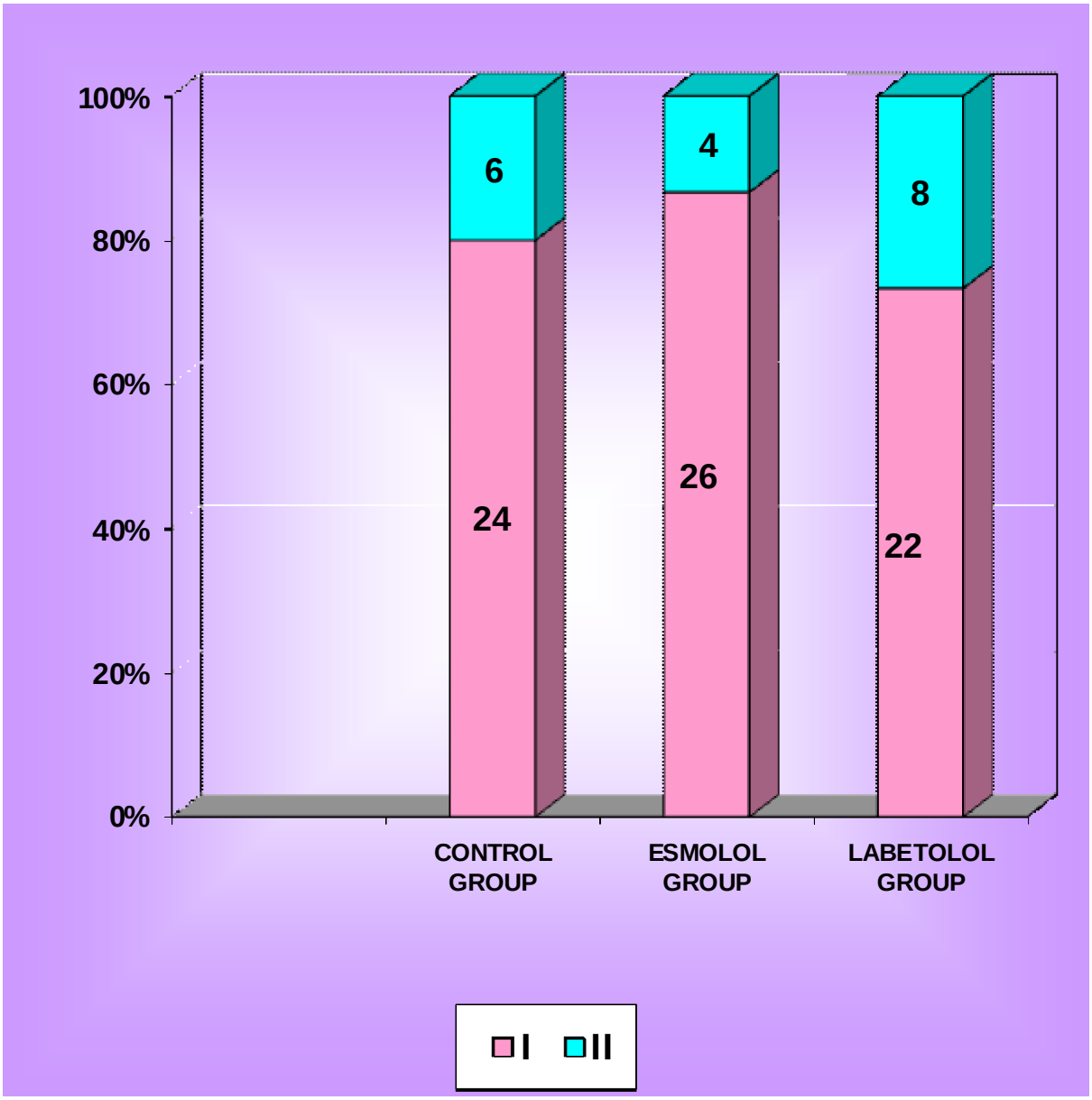


This graphs shows the sex distribution in all the three groups.This is not statistically significant.

Table A3 : ASA

Group	**ASA**			
	I		**II**	
	No	**%**	**No**	**%**
Control Group	24	80	6	20
Esmolol Group	26	86.7	4	13.3
Labetalol Group	22	73.3	8	26.7
'p' value between				
Control & Esmolol Group	0.3653			
Control & Labetolol Group	0.1667			
Esmolol & Labetolol Group	0.3805			

80% in group C & 86.7% in group E & 73.3% in group L comes under ASA I.20% in group C &13.3 & 26.7 group L comes under ASA II.ASA grading didnot show any statistical difference.



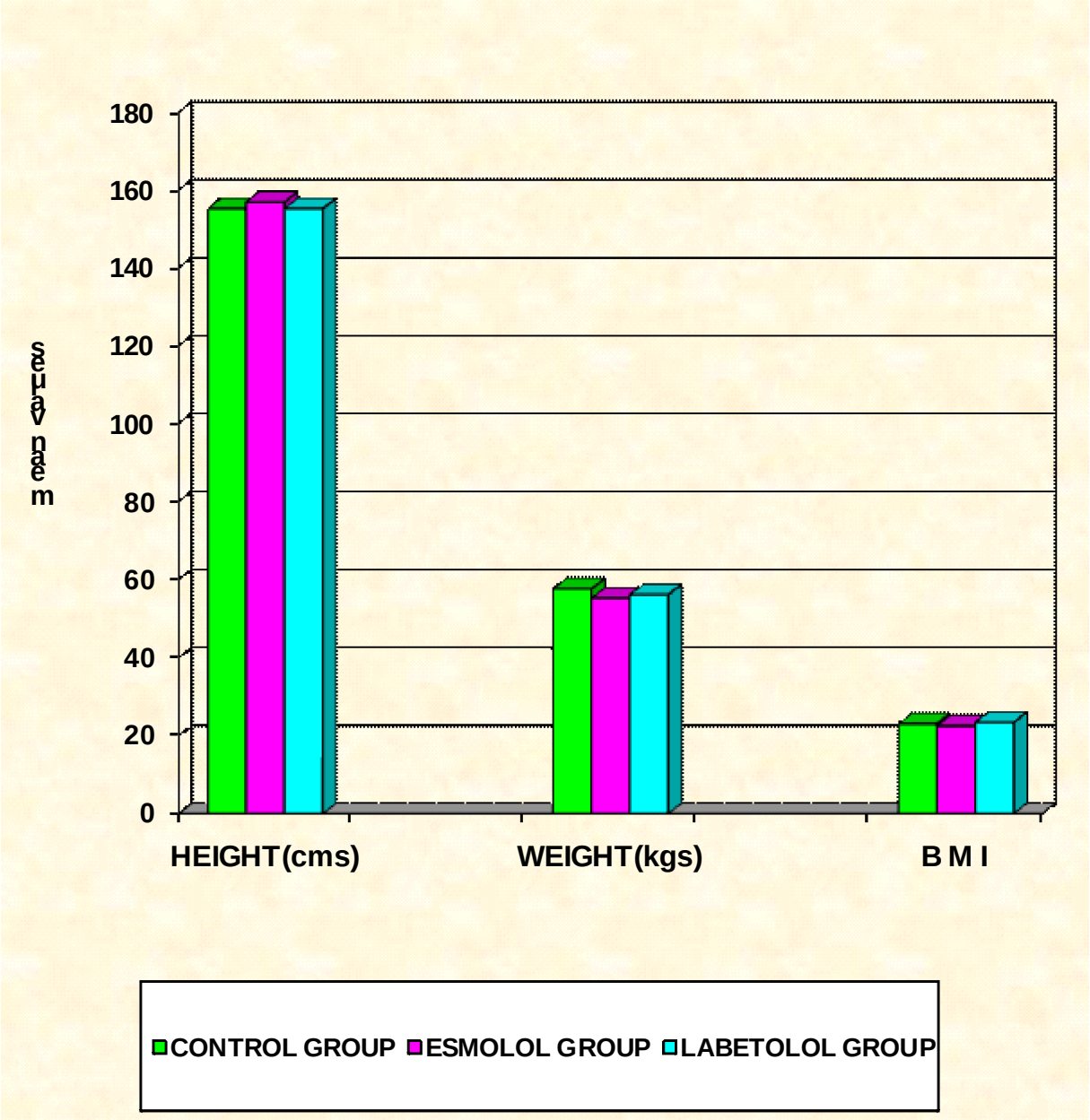
This graph shows the ASA of all the three groups.This is not statistically significant.

Table A4: Height / Weight / BMI

Group	Height (cms)		Weight (kgs)		BMI	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Control Group	158.2	8.4	57.7	6.8	23.1	2.9
Esmolol Group	156.9	2.3	55.3	7.8	22.5	3.2
Labetalol Group	155.2	6.8	56.2	7.2	23.4	3.2
'p' value between						
Control & Esmolol Group	0.0816		0.2077		0.4537	
Control & Labetolol Group	0.0705		0.4112		0.7193	
Esmolol & Labetolol Group	0.3737		0.6444		0.2952	

Mean BMI of C was 23.1 and Group E was 22.5 and group L was 23.4.

The mean BMI of these groups were not statistically significant .



This is the graphical representation of the BMI of three groups.This is not statistically significant.

