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Original Contribution

A cross-over, post-electroconvulsive therapy comparison of clinical recovery from rocuronium versus succinylcholine☆

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Abstract
Study Objective: To evaluate the effect of the neuromuscular blocking agent, rocuronium, on clinical recovery from electroconvulsive therapy (ECT) as compared with succinylcholine.
Design: Cross-over study.
Setting: University hospital.
Patients: 13 ASA physical status I and II patients, ages 18 to 60 years, receiving ECT three times a week.
Interventions: Each patient received either succinylcholine before the first ECT session (Group S) and rocuronium before the third ECT session (Group R). Muscle paralysis was produced with succinylcholine one mg kg^{-1} intravenously (IV) or rocuronium 0.3 mg kg^{-1} IV. Reversal of the residual neuromuscular block (Group R) was accomplished with 10 μg $kg^{-1}$of atropine and 20 μg $kg^{-1}$of neostigmine after completion of the ECT procedure.
Measurements: Motor seizure duration time, time to first spontaneous breathing, eye opening, head lift, and tongue depressor test were recorded.
Main Result: Motor seizure duration and time to first spontaneous breath was longer (33.6 sec vs. 24.2 sec; 9.46 min vs 8.07 min, respectively) in the rocuronium group than the succinylcholine group. No significant difference was detected between the two groups in eye opening, head lift, or tongue depressor testing.
Conclusion: Rocuronium, when used in conjunction with a reversal agent, may be an adequate alternative to succinylcholine as a neuromuscular blocker during ECT.

1. Introduction

Electroconvulsive therapy (ECT)-induced convulsive activity is accompanied by a generalized seizure, with potential complications such as neuromuscular injury, tooth

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fracture, tongue injuries, or bone fractures. Although serious complications are rare, fractures or dislocations have frequently been described when ECT treatments are performed without muscle relaxants [1-3]. For such a short procedure, succinylcholine may be an adequate neuromuscular blocking agent [4]. However, succinylcholine has some adverse affects, including myalgias and hyperkalemia. Moreover, succinylcholine is a potential triggering drug for malignant hyperthermia as well as neuroleptic malignant syndrome. There are reports of successful use of intermediate-acting, non-depolarizing muscle relaxants such as mivacurium, atracurium, and rapacuronium during ECT procedures in this patient population [5-10].

Rocuronium is a steroidal, nondepolarizing muscle relaxant with an intermediate duration of action [11]. Rocuronium 0.25 mg kg^{-1} intravenously (IV) has a time of onset to maximum neuromuscular block of the laryngeal adductor muscles of 1.6 minutes and a time to spontaneous 90% recovery of T1 twitch height at this muscle of approximately 10 minutes [12]. Rocuronium 0.3 mg kg^{-1} IV provides optimal intubation conditions for most patients [13]. However, there is no report of rocuronium as a neuromuscular blocking agent for ECT.

We designed a cross-over study to evaluate the effect of rocuronium on clinical recovery following ECT.

2. Materials and methods

Approval for the study was granted by the Dokuz Eylül University Hospital Institutional Review Board. Study subjects were 13 ASA physical status I and II patients, ages 18-60 years, receiving ECT three times a week to complete an average of 6 to 12 treatments. Patients with neuromuscular disorders, hypertension, heart disease, history of drug allergy, or taking medications with a potential for drug-drug interaction with neuromuscular relaxants were excluded from the study. Before ECT, all patients had preanesthetic evaluation. Informed consent was obtained from all patients. Nine patients were diagnosed with major depressive disorder, and 4 were diagnosed with schizophrenia. All patients were taking psychotropic medications, including antidepressants and antipsychotics, as appropriate, throughout the study.

Each patient received succinylcholine for the first ECT session (Group S) and rocuronium for the third ECT session (Group R). All patients received atropine (0.01 mg kg^{-1} IV) two to three minutes before anesthesia induction to avoid any unfavorable parasympathetic reflex. Subsequently, unconsciousness and loss of eyelash reflex were induced with propofol one mg kg^{-1} IV administered over 15 to 20 seconds. On loss of responsiveness to verbal commands and eyelash reflex, patients received a blood pressure cuff that was inflated 20 to 30 mmHg over systolic blood pressure (SBP) on the left arm to enable assessment of the duration of motor seizure activity. Succinylcholine one mg/kg IV (Group S) or rocuronium 0.3 mg kg^{-1} IV (Group R) was then administered for muscle relaxation and ventilation was assisted with a face mask and 100% oxygen [13]. Reversal of the residual neuromuscular block (Group R) was accomplished with 10 μg $kg^{-1}$of atropine and 20 μg $kg^{-1}$of neostigmine after completion of the ECT procedure.

