ABSTRACT
Introduction: ECT is widely used for treatment of severe psychiatric disorders. Although general anaesthesia has added to the patient safety and comfort, the haemodynamic pressor and neuroendocrine response associated with ECT remains a major concern due to associated cardiovascular morbidity. MgSO4 has unique pharmacological properties making it an important alternative for attenuation of pressor response to ECT. Present study was done to evaluate the efficacy of IV MgSO4 for attenuation of haemodynamic response to ECT when used in combination with propofol or thiopentone Na.

Material and Methods: In this prospective, randomized, double blind study we evaluated the efficacy of IV MgSO4 (30mg/kg) for attenuation of haemodynamic response to ECT when used in combination with Propofol or Thiopentone Na in 100 ASA I and II patients. We also evaluated time taken for spontaneous respiration, seizure duration and incidence of adverse effects.

Results: MgSO4 + Propofol combination effectively attenuates of both hypertensive and tachycardic response to ECT. MgSO4 + Thiopentone Sodium combination effectively attenuates hypertensive response but not heart rate response. The difference in the post ECT heart rate and rate-pressure product between the two groups is statistically highly significant (p<0.01). MgSO4 did not prolong the action of succinylcholine. Although Propofol shortened the duration of seizure, the duration was within therapeutic range.

Conclusion: MgSO4 + Propofol is a useful and effective combination for attenuation of ECT associated haemodynamic pressor response.

Keywords: Electro convulsive therapy (ECT), Haemodynamic response, Magnesium Sulphate, Thiopentone Sodium, Propofol

INTRODUCTION
Electroconvulsive therapy (ECT) is widely used in the treatment of severe psychiatric disorders. In the early days, ECT was often conducted without the benefits of general anaesthesia and neuromuscular blockade leading to physical and psychological trauma. Better understanding of physiology of ECT, improvement in ECT machines and technique, greater attention to anaesthetic management and preparation for emergencies has resulted in a high level of safety for ECT. The haemodynamic pressor and neuroendocrine response associated with ECT includes an initial parasympathetic discharge causing transient bradycardia for 10-12 seconds followed by an intense sympathetic discharge resulting in tachycardia, hypertension and a risk of arrhythmias for 5-7min.1-3 This response is undesirable in normal patients and is harmful to patients with ischemic heart disease, hypertension and cerebrovascular disease. A wide variety of drugs have been used with varying degrees of success in attenuating the acute haemodynamic response associated with ECT. Magnesium sulphate (MgSO4) has been successful in attenuation of the pressor response to intubation.4-6 and pneumoperitoneum.7 MgSO4 is vagolytic in nature and increases pulse rate. We hypothesized that MgSO4 would be useful in the setting of ECT and more effective if combined with Propofol, a vagomimetic induction agent.

The purpose of this study was to evaluate the efficacy of IV MgSO4 30 mg/kg for attenuation of the haemodynamic response to ECT and also to compare its combination with two short acting induction agents, Propofol or Thiopentone Sodium in attenuating the pressor response.

MATERIAL AND METHODS
After obtaining approval from hospital ethics committee and written, informed valid consent from the guardian (Parent / Sibling / Spouse), 100 ASA grade 1 and 2 patients between the age of 18-55 years, undergoing ECT session for a variety of psychiatric conditions were enrolled in this randomized, prospective, double blind study. Using computer generated randomization each patient was assigned to one of the two groups. Group T (T+M) received Thiopentone Sodium + Magnesium Sulphate and Group P (P+M) received Propofol + Magnesium Sulphate as part of induction. The study excluded patients with history of controlled and uncontrolled hypertension, Myocardial infarction in previous 6 months, Atrial fibrillation, Atrial flutter, Heart block or any other arrhythmias, Cerebrovascular accidents, raised ICT or Space occupying legion and patients whose guardians refused to give consent.

All patients underwent thorough medical evaluation and investigations. All the psychiatric medications were continued. After arrival to the ECT room, patients were administered oxygen by nasal prongs and cardioscope and pulse oximeter were attached. Sphygmomanometer cuff was applied on both arms, one for BP measurement and one used as torniquet to

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prevent succinylcholine induced paralysis so as to observe and record seizure duration. Although continuous NIBP monitoring would have been advantageous the same is unavailable in our ECT setup. Mercury sphygmomanometer was used as it is accepted as the ‘Gold Standard’ for clinical measurement of BP. Also it is undisputed that the mercury sphygmomanometer has the highest accuracy, with a high degree of technical agreement between devices of different producers.9,10

IV access was established with 22G angiocath on the dorsum of hand.

