Original Article

Modified electroconvulsive therapy in a resource-challenged setting: Comparison of two doses (0.5 mg/kg and 1 mg/kg) of suxamethonium chloride

ABSTRACT

Background: Suxamethonium has been shown to have a superior modification of the convulsion associated with ECT compared to other muscle relaxants. The dosage of suxamethonium used in ECT varies widely based on the experiences of practitioners. The study aimed to determine and compare the effectiveness and side effect profile of 0.5 mg/kg and 1 mg/kg in modified ECT.

Subjects and Methods: This was a prospective randomized crossover study, comparing the effects of suxamethonium at a dose of 0.5 mg/kg, and 1.0 mg/kg in 27 patients who had a total of 54 sessions of modified ECT. The primary outcome parameters were quality of convulsion and onset and duration of apnoea. The secondary outcome parameters were hemodynamic variables, arterial oxygen saturation, delayed recovery, muscle pain, vomiting, headache, prolonged convulsion, and serum potassium. Data collected were entered into proforma and analyzed using Statistical Package for Social Sciences (SPSS) version 17.0. Parametric variables are presented as means and standard deviations while non-parametric variables are presented as frequencies and percentages. The level of significance (*P*-value) was considered at 0.05.

Results: Sixteen patients (59%) had acceptable convulsion modification with 0.5 mg/kg suxamethonium compared to 23 patients (85%) with the use of 1.0 mg/kg suxamethonium (*P* = 0.016). There was no statistically significant difference in the duration of convulsion, the onset of apnoea, and the duration of apnoea with the two doses. Changes in heart rate, blood pressure, arterial oxygen saturation, and serum potassium level that accompany the mECT were comparable with the two doses of suxamethonium studied.

Conclusions: A better modification of convulsion with comparable hemodynamic and side effect profile is achieved during mECT with the use of 1.0 mg/kg suxamethonium compared to 0.5 mg/kg.

Key words: Electroconvulsive therapy; seizure modification; suxamethonium chloride

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Introduction

Electroconvulsive therapy (ECT) involves placing electrodes on the scalp and applying a current of electricity to induce a generalized therapeutic convulsion.[1,2] It has proven efficacy in patients with severe depression not responsive to first-line treatment options.[3] ECT without anesthesia has been shown to result in severe injuries in about 50% of patients.[4] Suxamethonium: The shortest acting neuromuscular blocker and a depolarizer, have remained the drug of choice in modified ECT (mECT) due to its rapid onset of action, and ability to produce acceptable muscle relaxation for a short period. Other relaxants when used are accompanied by prolonged muscle relaxation requiring the use of reversal agents. Rocuronium and its antagonist sugammadex have been considered as an alternative to suxamethonium in many procedures that require muscle relaxation for a short period. This is, however, not only expensive but also not readily available in a resource-challenged setting like ours. Suxamethonium has stood the test of time despite the reported complications, because of its unique features of rapid onset, good relaxation profile, short duration of action, nontoxic metabolites, and it's economy of use.[5]

Propofol: An alkylphenol group of intravenous induction agents has become a more popular choice of induction agent for mECT.[6] The dose of suxamethonium used in mECT varies widely based on the experiences of practitioners. While several studies have compared the effects of different induction agents and their doses on mECT, the qualities of convulsion, as well as the possible side effects of various doses of suxamethonium commonly used have not been satisfactorily evaluated. There is no report yet comparing the motor convulsion modification effects of anesthetics in our setting. This study compared the effectiveness of the two commonly used doses of suxamethonium for modification of convulsion, and the side effects profile in a propofol-based induction during a mECT.