Prior to entry into the study, each patient's ECT-induced seizure threshold was determined by recording the patient's age as a reference. The ECT stimulus was given repeatedly with an increasing intensity at 30-second intervals until a generalized motor seizure that lasted more than 20 seconds was obtained [14]. A supra-threshold stimulus was used throughout the study and was increased appropriately at each session to achieve a minimum seizure duration of 20 seconds. In both Group S at the end of the fasiculations and in Group R 90 seconds after receiving the muscle relaxant, a supra-threshold electrical stimulus was delivered via bifrontotemporal electrodes with a MECTA Model SR II apparatus (MECTA Corp., Portland, OR). Duration of the motor seizure in the isolated arm was measured by a study-blinded psychiatrist.

Non-invasive SBP, diastolic blood pressure (DBP), heart rate (HR), and peripheral oxygen saturation (SpO_2) were monitored (M1094B; Hewlett Packard, Saronno, Italy). Values were recorded before any medications were administered (baseline values), every 5 minutes during the procedure and 30 minutes after termination of the ECT session.

Recovery from anesthesia was assessed as the time from administration of the hypnotic agent until eye opening in response to simple commands.

Duration of neuromuscular block was evaluated by recording first the time frame between the application of neuromuscular relaxant and first spontaneous breath; second, the time frame between administration of neuromuscular relaxant and head lift for 5 seconds; and third, the time frame between administration of neuromuscular relaxant and induction of a positive tongue depressor test (standard wooden tongue depressor is placed between the patient's upper and lower incisor teeth; the patient is told not to let the clinician remove it) [15]. All measurements of neuromuscular block and eye opening were assessed at one-minute intervals for each subject during recovery after all of the study-related ECT sessions.

2.1. Statistical analyses

A priori power analysis indicated that a minimum of 13 patients in each group would demonstrate a difference of two minutes in the first spontaneous breath time, with a power of 83% at 0.05 level of significance (Number Cruncher Statistical Systems for Windows; NCSS, Kaysville, UT).

Study data were analyzed by using SPSS 8.0 (SPSS, Chicago, IL). Wilcoxon signed-rank test was used to compare measures of recovery between the two treatment

Table 1 Hemodynamic measures in the study groups

	Baseline	5 min	10 min	15 min	20 min	25 min	30 min
HR (bpm)							
Group S	84 ± 15	118 ± 18	110 ± 21	103 ± 18	99 ± 16	96 ± 14	91 ± 12
Group R	86 ± 17	113 ± 15	109 ± 16	103 ± 17	100 ± 15	98 ± 14	93 ± 13
SBP (mmHg)							
Group S	125 ± 10	155 ± 18	141 ± 17	131 ± 17	128 ± 15	125 ± 15	125 ± 10
Group R	125 ± 10	147 ± 19	143 ± 19	138 ± 15	131 ± 17	129 ± 12	128 ± 12
DBP (mmHg)							
Group S	84 ± 10	96 ± 10	88 ± 9	85 ± 8	84 ± 9	84 ± 9	82 ± 9
Group R	83 ± 11	90 ± 10	87 ± 9	86 ± 7	81 ± 8	81 ± 7	80 ± 8
SpO_2 (%)							
Group S	98 ± 1	97 ± 2	98 ± 1	99 ± 1	99 ± 1	100 ± 1	100 ± 1
Group R	99 ± 1	97 ± 1	98 ± 1	99 ± 1	99 ± 1	100 ± 1	100 ± 1

HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, SpO_2 = peripheral oxygen saturation.
All values are means ± SD.

groups. Significance level was set at $P < 0.05$. All reported P-values are two-sided.

3. Results

A total of 26 ECT treatments were evaluated in 13 patients (5 men and 8 women). The sample's mean age was 44 ± 14 years (mean ± SD; range, 27-60 yrs) and mean body weight was 71 ± 13 kg (mean ± SD; range, 57-107 kg). Mean propofol dose used was the same in each treatment group (90.3 ± 29.8 mg [mean ± SD]; range, 70-180 mg).