An anesthesiologist not involved in the study prepared and injected all the anaesthesia drugs. The induction agent was taken in a black plastic syringe and the study drug (Magnesium Sulphate 30 mg/kg diluted with 0.9% saline total volume of 10 ml) was prepared as ‘trial drug.’ During injection of drugs, patients hand was covered to ensure blinding. The Anaesthetist conducting the study monitored each specific parameter of the patient.

All patients received premedication with IV Glycopyrrolate 0.004 mg/kg. Anaesthesia was induced with Thiopentone Na 4 mg/kg or Propofol 1.25 mg/kg given over 10 sec as per the assigned group. After loss of Eye Lash reflex, ability to mask ventilate the patient was confirmed and the study drug MgSO4 30mg/Kg was injected over 30sec. The Sphygmomanometer cuff in the opposite arm was inflated and IV succinylcholine 0.5 mg/kg was injected followed by 5 ml of 0.9% saline to flush the line. The patients were manually ventilated with Oxygen enriched air, with bag and mask till fasciculations disappeared. As soon as the jaw was relaxed, mouth was opened and rubber bite block was placed between teeth to avoid injury to the teeth and tongue during the seizure, and ECT stimulus was administered.

The Psychiatrist applied bitemporal electrodes dipped in Normal Saline and a suprathreshold electrical stimulus of 70 to 100 Volts was applied for a period of 0.8 to 2 seconds. The magnitude of the energy setting for ECT stimulus was predetermined by age and weight for each patient. One more electrical stimulus at a higher energy level was given immediately after the initial stimulus (at the psychiatrist's discretion) if the seizure duration was not long enough (<20 sec). Once the twitching of the muscles passed off, the bite block was removed and patients were ventilated with oxygen enriched air with bag and mask till the return of spontaneous respiration. Visual diaphragmatic movement was used to assess the apnea time from induction of anesthesia to onset of spontaneous ventilation.

Heart rate, Systolic (SBP) and diastolic (DBP) arterial blood pressures and oxygen saturation (SpO2) values were recorded on arrival for the ECT (baseline value), after injection of induction agent, after injection of Trial Drug and succinylcholine and then at 0, 1, 3, 5 and 10 min after the end of the ECT-induced seizure. ‘0’ being immediately at the end of the seizure activity. Mean arterial pressure was calculated from the above readings.

Duration of seizure: The time from application of electrical stimulus to the last clonic movement. Duration of apnea: Time from injection of succinylcholine to the onset of first spontaneous post electroconvulsive breath.

Adverse events such as bradycardia, arrhythmias, hypotension, desaturation were looked for throughout the observation period and before discharge back to the ward.

Sample size: Sample size was calculated from a previous study11 on the basis of the anticipated difference in mean SBP between the two groups. The study revealed that the SBP increase induced by ECT was approximately 30%. Assuming Type I error of 5% and Type II error of 20% (Power 80%), a 50% reduction was considered as clinically significant with standard deviation of 25 mm. This required a sample size of 45 patients in each group. We used 50 patients in each group for a comfortable margin of error.

STATISTICAL ANALYSIS

Data was analyzed with SPSS statistical software. Data from both groups was compared between groups and within the group. Intergroup data was analyzed using t test for independent sample and intragroup data was evaluated by paired t-Test, with P values <0.05 considered statistically significant, P<0.001 highly significant and P>0.05 as non significant. Data is presented as mean ± SD.

RESULTS

A total of 100 patients were included in this prospective, randomized, double blind study with 50 patients in each group. The groups were comparable with regard to the demographic data, ASA grade, psychiatric diagnosis and baseline haemodynamic parameters (Table-1).

The baseline mean pulse rate (PR), pulse rate after injection of induction agent and after trial drug + succinylcholine was comparable between the groups. There was an increase in the mean pulse rate immediately after seizure (0 min) in Group T (Thiopentone Na + MgSO4) which was highly significant (p<0.01) when compared with the baseline pulse rate and this increase persisted till 10 minutes. In Group P (Propofol + MgSO4) the mean pulse was clinically and statistically comparable with baseline pulse rate at all times (p>0.05).

When compared between the two groups, the mean pulse rate in Group T was clinically and statistically higher than the pulse rate observed in Group P during the post ECT period; the statistical difference being significant at 0 and 1 minute (p<0.05) and 3, 5 and 10 minutes with p<0.001 (Table-1, Figure-1).

The baseline mean systolic blood pressure (SBP), SBP after injection of induction agent and trial drug + succinylcholine was comparable between the groups. In both Groups T (Thiopentone Na + MgSO4) and Group P (Propofol + MgSO4) there was no increase in SBP post ECT; and it was comparable with baseline SBP as well as with each other at all times (p>0.05) (Figure-2).

The baseline diastolic blood pressure (DBP), DBP after injection of induction agent and after trial drug + succinylcholine was comparable between the two groups. In both Groups T and Group P there was no increase in DBP and it was comparable with baseline value as well as with each other at all times during the observation period (p>0.05) (Graph 3).