Subjects and Methods

The study was a prospective, randomized, crossover study comparing 0.5 mg/kg and 1.0 mg/kg suxamethonium as a muscle relaxant in the first two successive treatment sessions of mECT carried out 48 h apart in patients who were referred for mECT at the mental health facility of a university teaching hospital located in south-western Nigeria. Ethical approval for the study was obtained from the institutional ethics board while written informed consent was obtained from the caregivers of each of the patients before the commencement of the study. Inclusion criteria were patients aged 18 to 65 years with consenting responsible next of kin, and American Society of Anesthesiologists' physical status I or II patients. Patients with non-consenting next of kin anticipated difficulty with mask ventilation or intubation, liver dysfunction as determined by liver function tests, recent major burns, history of ischemic heart disease, family history of malignant hyperthermia, or history of allergy to propofol or egg were excluded from the study. The sample size for the study was determined using sample size calculation for the difference of means.[7] in a comparative study of same outcome measures in same patient at different treatment session(n = 2/d ^ 2 xC) where: n = sample size, d (standardized difference) = (target difference)/(standard deviation), target difference = mean 1 - mean 2, and C = constant defined by the *P* value and power (0.05 and 80%, respectively). This resulted in a sample size of 23 patients. The addition of a 10% attrition rate yielded a total sample size of 26 patients. However, 27 patients that had a total of 54 mECT sessions and satisfied the inclusion criteria over the eight months study period were included in the study [see Figure 1].

The patients were randomized by the principal investigator (PI) to commence the ECT course with either of the two doses of suxamethonium (0.5 mg/kg and 1 mg/kg) being compared in the study by simple ballot. A patient who was administered with 0.5 mg/kg suxamethonium in the first session of ECT had 1.0 mg/kg at the second session and vice versa. The sessions were carried out according to the standard ECT protocol. The attending anesthetist prepared the propofol and suxamethonium used following the study protocol in equal volumes. The patients, the mental health physician who administered the shock, and the assisting psychiatry resident who administered the drugs were all blinded to the grouping. The PI observed and recorded the variables.

Patients were encouraged to empty their bladder before the procedure as incontinence is common during convulsions in ECT. The baseline heart rate (HR), systolic blood pressure (SBP), mean arterial pressure (MAP), and diastolic
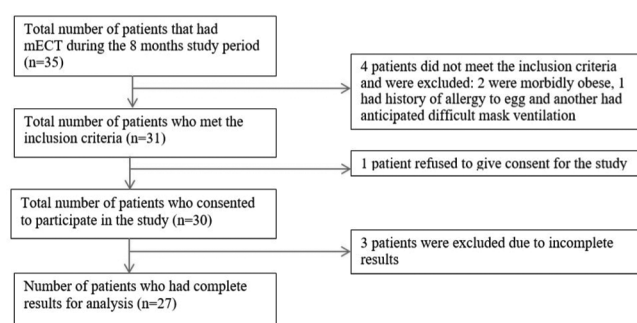

Figure 1: Flow diagram of patients from recruitment to completion of two successive mECT

blood pressure (DBP) were recorded before each treatment using a GE Dash 4000 multiparameter monitor (GE Healthcare, Milwaukee, Wisconsin, USA). The noninvasive blood pressure was programmed to cycle every 3 min during the procedure. Arterial oxygen saturation (SpO2) and the electrocardiogram were monitored continuously. Intravenous access was secured with a size 18G cannula for drugs and fluid administration. Normal saline was used in all the treatment sessions. Venous blood samples were taken before induction, and at the end of induced convulsion into lithium heparin bottles for serum potassium estimation. The blood samples were coded and analyzed at the chemical pathology laboratory of the hospital after each treatment session.

All patients had propofol 1 mg/kg intravenously for induction. The randomized dose of intravenous suxamethonium (0.5 mg/kg or 1 mg/kg) was administered after isolation of the second upper limb not used for drug administration with a manual sphygmomanometer cuff. At the onset of muscle paralysis and apnoea, oxygenation was maintained by manual mask ventilation with 100% oxygen at 6 L/min till resumption of spontaneous respiration. This was suspended for few seconds to allow delivery of the electric shock and resumed immediately after until patients recovered. A bite block was inserted into the mouth to protect the tongue immediately after noticing suxamethonium induced fasciculation before administration of the shock.