Table B4 : Changes in SPO2

Group	**SPO2**	
	mean	**SD**
Control Group	99.1	0.6
Esmolol Group	99.1	0.6
Labetalol Group	99.1	0.6
'p' value between		
Control & Esmolol Group	1.0	
Control & Labetolol Group	1.0	
Control Group	1.0	

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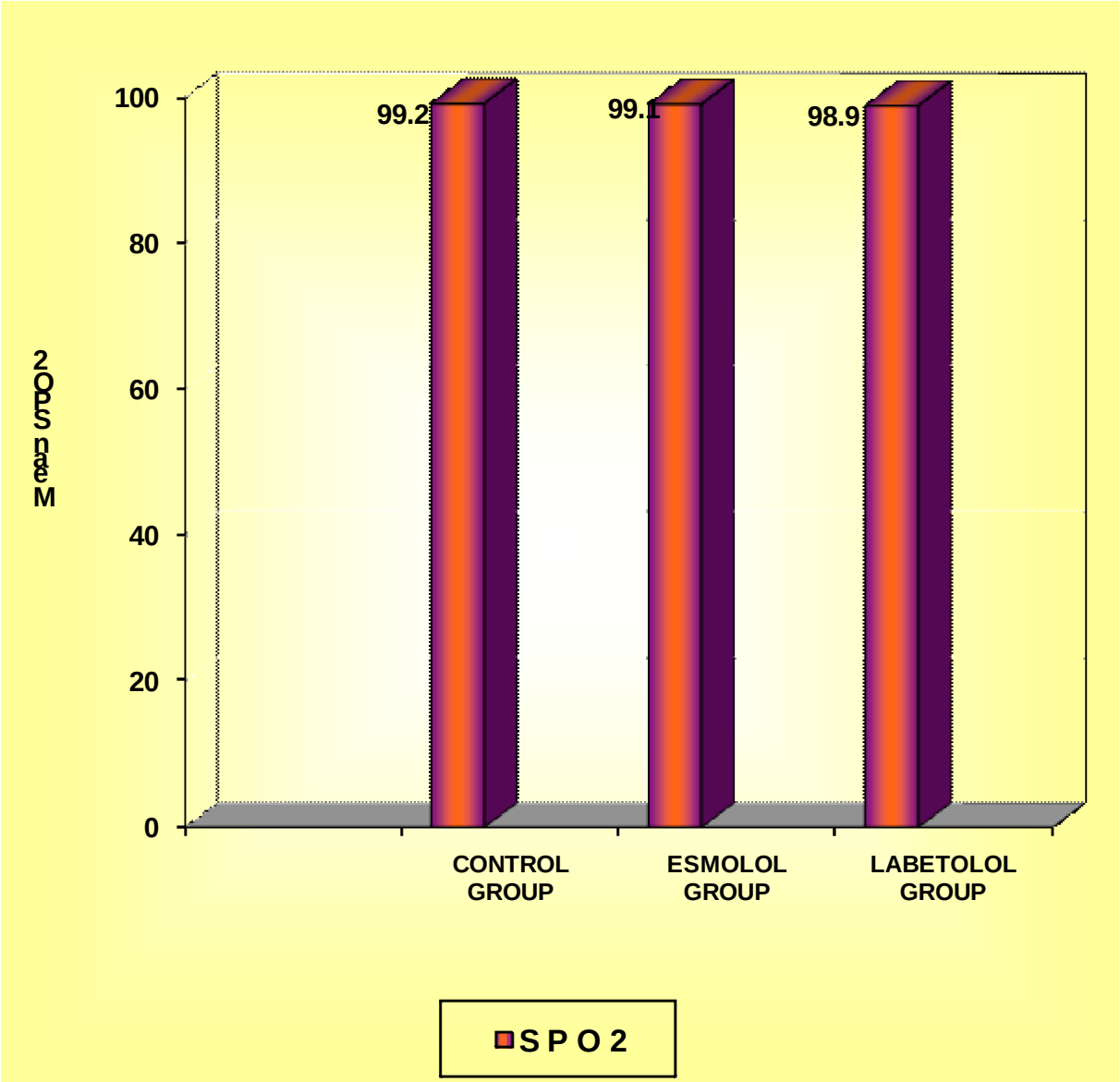
SPO2 of group C,group E,group L is 99.1.SPO2 is not statistically significant.



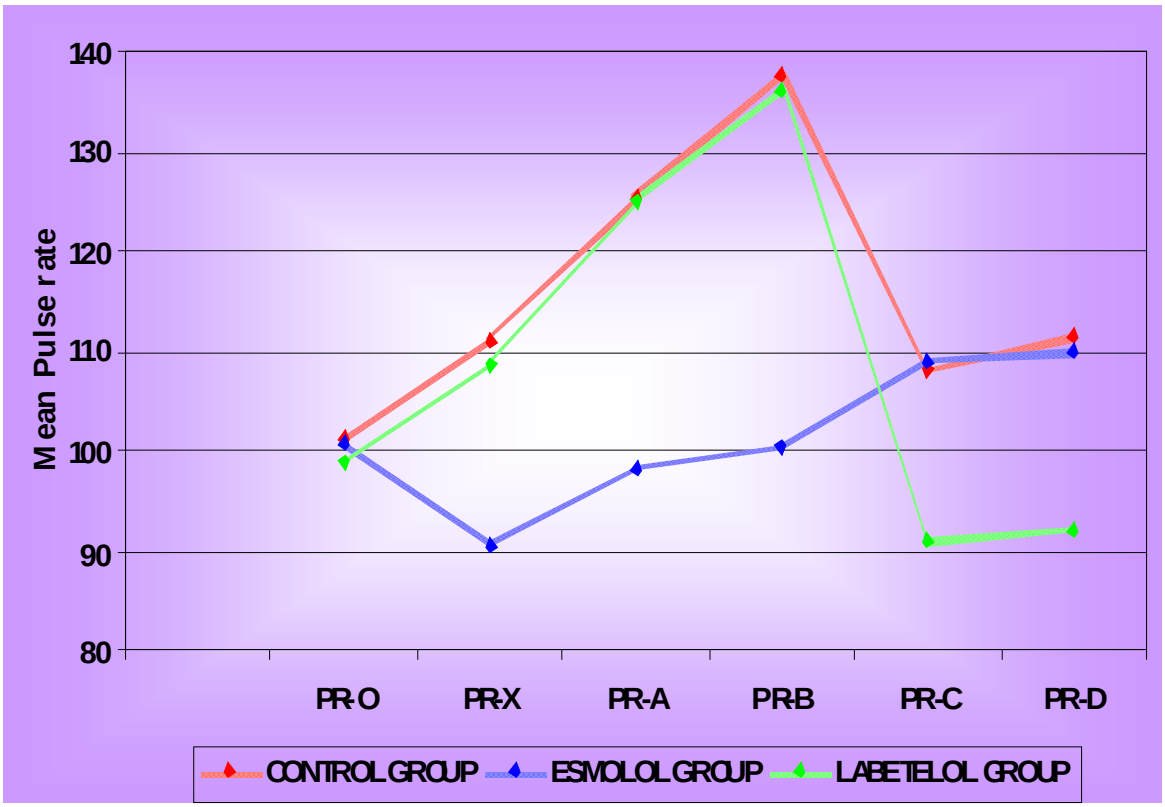
This the graphical representation of SPO2 of three groups.There is no significance.

B: EFFICACY OF THE THREE DRUGS

Table B1: Changes in Pulse Rate

Pulse Rate at	Pulse Rate of						'p' Value between		
	Control Group		Esmolol Group		Labetolol Group		Control & Esmolol groups	Control & Labetolol groups	Esmolol & Labetolol Groups
	Mean	SD	Mean	SD	Mean	SD			
P R – 0	101.1	3.1	100.7	3.1	99.1	3.8	0.28	0.1054	0.0693
P R – X	111.1	3.1	90.7	3.3	108.5	7.3	**<0.0001**	0.0716	**0.0001**
P R – A	125.2	5.9	98.3	2.5	125.0	4.1	**<0.0001**	0.8801	**<0.0001**
P R – B	137.5	3.1	100.5	3.0	136	2.5	**<0.0001**	0.3181	**<0.0001**
P R – C	108.1	2.8	109.0	5.5	91.1	3.1	0.4443	**<0.0001**	**<0.0001**
P R – D	111.4	5.6	109.9	4.0	92.1	3.3	0.2251	**<0.0001**	**<0.0001**