The MAP was calculated as per formula MAP=2/3DBP+1/3SBP in mmHg. The baseline mean arterial pressure (MAP), MAP after injection of induction agent and trial drug + succinylcholine was comparable between the two groups. In both Group T and Group P the MAP was comparable with baseline MAP as well as with each other at all times during the observation period (p>0.05) (Graph 4).
There was no statistical difference in the SPO2 and apnea time (Table-3) between the two groups. The seizure duration in group P was statistically significantly shorter as compared to in Group T (p<0.05) (Table-2). However this duration was clinically acceptable. None of the patient had seizure duration of < 30 seconds. There was no incidence of any adverse effect such as bradycardia, arrhythmias, hypotension, desaturation in any of the groups.

**DISCUSSION**

Electroconvulsive therapy (ECT) was introduced in 1934 as a treatment for Schizophrenia and is currently a widely used modality for treatment of severe psychiatric disorders. Today, an estimated 1 million people worldwide receive ECT every year.12

The goals of General anaesthesia for ECT are to provide the patient with lack of awareness with use of anaesthetic agents compatible with the psychotropic medications, attenuation of the haemodynamic response to ECT with minimal antagonistic effects on seizure activity, modification of the motor effects of seizure in order to prevent injury and ensure rapid recovery.13

Patients receive ECT repeatedly for several weeks; hence adjustment of dosages of induction agents, muscle relaxants, and adjuvant drugs as well as communication and coordination between anaesthesiologist and psychiatrist is essential.

Seizure activity which is the therapeutic aspect of ECT is accompanied by untoward physiologic cardiovascular response due to generalized autonomic nervous system stimulation resulting in initial parasympathetic outflow followed immediately by a more prominent sympathetetic response. The sequence described may result in an initial bradycardia lasting 10 to 15 seconds or even frank asystole, followed by tachycardia and hypertension lasting 5 minutes or longer.14-18

The cardiovascular response is associated with the release of catecholamines and/or vasopressin. Systolic blood pressure (SBP) transiently increases by 30%-40% and the heart rate (HR) by 20% or more, resulting in a two to fourfold increase in the rate-pressure product (RPP) which is an index of myocardial oxygen consumption. Older patients typically manifest a larger increase in RPP. In patients at risk, the hemodynamic response to ECT can produce myocardial ischemia, infarction and even cardiac rupture. Even in normal patients, ECT has been shown to reduce left ventricular systolic as well as diastolic function.19

A wide variety of drugs have been administered in an effort

<table>
<thead>
<tr>
<th>Table-1: Comparison of demographic data and Baseline parameters</th>
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<tbody>
<tr>
<td><strong>Group T (THIOPENTONE+MgSO4)</strong></td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>33.54</td>
</tr>
<tr>
<td>Weight (Kgs)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>27</td>
</tr>
<tr>
<td>ASA Grade</td>
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<tr>
<td>Diagnosis</td>
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<tr>
<td>BASeline pulse rate</td>
</tr>
<tr>
<td>Baseline systolic BP (mm of Hg)</td>
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<tr>
<td>BASELINE DIASTOLIC BP (mm of Hg)</td>
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<th>Table-2: Comparison of Mean Pulse Rate</th>
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<tbody>
<tr>
<td><strong>Time</strong></td>
</tr>
<tr>
<td>Arrival</td>
</tr>
<tr>
<td>85.82</td>
</tr>
<tr>
<td>After induction</td>
</tr>
<tr>
<td>After trial drug+sch</td>
</tr>
<tr>
<td>0 Min</td>
</tr>
<tr>
<td>1 Min</td>
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<tr>
<td>3 Min</td>
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<tr>
<td>5 Min</td>
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<tr>
<td>10 Min</td>
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<th>Table-3: Apnoea Time and Seizure Duration</th>
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<tr>
<td><strong>Group</strong></td>
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<tr>
<td>APNOEA Duration (Minutes)</td>
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<tr>
<td>4.049</td>
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<tr>
<td>SEIZURE Duration (Seconds)</td>
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<td>35.86</td>
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to minimize ECT induced haemodynamic changes. Nitroprusside, Nitroglycerine, Esmolol, Labetalol, Propranolol, Nicardipine, Diltiazem, Urapidil, Landiolol, Alfentanil, Remifentanil, Clonidine, and Dexmedetomidine have been used with varying results. Many of these drugs are unable to completely block the acute hypertensive response to ECT without causing prolonged hypotension, some led to shortening of the seizure reducing the efficacy of the treatment.

For over a century, MgSO4 has been used to treat tachyarrhythmias and myocardial ischemia, for tocolysis, control of convulsions in eclampsia, haemodynamic control in Pheochromocytoma, and in the management of autonomically unstable conditions such as tetanus. Recently it has been described as the emerging drug in anaesthesia practice.