Electric shock was administered with Ectonus® 5B, Serial Number 5CB 1012 (Ectron Ltd England) with a maximum output of 700 mC and input of 80 Watts. Bitemporal electrode placement was used for all patients. The dose of ECT (150-200 mC) determined by the attending Physician was used for all the treatment sessions. Electroencephalogram is the preferred mode of monitoring convulsion but could not be used for this study because it was not routinely available in (many resources constraint setting including) our treatment facility. Therefore, visible convulsion activity of muscles of the limbs and face were used as recommended by Whitehouse and Scott.[8] Convulsion duration was measured from the time of appearance of the tonic phase of contraction to the end of convulsion using a stopwatch. The disappearance of visible involuntary motor activity on the limbs or face was considered as the end of the seizure.

Quality of motor convulsion was scored between one and five inclusive, based on the location and intensity of convulsions[9] as follows: 1. Violent convulsions similar to that seen in straight (unmodified) ECT; 2. Bilateral motor convulsions that are equal in intensity in both cuffed and uncuffed limbs; 3. Bilateral motor convulsions with the intensity more in cuffed limb compared with corresponding uncuffed limb; 4. Motor convulsions are observed in cuffed limb and face; 5. A seizure is limited to the cuffed limb only. A score of 5 is the desired modification pattern in mECT. A score ≤2 indicates poor modification.

The major events during the procedure starting from the administration of propofol, suxamethonium, loss of spontaneous respiratory efforts, ECT stimulus application, the end of the physical convulsive activity and resumption of spontaneous breathing were all timed and recorded using a stopwatch by an anesthesia resident who was blinded to the dose of suxamethonium used. Another assistant, a psychiatrist, blinded to the dose of suxamethonium recorded the duration of the motor seizure. Both assistants assessed the extent of motor seizure using the five-point scale as stated above.

Data collected were entered into proforma and analyzed using Statistical Package for Social Sciences (SPSS) version 17.0. Parametric variables (height, weight, age, onset and duration of apnoea, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and serum potassium level) are presented in means and standard deviations, and test of significance was performed using Paired *t*-test. Non-parametric variables (convulsion modification and side effects) are presented as frequencies and percentages, and test of significance performed with the Chi-squared test or Fisher's exact test as appropriate. The level of significance (*P*-value) was considered at 0.05.

Results

Twenty-seven patients aged 18–62 years who participated in a total of 54 sessions of mECT were studied. There were 11 males (40.7%) and 16 females (59.3%). Nineteen of the patients (70.4%) were ASA physical status class I while the remaining 8 (29.6%) were class II. Patients' demographic parameters are as shown in Table 1. All patients had 0.5 mg/kg or 1.0 mg/kg suxamethonium in either of the two sessions compared. The indications for mECT are shown in Figure 2. Schizophrenia was the commonest indication for mECT (48%).

Table 2 shows the onset and duration of apnoea and duration of convulsion. The differences between the two doses of suxamethonium were not statistically significant. The quality of convulsion is shown in Table 3. Sixteen patients (59%) had acceptable convulsion modification with 0.5 mg/kg suxamethonium regimen compared to 23 patients (85%) with 1.0 mg/kg suxamethonium regimen. Convulsion modification

was poor in 11 (41%) patients in 0.5 mg/kg suxamethonium group compared to 4 (15%) patients in 1.0 mg/kg suxamethonium group. The differences were statistically significant ($P = 0.016$).

The mean heart rate, arterial oxygen saturation, systolic-, diastolic-, and mean arterial pressure for the two doses of suxamethonium were comparable as shown in Figures 3 and 4. Table 4 shows the comparison of pre-ECT and post-ECT mean serum potassium with the two doses of suxamethonium studied. There was a significant increase in the mean serum potassium post-ECT compared to the pre-ECT levels for both doses of suxamethonium studied ($P < 0.001$).