CHANGES IN PULSE RATE



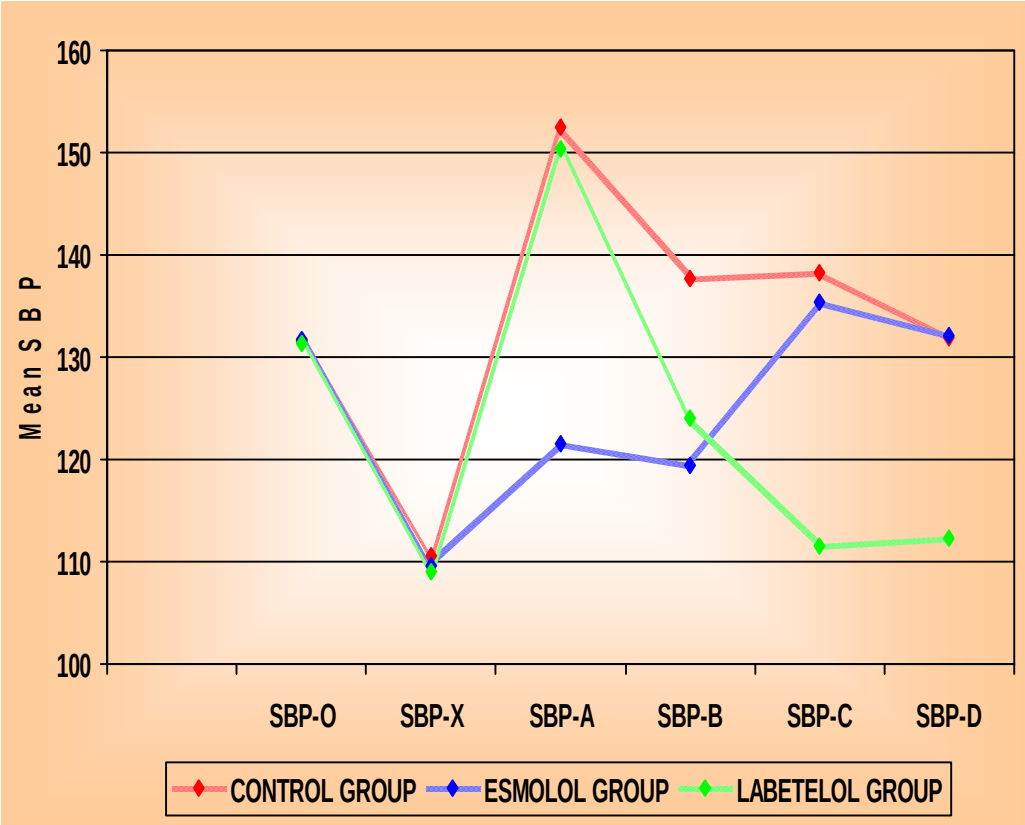
This graph shows the changes in heart rate during ECT in all groups

Table B2: Changes in Systolic Blood Pressure

Systolic Blood Pressure at	Systolic Blood Pressure of						'p' Value between		
	Control Group		Esmolol Group		Labetolol Group		Control & Esmolol groups	Control & Labetolol groups	Esmolol & Labetolol Groups
	Mean	SD	Mean	SD	Mean	SD			
SBP – 0	131.6	8.2	131.7	8.2	131.3	8.4	0.9501	0.8774	0.8288
SBP – X	110.6	7.0	109.7	7.0	109.1	5.2	0.608	0.3635	0.7384
SBP – A	152.5	7.6	121.5	4.3	150.3	5.0	**<0.0001**	0.1898	**<0.0001**
SBP – B	137.6	8.4	119.5	4.5	124.1	8.8	**<0.0001**	**<0.0001**	**0.0134**
SBP – C	138.3	8.9	135.4	7.3	111.6	5.5	0.1781	**<0.0001**	**<0.0001**
SBP – D	131.9	6.6	132.2	6.5	112.3	7.2	0.8756	**<0.0001**	**<0.0001**

This table shows the Systolic BP at various time during ECT in all the three groups.

CHANGES IN SYSTOLIC BLOOD PRESSURE



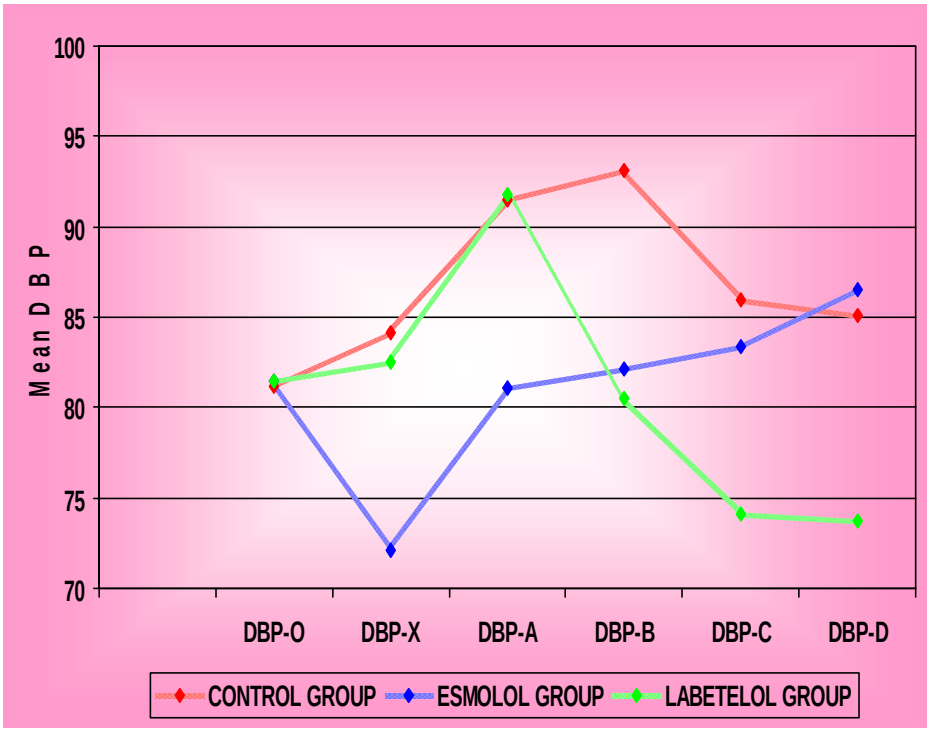
This graph shows the changes of systolic bp at various time in all three groups

Table B3: Changes in Diastolic B.P.

Diastolic B.P.at	Diastolic B.P. of						'p' Value between		
	Control Group		Esmolol Group		Labetolol Group		Control & Esmolol groups	Control & Labetolol groups	Esmolol & Labetolol Groups
	Mean	SD	Mean	SD	Mean	SD			
DBP – 0	81.2	5.3	81.5	5.1	81.5	5.5	0.8438	0.8114	0.9614
DBP – X	84.1	5.3	72.1	4.4	82.5	3.3	**<0.0001**	0.1666	**<0.0001**
DBP – A	91.5	5.6	81.1	5.1	91.8	6.0	**<0.0001**	0.8588	**<0.0001**
DBP – B	93.1	5.8	82.1	5.0	80.5	5.7	**<0.0001**	**<0.0001**	0.2337
DBP – C	86.0	3.6	83.4	6.0	74.1	5.8	0.1961	**<0.0001**	**<0.0001**
DBP – D	85.1	5.3	86.5	4.0	73.7	6.3	0.2325	**<0.0001**	**<0.0001**

This table shows the recorded values of Diastolic BP during ECT in all three groups.

CHANGES IN DIASTOLIC BLOOD PRESSURE



This Graph shows the Diastolic Blood Pressure change in all three groups.

REVIEW OF LITERATURE

1. Castelli I& Steiner in 1995 studied the comparative effects of Esmolol and Labetalol in attenuation of hemodynamic responses after ECT.In that study they studied 18 patients with atleast one cardiac risk factor.They compared the effects of five types of pretreatment.The patient did not receive any drug in the first session of ECT.Then the patient received Esmolol 1.3mg/kg and 4.4mg/kg,Labetalol 0.13mg/kg and 0.44mg/kg in subsequent sessions.They found that hemodynamic responses (rise in heart rate,systolic bp,diastolic bp) occurs 1 minute after ECT.They concluded that hemodynamic responses were attenuated (50% reduction in HR &BP) by Esmolol 1.3mg/kg and Labetalol 0.13mg/kg.These responses are almost eliminated at the doses of Esmolol 4.4mg/kg and Labetalol 0.44mg/kg. Even after 10 minutes of ECT systolic BP was low after Labetalol treatment but not so after Esmolol.

2. Howie et al defined the dose range of Esmolol in attenuation of hemodynamic responses after ECT.They divided 20 patients into placebo group and Esmolol group.Esmolol group received Esmolol 500mic/kg/minute followed by Esmolol 300mic/kg/minute (high dose) or 200mic/kg/minute (medium dose) or 100mic/kg/minute (low dose) infusion during ECT.

each patient given either placebo or Esmolol 500mic/kg/minute bolous followed by high or medium or low dose infusion.The infusion or placebo stopped 3 minutes after ECT.They found that mean heart rate was decreased significantly from 3-7 minutes.The decrease in heart rate was high dose>medium dose>low dose infusion.They concluded that Esmolol bolus dose of 500mic/kg/minute followed by 300mic/kg/minute of infusion reduces heart rate maximum when compared to medium or high dose of infusion.

3.Avramom MN et al studied the efficacy of IV nicardipine in attenuating hemodynamic responses after ECT when used alone or combined with Labetalol.Patient underwent series of studies.Patient received either placebo or IV nicardipine by rapid infusion(1, 2.5, 5, 10, and 15 mg) or bolus injection (1.25, 2.5, and 5 mg), either alone or in combination with Labetalol 10mg IV.At 1- to 5-minute intervals heart rate (HR) and Mean arterial pressure (MAP) were recorded. When nicardipine 5 mg i.v.given as rapid infusion decreases the MAP significantly.If they increases the nicardipine dosages of 10 to 15 mg i.v. did not decrease the MAP greater than 5mg bolus dose of iv nicardipine.The heart rate increased when MAP decreased after giving the bolus dose of 5mg nicardipine. The hemodynamic responses after ECT was attenuated effectively by nicardipine 2.5 to 5 mg i.v. bolus, in combination with labetalol 10 mg i.v.Nicardipine does not significantly affect the seizure duration.