MgSO4 is involved in control of vasomotor tone and produces vasodilatation by acting directly on blood vessels. It reduces release of catecholamines, vasopressin, or both. It attenuates vasopressin stimulated vasoconstriction and normalizes sensitivity to vasopressin. In a dose of 30-40 mg/kg MgSO4 has been shown to be effective in attenuating the pressor response to tracheal intubation and pneumoperitoneum. It has immediate onset of action when given IV and the action lasts for 30 minutes.

In view of these pharmacological properties of Magnesium sulphate, we decided to investigate whether MgSO4 in a dose of 30mg/Kg, attenuates the haemodynamic stress response to ECT in this prospective, randomized, double-blind study. MgSO4 is vagolytic in nature. In a previous study, MgSO4 was found to have no action on heart rate response to ECT. In the pilot study using Thiopentone Sodium as a standard induction agent, we observed that although MgSO4 attenuated hypertensive response to ECT, it was associated with increase in pulse rate. Thus we decided to evaluate whether the combination of MgSO4 with Propofol which has intrinsic vagomimetic property provides better attenuation of haemodynamic response to ECT.

The 2 groups were comparable with respect to demographic parameters, psychiatric diagnosis, ASA grade and baseline hemodynamic parameters. IV glycopyrrolate was administered to all patients to avoid excessive secretions as well as to prevent bradycardia and reduced cerebral oxygenation/perfusion associated with ECT induced parasympathetic outflow in the stimulation phase of seizure. Both Thiopentone Sodium and Propofol have been used effectively for ECT. As both have anticonvulsant properties, we selected comparable doses proven to have least effect on the duration of seizure. Propofol produces similar dose-dependent effects (slow waves with high gamma activity) on EEG activity in patients with or without a history of seizure disorders. While induction of anesthesia with higher doses of propofol (>1.5 mg/kg) in patients with well controlled seizure disorder is safe, smaller sedative doses should be administered with caution to epileptic patients. Succinylcholine was used in the dose...
recommended by Royal college of Psychiatrists. The mean pulse rate, SBP, DBP and MAP after injection of induction agent and succinylcholine + trial drug in both the groups were comparable with baseline values as well as with each other.

There was no increase in mean pulse rate in Group P (Propofol + MgSO4) at any time during the observation period. Group P had a statistically significant attenuation of mean pulse rate when compared with Group T (Thiopentone Sodium + MgSO4) at all times post ECT. These findings indicate that MgSO4 has less effect on the post ECT increase in pulse rate. Propofol + MgSO4 combination provides attenuation of ECT related tachycardia as propofol counters the vagolytic action of MgSO4. Therefore the authors recommend this combination for ECT anaesthesia.

Patients in both Group T and Group P had a statistically significant attenuation of SBP, DBP and MAP at all times post ECT. These findings indicate that MgSO4 is effective in attenuation of hypertensive response to ECT.

Dirk H, van Zijl et al compared Remifentanil and MgSO4 with placebo for attenuation of haemodynamic response to ECT. They found that there was a rise in heart rate in both MgSO4 and placebo group at all time post ECT. They observed that MgSO4 attenuated increases in SBP at 0, 1 and 3 min post ECT and neither MgSO4 nor placebo attenuated the heart rate increase at 1 and 3 min. They recommended MgSO4 for attenuation of hypertensive response in patient at risk of developing post ECT bradycardia but not in patients of ischaemic heart disease. MgSO4 has a potential to cause of hypotension due to its direct depressant effect on myocardial and vascular smooth muscle and reduction in release of catecholamines. However in our study no patient had hypotension.

Propofol significantly shortened the seizure duration. However the seizure duration was > 30 seconds in all patients and was in the therapeutic range. The apnoea time was comparable in all the 3 groups. There was no incidence of desaturation, arrhythmias or any other adverse effect observed in the study.

CONCLUSION

Our results show that Propofol and MgSO4 combination is effective in attenuation of the sympathetic haemodynamic response to ECT. It attenuates increase in heart rate, systolic, diastolic blood pressure and hence the rate pressure product. Propofol reduces Seizure duration; but it remains in the therapeutic range which is primary aim of the therapy. Thiopentone Sodium and MgSO4 combination is effective in attenuation of hypertensive response but not the heart rate response.

In elderly patients and those with ischemic heart disease, propofol + MgSO4 combination will be advantageous. Because MgSO4 has less effect on heart rate, Thiopentone Sodium + MgSO4 might offer advantages in patients at risk for post-ECT bradycardia.

The limitation of our study is that we did not have a placebo control group. A pilot study of using placebo control groups as well as plenty of studies in literature have revealed that a haemodynamic response is associated with ECT and is undesirable.

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