Table 1: Patients' demographic characteristics (*n*=27)

Variables	Mean (SD)
Age (years)	34.9 (11.3)
Weight (kg)	58.2 (11.6)
Height (m)	1.6 (0.8)
BMI (kg/m²)	22.2 (3.7)

Table 2: Comparison of onset of apnoea, duration of apnoea, and duration of convulsion between 0.5 mg/kg and 1.0 mg/kg suxamethonium

Variable	0.5 mg/kg (*n*=27) mean (SD)	1.0 mg/kg (*n*=27) mean (SD)	*P*
Onset of apnoea (s)	62.15 (13.14)	61.41 (12.02)	0.785†
Duration of apnoea (s)	112.44 (31.24)	125.74 (35.40)	0.112†
Duration of convulsion (s)	30.26 (5.95)	29.00 (7.83)	0.498†

†Not Significant

Table 3: Quality of convulsion with the two doses of suxamethonium

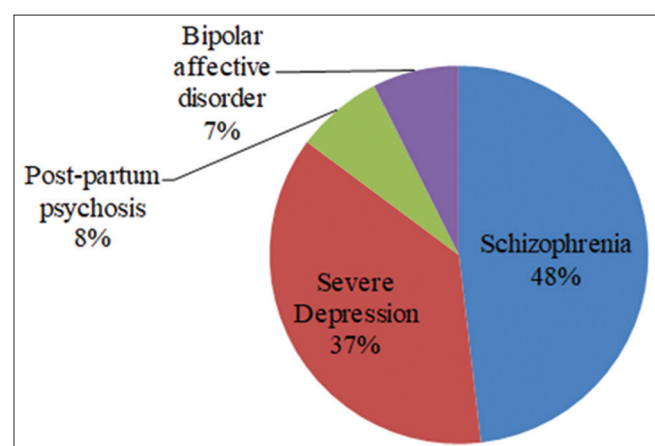| Convulsion modification	Dose of suxamethonium		*P*
	0.5 mg/kg (*n*=27)	1.0 mg/kg (*n*=27)	
Poor	11 (41%)	4 (15%)	*0.016††
Acceptable	16 (59%)	23 (85%)	

††Significant. *Fisher's Exact Test

Figure 2: Showing the indications for mECT in the studied population

However, the increase in mean serum potassium following the use of 0.5 mg/kg and 1.0 mg/kg suxamethonium were comparable (0.20 mmol/L versus 0.25 mmol/L, $P = 0.192$).

The incidence of side effects during the twelve hours follow-up period after the procedure was comparable with the two doses of suxamethonium. Muscle pain was the most common side effect. This was recorded in 5 patients (19%) with 0.5 mg/kg and 4 patients (15%) with 1.0 mg/kg ($P = 0.133$). Two patients complained of headache with 1.0 mg/kg suxamethonium regimen and one patient with 0.5 mg/kg regimen ($P = 0.353$). The incidences of headache and muscle pain between the two doses were comparable.

Discussion

The effectiveness of ECT depends on the quality of generalized convulsion activity,[10] therefore adequate but well-controlled convulsions are important in ECT. While cerebral seizure is required for treatment, its associated adverse physical effects including injury to bones, teeth and soft tissues should be prevented through appropriate anesthesia in an mECT session, and the patient should be adequately monitored without compromising the efficacy of treatment.

This study has demonstrated that 1.0 mg/kg suxamethonium regimen is more effective than a 0.5 mg/kg regimen as a muscle relaxant for electroconvulsive therapy. The former had a better modification effect on the induced convulsions using an objective scale. Time of onset as well as the duration of apnoea, changes in heart rate, blood pressure and incidence of adverse effects was similar when either of the doses was used in the same patient during a course of ECT treatments. This is in keeping with the findings of an earlier study by Murali *et al.*[9] where similar doses were compared during ECT using a different hypnotic, sodium thiopentone as an induction
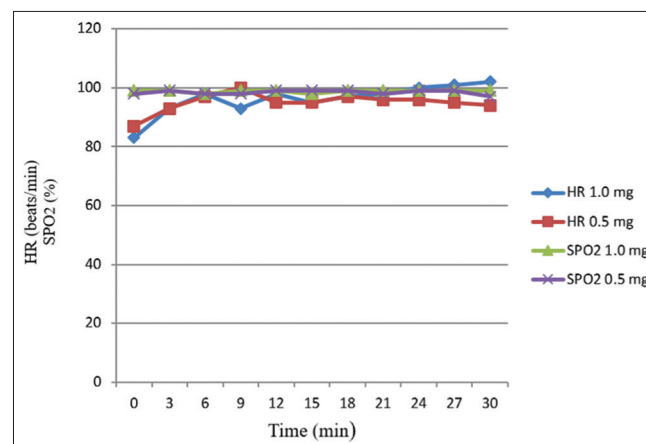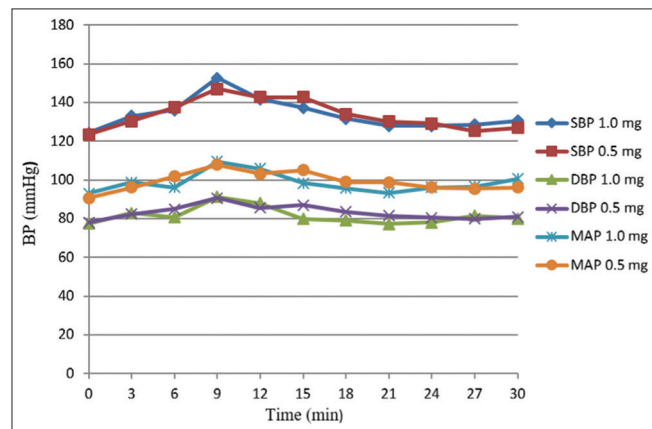
Figure 3: Showing the mean heart rate and SpO2 of the two groups during mECT