They concluded that hemodynamic responses after ECT was significantly affected by Nicardipine 2.5 mg i.v. bolus in combination with labetalol 10 mg i.v.It was found that this combination reduces the mean arterial pressure 20% before ECT and at the time of discharge.

4.Kovac et al compared placebo with 2 doses of Esmolol in attenuation of hemodynamic responses after ECT.Patient received either placebo or Esmolol 100mg or 200 mg as bolus.Both the doses of Esmolol reduces hemodynamic responses after ECT significantly when compared to placebo.It was found that Esmolol bolus dose of 100 mg significantly reduces heart rate and mean arterial pressure up to 4 minutes after ECT where as bolus dose of 200mg reduces heart rate and mean arterial pressure up to 18 minutes after ECT.But Esmolol bolus dose of 200mg shorten the duration of seizures.So low dose of Esmolol found to be effective without altering the seizure duration.

5.Sarvesh P singh et al studied the effects of Esmolol and Labetalol in attenuation of sympathetic response to laryngoscopy and intubation.They divided the patients into 3 groups(control group received saline,esmolol group received 0.5mg/kg esmolol and labetalol group received 0.25mg of labetalol)Test drugs were given 2 minutes before laryngoscopy.Heart rate,Systolic BP and Diastoloc BP were measured prior to intubation and after 1,3,5,10 of intubation.

Both the drugs in low dose raduces sympathetic responses.They concluded that labetalol 0.25mg/kg is the better agent in reducing the sympathomimetic responses during laryngoscopy and intubation.

6. Jung Hee Ryu et al compared the effects of IV Labetalol 0.4 mg/kg and IV Nicardipine 20 mic/kg to attenuate the hemodynamic responses during laryngoscopy and endotracheal intubation.Both the drugs were given 4 minutes before intubation.120 patients were divided into four groups.40 patients received 0.4 mg/kg of labetalol or 20 mic/kg of nicardipine (40 patients) before intubation in part I.In part II to receive 0.4 mg/kg of labetalol(40 patients) or 20 mic/kg of nicardipine (40 patients) after intubation if hypertension occurred.The amount of additional drug needed to reduce the hemodynamic responses wera noted. In part I and part II patients who had taken nicardipine required additional dose of drug less likely when compared to labetalol.But labetalol reduces the incidence of tachycardia when compared with nicardipine during intubation.SO they concluded that labetalol reduces the hemodynamic responses significantly without increasing the heart rate when compared to nicardipine.

7. Mulgaokar G D et al assesed the cardiac function changes in patients undergoing ECT.80 psychiatric patients underwent ECT was included in that study.ECT resulted in increased blood pressure and rate pressure product and also shortening of preejection period.

Cardiac contractility and myocardial oxygen demand was increased as a result of changes in rate pressure product and shortening of pre ejection period.These effects were mainly due to catecholamines such as epinephrine and norephinephrine released during ECT.

8.Mohammad umar zhoor et al studied the use of lidocaine and nitroglycerine in attenuation of stress response during ECT.Patients were allocated into 3 groups. Group A is control group,group B received lidocaine 1mg/kg and group c received nitroglycerine 3 mic/kg after induction.Heart rate,MAP was 2 minutes of administration of test drug and 1min after ECT.65% patients showed significant reduction of HR and MAP in group B compared to group A.52% showed significant reduction of HR and MAP in group C compared to group A.It was concluded that NTG provided more hemodynamic stability in post-ECT period as compared to lignocaine which only prevented a surge in HR without any effect on MAP.It was concluded that NTG can safely be instituted for anaesthesia in ECT patients for prevention of hemodynamic stress response.

9. D O'Flaherty et al compared the haemodynamic responses in 82 patients underwent electroconvulsive treatments were randomly assigned to receive either nitroglycerin 3 micrograms.kg-1, esmolol 2 mg.kg-1 or placebo. These drugs were given shortly after the suxamethonium and 2 min before the electroconvulsive therapy in all cases.

Heart rate was significantly lower with esmolol 1 min after therapy as was blood pressure (systolic and diastolic). The pulse rate was higher following nitroglycerin than placebo, which in turn was higher than esmolol. The three groups did not differ with regard to seizure duration. The results demonstrate that esmolol is more effective than nitroglycerin in controlling the haemodynamic response to electroconvulsive therapy. With recent emphasis on stabilisation of heart rate in preference to blood pressure in at-risk cardiac patients, our study suggests that, in the doses selected, esmolol is preferred to nitroglycerin to control the heart rate response to electroconvulsive therapy.

10. MB Weinger at al studied the cardiovascular effects of ECT after pre-treatment of 10 patients with esmolol (1.0 mg/kg), fentanyl (1.5 micrograms/kg), labetalol (0.3 mg/kg), lidocaine (1.0 mg/kg), and saline solution (control), using a double-blind, randomized block-design. Each patient received all five pretreatment regimens over the course of five ECT sessions. During control studies, arterial blood pressure and heart rate increased significantly in all patients after ECT (P less than 0.05 and P less than 0.01, respectively). The rate-pressure product increased by an average of 336% +/- 14% (P less than 0.01).

There were appreciable individual differences in the cardiovascular response to ECT, independent of pretreatment (P less than 0.01). Pretreatment with esmolol and labetalol significantly reduced the hemodynamic response to ECT, compared with fentanyl, lidocaine, or saline solution (P less than 0.05). Esmolol attenuated arterial blood pressure to a larger extent than did labetalol (P less than 0.05). Compared with saline solution (control), pretreatment with labetalol, fentanyl, or lidocaine significantly reduced seizure duration (P less than 0.05) and increased the frequency with which a second electrical stimulus was required. In contrast, esmolol pretreatment did not significantly affect seizure duration. Esmolol (1 mg/kg), administered 1 min before induction of anesthesia, produced significant amelioration of the cardiovascular response to ECT with minimal effect on seizure duration.

In this study comparison of Esmolol and Labetalol in attenuating hemodynamic responses after ECT was done.90 patients were divided randomly into 3 groups.Each group contains 30 patients.Patients in each group received saline or either bolus dose of Esmolol 1mg/kg or Labetalol 0.25mg/kg just after induction with propofol.ECT was given after 2 minutes of test drug.

Heart rate, Systolic BP,Diastolic BP were recorded before ECT,1 minute after test drug and 1,3,5,10 minutes after ECT.It was found that Esmolol 1mg/kg was significantly attenuates the hemodynamic responses by reducing the Heart rate,Systolic BP and Diastolic BP up to 3 minutes after ECT. Where as Labetalol reduces the Heart rate from 5 minutes to 10 minutes, and reduces Systolic BP and Diastolic BP from 3 minutes to 10 minutes.

DISCUSSION

Electroconvulsive therapy (ECT) is used to treat severe depression resistant to pharmacological treatment.It is used for the past 50 years.In the initial period ECT was given without anaesthesia.Now a days ECT is administered with anaesthesia to eliminate the advers events of the unmodified ECT.The goal of anaesthetist is to provide anaesthesia without affecting the therapeutic effects of ECT.The therapeutic effects of ECT is due to central nervous system activation,but the exact mechanism of the beneficial effects is not known.During ECT after application of electric current tonic clonic seizures occurs.During the period of tonic clonic seizures parasympathetic discharge occurs which may cause bradycardia or even asystole.But it lasts for few seconds(10-15 sec),which is followed by sympathetic discharge occurs.Sympathetic discharge is due to the release of adrenaline and noradrenaline.Adrenaline level increased 15 times and comes to normal level after 10 minutes of ECT.Noradrenaline level increases 3 times and remains increased for twice as long.Peak level occurs at 60 sec after ECT. This leads to increases in Heart rate,Systolic BP,Diastolic BP and cardiac output.During ECT myocardial oxygen demand increases and myocardial oxygen supply decreases.SO, patients with comorbidities are at risk of developing ischemia or infarction.Cerebral blood flow and intracranial pressure also increases.

During ECT intra ocular pressure and intragastric pressure increases.It is necessary to attenuate the hemodynamic responses after ECT.For that a short acting beta-blocker or drug that have both alpha and beta blocking property can be used to blunt the stress response caused by catecholamines.Mortality rate is 0.03% if patients with cardiovascular disease undergo ECT.Many drugs are used to attenuate the hemodynamic responses after ECT.These include antihypertensive drug including trimethaphan, nitroprusside,nitroglycerin,beta blockers like propranolol, alprenolol, esmolol,labetalol, alpha agonists like clonidine, dexmedetomidine, urapidil, and calcium channel blockers like nicardipine.There is no standard regimen to blunt the hemodynamic responses after ECT.The property of the ideal drug should be more convenient to the patient.It must be easily available,cheap,easy to prepare and administer,onset of action must be rapid.It should not produce any toxic effects and have minimal side effect.

Esmolol hydrochloride is an ultra-short acting,cardio selective beta blocker(beta 1).Its distribution half life is 2 minutes.Elimination half life of Esmolol is 9 minutes. Esmolol is also more useful in attenuating the stress response during laryngoscopy and intubation and also used to reduce the stress intraoperatively and postoperatively.Labetolol is adrenergic receptor blocking agent with mild alpha1 and predominant beta-adrenergic receptor blocking actions.

Ratio of alpha:beta blockade is 1:7 when it is administered intravenously and 1:3for PO administration. Labetalol onset of action is 2-5 minutes with peak effect at 5-15 minutes.These properties like rapid onset of the drug makes the drug useful in attenuating the hemodynamic responses after ECT.It will take 10-20 minutes to decrease the adrenaline and noradrenaline level to normal after ECT. Hemodynamic changes occurs after ECT lasts for 10 minutes.After ECT for a period of ten minutes Esmolol and Labetolol take part in reducing the hemodynamic changes.It was found that Esmolol dose of 1mg/kg was effective in attenuating the increase in Heart rate,Systolic BP,Diastolic BP up to 3 minutes but not effective in the later period of ECT(3-10 min).The time coinsides with the onset and peak time of the Esmolol.This results is similar to that found in study conducted by kovac et al.This study found that 0.25mg/kg Labetolol is not effective in attenuating the increase in mean Heart rate in the first 5 minutes and Systolic BP and Diastolic BP in the first 3 minutes.But Labetalol is effective in attenuating the Heart rate after 5-10 minutes of ECT and Systolic BP and Diastolic BP after 3-10 minutes of ECT.The time coinsides with the onset and peak time of the Labetalol.This results is similar to that found in study conducted by Castelli I& Steiner in 1995.

Demographic profile:

The mean age ,sex distribution, the BMI, ASA classification were comparable in all the three groups and there was no statistical difference between these groups.

between these groups.

CHANGES IN HEART RATE

Comparison of Esmolol with Control group

In both Control and Esmolol group baseline mean heart rate was same.The difference between mean Heart rate was not statistically significant(P value=0.28).After 1 min of ECT the mean heart rate in Control group was 125.2 and where as in Esmolol group was 98.3.The difference between the mean heart rate was statistically significant(P value =<0.05).After 3 min of ECT the mean heart rate in Control group was 137.5 and in Esmolol group was 100.5.The difference in the mean heart rate between the Control group and Esmolol group was statistically significant(P value =0.0001).The mean heart rate in Control group after 5 minutes and 10 minutes of ECT was 108.1 and 111.4 and in Esmolol group was109.0 and 109.9.

The difference between mean heart rate between the Control group and in Esmolol group after 5 and 10 minutes ECT was statistically insignificant(P value =0.44 and 0.22 respectively).This clearly shows that Esmolol was effective in attenuating the increase in heart rate in the immediate period that is 1 minute and 3 minutes after ECT but not effective in attenuating the rise in heart rate in the later period (5-10minutes after ECT).This results is similar to result of the study conducted by **D O'Flaherty et al** who found that esmolol is preffered to nitroglycerine to control the heart rate.

Comparison of Labetalol with Control group

In both Control and Labetalol group baseline mean heart rate was same.The difference between mean Heart rate was not statistically significant(P value=0.105).After 1 min of ECT the mean heart rate in Control group was 125.2 and where as in Labetalol group was125.0.The difference between the mean heart rate was statistically insignificant(P value =0.88).After 3 min of ECT the mean heart rate in Control group was 137.5 and in Labetalol group was 136.0.The difference in the mean heart rate between the Control group and Labetalol group was statistically insignificant(P value =0.32).The mean heart rate in Control group after 5 minutes and 10 minutes of ECT was 108.1 and 114.4 and in Labetalol group was 91.1 and 92.1.

The difference between mean heart rate between the Control group and in Labetalol group after 5 and 10 minutes of ECT was statistically significant (P value =<0.0001).This clearly shows that Labetalol was not effective in attenuating the increase in heart rate in the immediate period that is 1 minute and 3 minutes after ECT but effective in attenuating the rise in heart rate in the later period (5-10minutes after ECT).This results is similar to the study conducted by **Jung Hee Ryu et al** who compare the effects of labetelol and nicardepine in attenuating the stress response in ECT.

CHANGES IN SYSTOLIC BP

Comparison of Esmolol with Control group

In both Control and Esmolol group baseline Systolic BP was same.The difference between mean Systolic BP is not statistically significant(P value=0.95).After 1 min of ECT the mean Systolic BP in Control group was 152.5 and where as in Esmolol group was121.5.The difference between the mean Systolic BP was statistically significant (P value =<0.0001).After 3 min of ECT mean Systolic BP in Control group was 137.6 and in Esmolol group was 119.5.The difference in the mean Systolic BP between the Control group and Esmolol group was statistically significant(P value =<0.0001).The mean Systolic BP in Control group after 5 minutes and 10 minutes of ECT was 138.3 and 131.9 respectively and in Esmolol group was135.4 and 132.

The difference in mean Systolic BP between the Control group and in Esmolol group after 5 and 10 minutes of ECT was statistically insignificant(P value =0.18 and 0.88 respectively).This clearly shows that Esmolol was effective in attenuating the increase in Systolic BP in the immediate period that is 1 minute and 3 minutes after ECT but not effective in attenuating the rise in Systolic Blood Pressure in the later period (5-10minutes after ECT).This results is similar to result of the study conducted by **Castelli I& Steiner in 1995** who compared the effects of esmolol and labetalol in ECT for stress attenuation.

Comparison of Labetalol with Control group

In both Control and Labetalol group baseline Systolic BP is same.The difference between mean Systolic BP was not statistically significant(P value(0.88).After 1 min of ECT the mean Systolic BP in Control group was 152.3 and where as in Labetalol group was150.3.The difference between the mean Systolic BP was statistically insignificant(P value =0.19).After 3 min of ECT the mean Systolic BP in Control group was 137.6 and in Labetalol group was 124.1.The difference in the mean Systolic BP between the Control group and Labetalol group was statistically significant(P value =<0.0001).The mean Systolic BP in Control group after 5 minutes and 10 minutes of ECT was 138.3 and 131.9 and in Labetalol group was111.6 and 112.3.

The difference between Systolic BP between the Control group and in Labetalol group after 5 and 10 minutes of ECT was statistically significant(P value =<0.0001).This clearly shows that Labetalol was not effective in attenuating the increase in Systolic BP in the immediate period that is 1 minute and after ECT but effective in attenuating in the rise Systolic BP in the later period (3-10minutes after ECT).This results is similar to result of study conducted by **MB Weinger et al** who found that labetalol is preffered over fentanyl in stress attenuation in ECT.

CHANGES OF DIASTOLIC BP

Comparison of Esmolol with Control group

In both Control and Esmolol group baseline Diastolic BP is same.The difference between mean Diastolic BP was not statistically significant(P value=0.84).After 1 min of ECT the mean Diastolic BP in Control group was 91.5 and where as in Esmolol group was 81.1.The difference between the mean Diastolic BP was statistically significant(P value =<0.0001).After 3 min of ECT mean Diastolic BP in Control group was 93.1 and in Esmolol group was 81.1.The difference in the mean Diastolic BP between the Control group and Esmolol group was statistically significant(P value =<0.0001).The mean Diastolic BP in Control group after 5 minutes and 10 minutes of ECT was 86.0 and 85.1 respectively and in Esmolol group was 83.1 and 86.5.

The difference in mean Diastolic BP between the Control group and in Esmolol group after 5 and 10 minutes of ECT was statistically insignificant(P value =0.19and 0.23 respectively).This clearly shows that Esmolol was effective in attenuating the increase in Diastolic BP in the immediate period that is 1 minute and 3 minutes after ECT but not effective in attenuating the rise in Diastolic BP in the later period (5-10minutes after ECT).This results is similar to result of the study conducted by **Howie et al** who defined the dose of esmolol in stress attenuation during ECT.

Comparison of Labetalol with Control group

In both Control and Labetalol group baseline Diastolic BP is same.The difference between mean Diastolic BP was not statistically significant(P value=0.81).After 1 min of ECT the mean Diastolic BP in Control group was 91.5 and where as in Labetalol group was 91.8.The difference between the mean Diastolic BP was statistically insignificant(P value =0.86).After 3 min of ECT the Diastolic BP in Control group was 93.1 and in Labetalol group was 80.5.The difference in the mean Diastolic BP between the Control group and Labetalol group was statistically significant(P value =<0.0001).

The mean Diastolic BP in Control group after 5 minutes and 10 minutes of ECT was 86.0 and 85.1and in Labetalol group was 74.1 and 73.7. The difference between Diastolic BP between the Control group and in Labetalol group after 5 and 10 minutes of ECT was statistically significant(P value =<0.0001).This clearly shows that Labetalol was not effective in attenuating the increase in Diastolic BP in the immediate period that is 1 minute and after ECT but effective in attenuating the rise in Diastolic BP in the later period (3-10minutes after ECT).This results is similar to results of the study conducted by **Sarvesh P singh et al** who compared the effects of esmolol and labetalol in attenuation of hemodynamic responses in laryngoscopy and intubation.

Side effects

one patient from the study group C,2 patients of E group and 3 patients of Lgroup developed bradycardia who were managed by I/V atropine bolus dose.3 patients developed hypotension ;1 from E and 2from L group which was managed by I/V fluids and intravenous ephedrine bolus.However the incidence of complications among all the three groups were statistically insignificant.