Table 4: Showing comparison of pre-ECT and post-ECT serum potassium with the two doses of suxamethonium

Suxamethonium dose (mg/kg)	Serum Potassium (mmol/L)		Change Mean (SD)	P
	Pre-ECT Mean (SD)	Post-ECT Mean (SD)		
0.5 (n=27)	3.52 (0.32)	3.72 (0.32)	0.20 (0.11)	<0.001[††]
1.0 (n=27)	3.67 (0.27)	3.92 (0.32)	0.25 (0.15)	<0.001[††]

[††]Significant

Figure 4: Showing the mean Systolic BP, Diastolic BP and MAP of the two groups during mECT

agent. Propofol was used as the induction agent in our study and this may explain the shorter duration of convulsion observed in this study compared to those reported by Murali *et al*.[9] (30.26 s versus 54.2 s; and 29.0 s versus 54.5 s) for 0.5 mg/kg and 1.0 mg/kg, respectively. This is in tandem with reports that propofol reduces seizure duration during ECT.[6,10]

A dose of as low as 0.5 mg/kg of suxamethonium is thought to be effective in modifying motor activities associated with ECT because invasive airway manipulations are not required.[11] In this study, however, modification of convulsions was more acceptable with the 1.0 mg/kg regimen than with a 0.5 mg/kg regimen (*P* = 0.016). A poor modification is characterized by vigorous convulsions as observed in 41% of patients in 0.5 mg/kg suxamethonium group due to inadequate muscle relaxation. This increases the risk of physical injury.

With well-modified convulsions, there is a reduced requirement for physical restraint that projected ECT as a harmful procedure in time past. Despite the difference in the quality of convulsion modification, duration of convulsion, the onset of apnoea, and duration of apnoea were comparable between 0.5 mg/kg and 1.0 mg/kg regimens, (*P*-values of 0.498, 0.785, and 0.112, respectively). Konarzewski *et al*.[12] reported better convulsion modification in patients who received 50 mg suxamethonium compared with 15 mg suxamethonium. The dosage was, however, not based on a kilogram per body weight, making it unreliable. Besides, dose-comparison was done between different patients; patient variability may thus have affected the result.

The cardiovascular changes associated with ECT are of clinical importance. The initial parasympathetic stimulation results in bradycardia, or rarely asystole which is often brief and likely unnoticed.[13] The sympathetic discharge that follows thereafter causes tachycardia, hypertension, and may lead to arrhythmias. The hemodynamic changes are self-limiting and resolved within 20 min.[14] Changes in hemodynamic parameters from the baseline values following ECT observed were significant with both 0.5 mg/kg and 1.0 mg/kg regimen. These changes were however not significant when compared between the two doses.

Conclusion

This study has shown that 1.0 mg/kg suxamethonium regimen provides a better modification of motor seizure activities than 0.5 mg/kg suxamethonium when used as a muscle relaxant for electroconvulsive therapy.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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