SUMMARY

This study was conducted in 90 patients undergoing Electroconvulsive therapy.

These patients were randomly divided into three groups with 30 patients in each group.Age between 18 and 65 years,either sex,belonging to ASA I and II were included in this study.Patients with II degree AV conduction block or greater,bradycardia Heart rate less than 50/min,systolic Blood pressure less than 90mmhg,asthmatic patients,patients with history of drug allergy,recent Myocardial infarction(with in 3 months) were excluded from this study. Patient was shifted to ECT room and secured large bore IV cannula.Baseline parameters were recorded and marked as "0".All patients were preoxygenated with 100% O2.Patients were induced with inj.Propofol 1-2mg/kg.Test drug was given immediately after induction and the time was noted. Group C received normal saline.Group E received Esmolol 1mg/kg IV and Group L received Labetalol 0.25mg/kg. Heart rate,Systolic BP and Diastolic BP were recorded 1min after test drug and marked as X. Inj.succinylcholine 1mg/kg was given. Two minutes after test drug electric current was applied bitemporally.Visible tonic-clonic contractions shows the efficacy of ECT.Ventilation was assisted with 100% O2 until spontaneous respiration recovered.Heart rate,Systolic BP and Diastolic BP were recorded 1,3,5 and 10 minutes after ECT and marked as A,B,C,D.

The following table shows the results obtained from this study

PARAMETERS	CONTROL	ESMOLOL	LABETALOL
Mean age in years	35.2	31.5	33.5
Mean weight in Kg	57.7	55.3	56.2
Mean height in cm	158.2	156.9	155.2
Mean baseline HR	101.1	100.7	99.1
Mean HR 1 min after test drug	111.1	90.7	108.5
Mean HR 1 min after ECT	125.2	98.3	128.0
Mean HR 3 min after ECT	137.5	100.5	136.0
Mean HR 5 min after ECT	108.1	109.0	91.1
Mean HR 10 min after ECT	111.4	109.9	92.1
Mean baseline SYS BP	131.6	131.7	131.3
Mean SYS BP I min after test drug	110.6	109.7	109.1
Mean SYS BP 1 min after ECT	152.5	121.5	150.3

Mean SYS BP 3 min after ECT	137.6	119.5	124.1
Mean SYS BP 5 min after ECT	138.3	135.4	111.6
Mean SYS BP 10 min after ECT	131.9	132.2	112.3
Mean baseline DIA BP	81.2	81.5	81.5
Mean DIA BP 1 min after test drug	84.1	72.1	82.5
Mean DIA BP 1 min after ECT	91.5	81.1	91.8
Mean DIA BP 3 min after ECT	93.1	82.1	80.5
Mean DIA BP 5 min after ECT	86.0	83.4	74.1
Mean DIA BP 10 min after ECT	85.1	86.5	73.7

The observation noted in this study are ,

1)By using the statistical analysis system,statistical analysis was done. t' test was used to test the significance of difference between quantitative variables and Yate's and Fisher's chi square tests for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

2)Demographic profile was similar in all the three groups and there

was no statistical significant difference between these three groups .

3) During ECT after application of electric current tonic clonic seizures occurs.During the period of tonic clonic seizures parasympathetic discharge occurs which may cause bradycardia or even asystole.But it lasts for few seconds(10-15 sec),which is followed by sympathetic discharge occurs.Sympathetic discharge is due to the release of adrenaline and noradrenaline.Adrenaline level increased 15 times and comes to normal level after 10 minutes of ECT.Noradrenaline level increases 3 times and remains increased for twice as long.Peak level occurs at 60 sec after ECT.This leads to increases in Heart rate,Systolic BP,Diastolic BP and cardiac output.

Esmolol hydrochloride is an ultra-short acting,cardio selective beta blocker(beta 1).Its distribution half life is 2 minutes.Elimination half life of Esmolol is 9 minutes.Peaks action at onset of action 1-2 minutes and peak effects at 3 minutes of administration.Labetolol is adrenergic receptor

blocking agent with mild alpha1 and predominant beta-adrenergic receptor blocking actions. Labetalol onset of action is 2-5 minutes with peak effect at 5-15 minutes.These properties like rapid onset of the drug makes the drug useful in attenuating the hemodynamic responses after ECT.

4)Esmolol significantly reduces the heart rate,systolic blood pressure and diastolic blood pressure from one to three minutes after ECT where as Labetalol did not produce any significant changes during that period.

5)Labetalol significantly reduces the heart rate,systolic blood pressure and diastolic blood pressure from three to ten minutes after ECT where as Esmolol did not produce any significant changes during that period.

CONCLUSION

It is concluded that a dose of 1mg/kg of Esmolol is effective in attenuating the hemodynamic responses to ECT in the first 3 minutes whereas a dose of 0.25mg/kg of Labetalol is effective in attenuating the responses to ECT in the period from 3-10 minutes.

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PROFORMA

NAME :

I.P.NO :

AGE & SEX :

ASA :

WEIGHT :

HEIGHT :

DATE& TIME OF ADMISSION :

DATE& TIME OF DISCHARGE :

DIAGNOSIS :

HISTORY :

HYPERTENSION

OTHER SYSTEMIC ILLNESS

ACUTE OR CHRONIC EYE DISEASE

DRUG THERAPY

ALLERGY TO DRUGS

CLINICAL EXAMINATION :

PULSE RATE

BLOOD PRESSURE

SPO2

PALLOR,ICTERUS,CLUBBING,CYANOSIS,LYMPHADENOPATHY,

EDEMA CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

ORAL CAVITY

AIRWAY

NECK & SPINE

BASIC INVESTIGATIONS:-

HAEMOGLOBIN

RENAL PARAMETERS & SERUM ELECTROLYTES,

ECG

CHEST X RAY PA VIEW

BT, CT

RBS

GROUP:

TIME OF INDUCTION:

TIME OF ADMINISTRATION OF TEST DRUG:

	HEART RATE	SYSTOLIC BP	DIASTOLIC BP
BASE LINE			
1 MIN AFTER TEST DRUG			
1MIN AFTER ECT			
3 MIN AFTER ECT			
5 MIN AFTER ECT			
10 MIN AFTER ECT			

COMPLICATIONS IF ANY:

S.NO	NAME	GROUP	AGE	SEX	ASA	WEIGHT	HEIGHT	PR-O	PR-X	PR-A	PR-B	PR-C	PR-D	SYS BP-O	SYS BP-X	SYS BP-A	SYS BP-B	SYS BP-C	SYS BP-D	DIA BP-O	DIA BP-X	DIA BP-A	DIA BP-B	DIA BP-C	DIA BP-D	SP02
1	SASIKALA	CONTROL	34	FEMALE	I	52	156	102	112	130	139	110	102	110	100	132	116	118	116	66	74	80	82	78	70	99
2	SUKUMAR	CONTROL	38	MALE	ii	48	157	100	110	126	137	106	110	122	116	148	128	130	120	72	76	82	84	82	74	99
3	MUNIYAMMAL	CONTROL	40	FEMALE	I	52	165	96	106	122	131	104	108	140	120	158	146	144	140	86	90	98	100	90	88	99
4	MANI	CONTROL	32	MALE	I	54	160	100	110	126	136	108	114	124	100	148	132	130	130	80	84	92	92	82	84	100
5	SRITHAR	CONTROL	28	MALE	I	48	159	104	114	120	140	110	114	122	108	146	130	128	122	76	82	90	92	82	80	99
6	SELVI	CONTROL	26	FEMALE	I	50	154	102	112	130	138	108	102	126	102	150	132	130	128	78	78	86	88	84	82	100
7	RAVI	CONTROL	26	MALE	I	54	159	104	114	120	140	110	116	138	114	156	142	140	136	84	84	92	94	88	88	99
8	BABU	CONTROL	39	MALE	II	57	158	96	106	122	133	102	106	140	120	160	146	148	136	90	94	100	102	84	94	100
9	MARI	CONTROL	37	FEMALE	I	51	156	106	116	134	142	112	108	132	110	156	144	146	136	82	84	90	92	86	86	99
10	IRULANDI	CONTROL	42	MALE	II	59	160	102	112	130	139	110	104	138	118	156	142	142	134	84	88	94	96	88	86	100
11	SATHYA	CONTROL	18	FEMALE	I	52	155	98	108	114	133	106	112	128	106	146	132	134	130	78	82	88	90	84	82	99
12	RAJASEKAR	CONTROL	47	MALE	I	74	158	106	116	134	141	112	120	140	118	158	144	144	138	84	88	84	86	90	88	99
13	VASANTHI	CONTROL	39	FEMALE	I	56	164	100	110	126	137	106	112	140	116	158	144	146	138	86	86	94	94	90	90	100
14	GOPI	CONTROL	36	MALE	I	52	160	102	112	130	136	108	114	132	110	150	140	140	134	82	88	92	98	88	86	99
15	RAJAM	CONTROL	41	FEMALE	ii	52	157	94	104	120	132	104	110	136	114	156	144	148	136	82	86	92	96	86	86	98
16	RAJESH	CONTROL	38	MALE	I	56	159	100	110	126	137	106	112	134	110	154	142	146	138	80	84	94	94	88	84	100
17	AMBAL	CONTROL	28	FEMALE	I	64	154	102	112	130	139	110	104	136	112	158	146	144	132	84	88	98	96	90	88	99
18	ARULRAJ	CONTROL	32	MALE	I	58	159	98	108	114	135	104	112	130	106	152	140	144	132	82	84	96	94	88	84	99
19	BHUVANA	CONTROL	46	FEMALE	II	72	156	96	106	122	132	104	112	138	108	156	138	136	136	84	88	96	98	86	88	98
20	BALAKUMAR	CONTROL	28	MALE	I	60	160	100	110	126	135	110	116	140	122	158	144	142	136	90	86	98	100	88	94	99
21	RAJESHWARI	CONTROL	39	FEMALE	I	56	157	104	114	120	140	110	116	138	114	162	150	148	134	86	92	98	100	86	90	100
22	MOHAN	CONTROL	20	MALE	I	57	158	98	108	114	136	108	112	136	110	156	138	148	132	82	86	94	96	86	86	99
23	JEYARAJ	CONTROL	54	MALE	II	62	155	100	110	126	137	106	112	138	120	158	140	138	140	84	88	98	100	90	88	99
24	SARASWATHI	CONTROL	41	FEMALE	I	62	163	102	112	130	139	110	122	134	100	160	144	142	134	86	90	96	98	92	90	100

S.NO	NAME	GROUP	AGE	SEX	ASA	WEIGHT	HEIGHT	PR-O	PR-X	PR-A	PR-B	PR-C	PR-D	SYS BP-O	SYS BP-X	SYS BP-A	SYS BP-B	SYS BP-C	SYS BP-D	DIA BP-O	DIA BP-X	DIA BP-A	DIA BP-B	DIA BP-C	DIA BP-D	SP02
25	PRASATH	CONTROL	26	MALE	I	68	158	106	116	134	143	110	120	136	122	156	136	140	134	80	78	86	88	86	86	99
26	MAHALAKSHMI	CONTROL	42	FAMALE	I	58	153	102	112	130	139	110	104	130	108	154	134	138	132	82	80	86	88	88	86	98
27	KUMAR	CONTROL	32	MALE	I	70	158	104	114	120	138	112	118	126	104	146	134	132	130	78	80	88	90	84	82	99
28	KANNAN	CONTROL	38	MALE	I	63	168	102	112	130	139	108	108	130	108	154	134	140	132	78	84	94	92	84	84	100
29	SIVANAMMAL	CONTROL	33	FEMALE	I	56	153	102	112	130	139	112	104	124	102	144	132	130	130	80	82	90	94	86	84	100
30	PANDI	CONTROL	35	MALE	I	57	157	104	114	120	142	108	118	110	100	130	114	112	112	70	70	80	78	76	74	99
31	MAHARANI	ESMOLOL	22	FEMALE	I	42	156	102	92	98	100	102	110	112	100	108	106	116	114	66	62	68	70	82	82	99
32	CATHERINE	ESMOLOL	26	FEMALE	I	46	157	102	90	96	98	110	110	120	110	118	114	128	126	74	68	72	74	88	86	99
33	LAKSHMI	ESMOLOL	40	FEMALE	I	53	155	98	90	98	100	104	116	140	120	124	122	144	140	86	78	86	88	84	80	99
34	BALU	ESMOLOL	20	MALE	I	50	160	100	92	100	100	110	108	126	100	120	116	130	128	80	70	80	80	84	88	100
35	JOTHIBASU	ESMOLOL	18	MALE	I	48	159	98	90	100	102	116	106	122	108	118	114	126	124	78	70	76	76	86	88	99
36	MALLIKA	ESMOLOL	24	FEMALE	I	50	154	102	92	98	102	118	110	126	102	120	118	130	128	78	66	78	80	78	82	99
37	MURUGAN	ESMOLOL	25	MALE	I	44	159	104	94	98	100	104	112	138	114	122	120	142	136	84	78	82	80	82	80	99
38	VASANTHI	ESMOLOL	39	MALE	II	57	158	96	88	98	100	118	104	142	120	124	122	140	136	90	80	90	82	86	84	100
39	KAVITHA	ESMOLOL	37	FEMALE	I	51	156	106	96	98	98	106	114	130	110	122	120	140	136	82	72	82	90	80	92	99
40	MARIAPPAN	ESMOLOL	42	MALE	II	49	160	98	90	98	104	108	118	138	108	126	124	142	136	84	74	84	86	82	86	100
41	GANDHIMATHI	ESMOLOL	19	FEMALE	I	52	155	98	88	98	100	108	106	128	106	122	120	132	130	78	68	76	76	88	90	99
42	NARAYANAN	ESMOLOL	47	MALE	I	74	158	106	98	100	104	116	114	142	112	124	122	144	138	84	74	84	84	84	84	99
43	MUTHULAKSHMI	ESMOLOL	39	FEMALE	I	56	154	102	92	98	100	112	110	140	116	124	124	144	136	86	74	86	88	86	86	100
44	KARUNAKARAN	ESMOLOL	26	MALE	I	52	160	102	92	98	100	112	110	134	106	122	120	138	134	82	78	82	84	82	94	99
45	SHANTHI	ESMOLOL	41	FEMALE	I	49	157	104	86	94	96	104	112	136	110	126	124	140	136	84	74	82	82	86	88	98
46	DURAI	ESMOLOL	27	MALE	I	54	159	100	90	100	102	100	108	134	124	124	120	140	138	80	70	80	80	88	92	99
47	GOMATHI	ESMOLOL	28	FEMALE	I	56	154	98	92	102	104	108	106	136	110	124	124	140	134	84	74	84	84	82	86	99
48	SARAVANAN	ESMOLOL	22	MALE	I	58	159	98	90	100	102	104	106	128	106	122	120	138	132	82	70	82	82	82	90	99

S.NO	NAME	GROUP	AGE	SEX	ASA	WEIGHT	HEIGHT	PR-O	PR-X	PR-A	PR-B	PR-C	PR-D	SYS BP-O	SYS BP-X	SYS BP-A	SYS BP-B	SYS BP-C	SYS BP-D	DIA BP-O	DIA BP-X	DIA BP-A	DIA BP-B	DIA BP-C	DIA BP-D	SP02
49	SUNDARI	ESMOLOL	46	FEMALE	II	72	156	96	86	98	100	106	114	138	108	126	124	138	136	84	70	84	86	86	88	98
50	RANJITH	ESMOLOL	30	MALE	I	60	160	100	90	102	106	104	108	140	122	124	122	140	136	88	74	90	90	82	82	99
51	RAJI	ESMOLOL	29	FEMALE	I	55	157	102	92	104	106	102	110	138	116	122	120	140	138	86	78	86	86	92	90	100
52	MATHAN	ESMOLOL	20	MALE	I	56	158	96	92	98	104	106	104	136	110	120	118	138	132	84	80	82	84	86	80	99
53	ARAYEE	ESMOLOL	54	FEMALE	II	62	155	102	86	90	92	108	102	138	108	124	122	136	138	84	70	84	84	88	92	99
54	FATHIMA	ESMOLOL	31	FEMALE	I	52	153	104	94	96	98	102	112	132	100	122	120	132	134	88	76	86	88	86	90	99
55	AYYAPPAN	ESMOLOL	24	MALE	I	68	158	106	96	96	98	106	114	136	122	124	122	136	134	80	70	80	82	88	82	99
56	KARPAGAM	ESMOLOL	32	FAMALE	I	58	153	98	88	98	100	114	106	130	108	124	122	134	132	82	72	82	82	82	90	98
57	ARASI	ESMOLOL	32	FEMALE	I	70	158	104	94	100	100	114	112	126	104	120	120	134	130	78	68	78	80	86	84	99
58	NAMBIRAJ	ESMOLOL	38	MALE	I	51	158	98	86	98	100	118	116	130	108	122	120	134	132	78	70	78	84	84	86	100
59	SUTHA	ESMOLOL	33	FEMALE	I	56	153	98	90	98	96	116	106	126	102	120	118	132	130	80	70	80	80	90	90	100
60	SENTHIL	ESMOLOL	35	MALE	I	57	157	104	84	98	102	114	112	110	100	108	106	114	112	70	86	70	72	86	84	99
61	SARATHA	LABETOLOL	32	FEMALE	I	44	156	100	106	116	136	88	90	108	106	156	104	102	102	66	82	82	72	62	60	99
62	KALYANI	LABETOLOL	26	FEMALE	I	56	157	106	104	118	138	90	92	122	116	154	108	110	118	72	84	82	72	66	64	98
63	BHUVANA	LABETOLOL	40	FEMALE	I	54	155	102	110	124	136	96	98	140	112	156	128	110	122	88	86	100	90	82	80	99
64	KALAIARASAN	LABETOLOL	30	MALE	I	50	160	100	106	128	138	94	92	124	110	154	116	112	102	80	80	92	76	70	68	100
65	KAVITHA	LABETOLOL	18	FEMALE	I	46	159	96	108	116	136	86	86	120	108	140	114	106	110	78	86	90	80	76	74	99
66	VALARMATHI	LABETOLOL	24	FEMALE	I	52	154	100	106	122	134	92	94	126	110	156	116	107	104	78	88	86	76	70	84	98
67	ANBARASU	LABETOLOL	35	MALE	I	46	152	92	108	124	140	86	86	138	110	158	128	116	116	86	78	94	84	78	78	99
68	XAVIER	LABETOLOL	39	MALE	II	59	158	94	104	126	136	90	92	140	114	152	130	116	122	90	80	100	90	84	82	100
69	CHINNATHAI	LABETOLOL	37	FEMALE	I	51	156	98	106	120	142	92	94	132	110	142	120	110	112	82	84	90	76	70	68	99
70	KALAIARASAN	LABETOLOL	42	MALE	II	51	154	96	108	132	134	90	92	138	112	154	132	118	120	84	88	96	84	80	78	100
71	PRIYA	LABETOLOL	29	FEMALE	I	54	155	94	100	120	134	88	90	128	106	144	118	110	108	78	82	86	80	74	86	99
72	RAJAN	LABETOLOL	47	MALE	ii	74	158	104	102	124	132	94	92	140	118	154	130	114	120	84	78	84	74	70	72	99

S.NO	NAME	GROUP	AGE	SEX	ASA	WEIGHT	HEIGHT	PR-O	PR-X	PR-A	PR-B	PR-C	PR-D	SYS BP-O	SYS BP-X	SYS BP-A	SYS BP-B	SYS BP-C	SYS BP-D	DIA BP-O	DIA BP-X	DIA BP-A	DIA BP-B	DIA BP-C	DIA BP-D	SP02
73	MANJULA	LABETOLOL	39	FEMALE	I	58	154	92	108	128	138	86	86	140	110	144	130	118	118	86	84	94	84	78	76	100
74	VEERANAN	LABETOLOL	26	MALE	I	52	153	98	114	128	136	92	94	132	102	150	120	110	112	82	78	92	82	76	74	99
75	DEVI	LABETOLOL	41	FEMALE	iii	51	150	102	108	124	136	96	98	136	112	156	128	110	116	82	88	88	78	70	72	98
76	GOVINDAN	LABETOLOL	37	MALE	I	54	159	100	106	122	138	94	92	132	110	152	126	114	112	80	76	94	84	76	74	99
77	RADHA	LABETOLOL	28	FEMALE	I	56	154	102	112	130	140	90	92	136	112	146	128	112	114	84	82	98	78	72	70	98
78	JAYAKUMAR	LABETOLOL	32	MALE	I	56	159	94	110	128	138	90	92	130	106	152	124	108	112	82	80	96	72	70	68	99
79	THAMARAI	LABETOLOL	46	FEMALE	II	72	156	100	104	130	136	94	92	136	110	148	132	120	110	84	82	100	88	80	78	98
80	MANICKAM	LABETOLOL	30	MALE	I	60	150	102	108	124	138	96	98	140	122	152	130	122	124	90	84	98	88	84	82	99
81	THANGAM	LABETOLOL	29	FEMALE	I	55	157	100	106	128	132	92	94	138	110	150	140	124	116	88	82	98	88	82	80	100
82	PERUMAL	LABETOLOL	20	MALE	I	58	158	102	108	126	134	96	98	136	110	152	128	106	112	82	80	94	84	78	76	99
83	SIGAPPI	LABETOLOL	54	FEMALE	II	62	155	98	104	132	138	90	92	138	114	148	136	116	122	86	84	100	84	64	64	99
84	JOTHI	LABETOLOL	31	FEMALE	I	54	153	96	112	128	136	90	92	132	100	154	130	110	102	86	86	96	86	78	76	98
85	SHANKAR	LABETOLOL	24	MALE	ii	68	151	102	116	124	138	94	92	136	110	152	128	106	122	80	80	86	76	70	68	99
86	PREMA	LABETOLOL	32	FAMALE	I	58	153	106	114	126	134	86	86	130	108	148	130	112	108	82	82	86	76	70	76	98
87	PARVATHI	LABETOLOL	32	FEMALE	I	70	152	98	116	124	142	92	94	126	104	150	118	100	104	78	80	88	78	72	70	99
88	DHARMARAJ	LABETOLOL	38	MALE	ii	51	158	104	112	128	138	88	90	130	100	152	124	112	108	78	82	94	84	80	76	100
89	SHANKARI	LABETOLOL	33	FEMALE	I	56	153	96	116	124	136	90	92	124	102	146	122	108	102	80	88	90	80	74	72	98
90	ALLIRAJA	LABETOLOL	35	MALE	I	57	157	98	114	126	138	90	92	110	100	138	104	110	100	70	82	80	70	68	66	99

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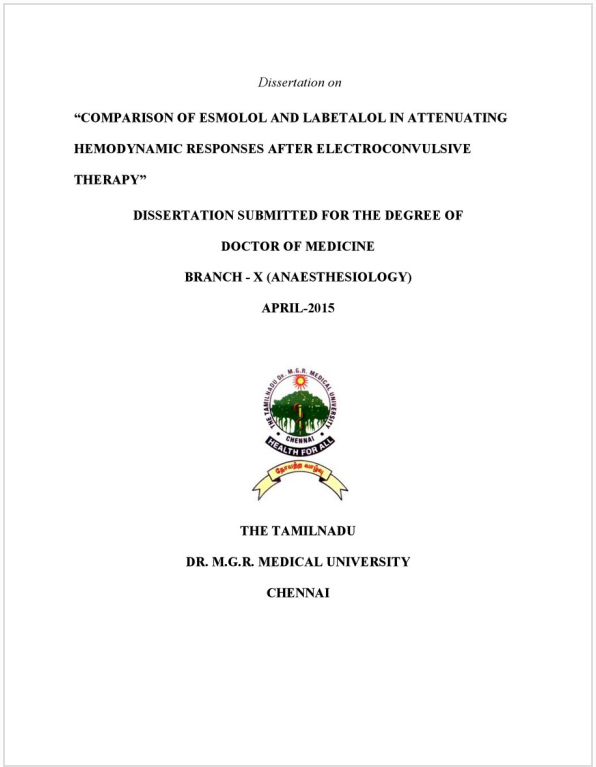

Dissertation on

“COMPARISON OF ESMOLOL AND LABETALOL IN ATTENUATING HEMODYNAMIC RESPONSES AFTER ELECTROCONVULSIVE THERAPY”

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH - X (ANAESTHESIOLOGY)

APRIL-2015

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

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Ref.No.4459/E1/5/2014

Madurai Medical College,
Maduai -20. Dated: 05 .2014.

Institutional Review Board/Independent Ethics Committee
Capt.Dr.B.Santhakumar,MD (FM). deanmdu@gmail.com
Dean, Madurai Medical College &
Government Rajaji Hospital, Madurai 625 020 . Convenor

Sub: Establishment – Madurai Medical College, Madurai-20 –
Ethics Committee Meeting – Meeting Minutes - for May 2014 –
Approved list – reg.

The Ethics Committee meeting of the Madurai Medical College, Madurai was held on 12th May 2014 at 10.00 Am to 12.00 Noon at Anaesthesia Seminar Hall at Govt. Rajaji Hospital, Madurai . The following members of the Ethics Committee have attended the meeting.

1.Dr.V.Nagarajan,M.D.,D.M(Neuro) Ph: 0452-2629629 Cell No.9843052029 nag9999@gmail.com.	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2.Dr.Mohan Prasad, MS.M.Ch. Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology (Retired) D.No.32, West Avani Moola Street, Madurai.-1	Member Secretary
3.Dr.K.Parameswari, MD(Pharmacology) Cell No.9994026056 drparameswari@yahoo.com.	Director of Pharmacology Madurai Medical College.	Member
4.Dr.S.Vadivel Murugan, MD., (Gen.Medicine) Cell No.9566543048 svadivelmurugan_2007@rediffmail.com.	Professor & H.O.D of Medicine Madurai Medical College	Member
5. Dr.L.Santhanalakshmi, MD (Physiology) Cell No.9842593412 dr.l.santhanalakshmi@gmail.com.	Vice Principal, Prof. & H.O.D. Institute of Physiology Madurai Medical College	Member
6.Dr.A.Sankaramahalingam, MS., (Gen. Surgery) Cell.No.9443367312 chandrahospitalmdu@gmail.com	Professor & H.O.D. Surgery Madurai Medical College. Madurai	Member
7.Mrs.Mercy Immaculate Rubalatha, M.A., Med., Cell.No.9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's Quarters, Gandhi Museum Road, Thamukam, Madurai-20.	Member
8.Thiru.Pala.Ramasamy, B.A.,B.L., Cell.No.9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72,Palam Station Road, Sellur, Madurai-20.	Member
9.Thiru.P.K.M.Chelliah, B.A., Cell No.9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20.	Member

The following project was approved by the committee

Name of the PG Student	Course	Name of the project	Remarks
Dr.M.Ranimariammal, mdr.rani@yahoo.co.in	PG in MD (Anesthesiology), Madurai Medical College and Government Rajaji Hospital, Madurai	Comparative study of esmolol and labetalol to attenuate hemodynamic responses after electroconvulsive therapy.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.

2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the E thical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Chairman
Ethical Committee

27.05.2014.
for Member Secretary

27.5.14
DEAN/Convenor
Madurai Medical College & Govt.
Rajaji Hospital, Madurai- 20.

To
The above Applicant
-thro. Head of the Department concerned