There were no significant differences between the two groups either in baseline values of HR, SBP, DBP, and SpO_2 or those values during the ECT procedure (Table 1). The groups also showed no significant differences in these measurements at 30 minutes following the ECT procedure (Table 1).

Motor seizure duration and time to first spontaneous breath was longer (33.6 ± 10.2 vs. 24.2 ± 4.0 sec; 9.46 ± 2.32 vs. 8.07 ± 1.57 min, respectively) in the rocuronium group than the succinylcholine group (Table 2).

No significant difference was detected in values for eye opening, head lift, or tongue depressor test between the two groups (Table 2).

4. Discussion

Rocuronium when used in conjunction with a reversal agent may be an effective and reliable muscle relaxant for ECT during propofol anesthesia.

Rocuronium is an aminosteroidal muscle relaxant with a lower potency than other aminosteroidal muscle relaxants. Onset time is fast because of the drug's lipophilic properties. Accordingly, its diffusion through biological membranes is faster. A dose of 0.3 mg kg^{-1} IV is rocuronium's ED_{95} dose at the adductor pollicis muscle (as estimated by supramaximal single twitch stimulation at 0.1 Hz), and its ED_{50} dose for the laryngeal adductor muscles [12,13]. Rocuronium 0.3 mg kg^{-1} IV dose is half of the recommended intubating dose for rocuronium [12,13]. Since only partial paralysis is required for ECT, we also chose to use rocuronium 0.3 mg kg^{-1} IV for ECT applications.

Table 2 Measures of motor seizure duration, time to first spontaneous breath, eye opening, head lift time, tongue depressor test time in the study groups after electroconvulsive therapy

	Group R	Group S	P-value
Motor seizure duration time (sec)	33.6 ± 10.2 * (25-60)	24.2 ± 4.0 (20-28)	0.04
First spontaneous breath time (min)	9.46 ± 2.32 * (7-15)	8.07 ± 1.57 (6-14)	0.02
Opens eyes (min)	10.77 ± 1.88 (75-15)	8.97 ± 2.22 (6-14)	0.07
Head lift time (min)	14.04 ± 3.23 (12-20)	12.81 ± 4.20 (8-20)	0.34
Tongue depressor test time (min)	14.8 ± 2.25 (10-20)	13.06 ± 3.43 (8-22)	0.16

All values are means ± SD, with ranges in parentheses.
* $P < 0.05$.

Rocuronium at a dose of 0.25 mg kg^{-1} IV has an onset time of 1.6 minutes for achieving maximum neuromuscular block for the laryngeal adductor muscles [12,16]. We elected to wait 90 seconds before inducing ECT, since further delay possibly would have resulted in recovery from anesthesia with no additional administration of propofol. Besides, Naguib and Samarkandi [17] showed that good Laryngeal Mask Airway (LMA) insertion could be achieved after 90 seconds following a dose of 0.3 mg kg^{-1} IV rocuronium.

Measures of recovery from rocuronium (0.3 mg kg^{-1} IV) were similar to those after succinlycholine one mg kg^{-1} IV except for time to first spontaneous breath. After injection of rocuronium 0.25 mg/kg IV, maximum neuromuscular block of the adductor pollicis is approximately 70%, and time to spontaneous 90% recovery of T1 twitch height for this muscle is about 10 minutes [12]. Given these measurements, we believe a dose of rocuronium 0.3 mg kg^{-1} IV would be appropriate for such ECT applications. In addition, low-dose rocuronium should always be reversed pharmacologically when used for ECT.

These findings encourage use of rocuronium as an adequate alternative neuromuscular blocker to succinylcholine for ECT applications during propofol anesthesia in cases where use of succinylcholine is contraindicated. At our institution, we prefer succinylcholine in routine ECT applications and substitute rocuronium in cases with a partial or definitive contraindication for use of succinylcholine.

We found longer motor seizure duration in the rocuronium group as compared with the succinylcholine group. There are no data available in the literature for explaining such differences between rocuronium and succinylcholine. One possible explanation may be the fact that in Group S, electrical stimulus was delivered after cessation of fasciculations and in Group R, electrical stimulus was delivered 90 seconds after receiving the muscle relaxant. This might have led to higher propofol serum levels in Group S than Group R. Consequently, while Group S was still under the influence of the central nervous system depressant effect, Group R might have recovered from the depressant effect of propofol leading to longer motor seizure duration. In this study, the time interval between administration of succinylcholine and cessation of fasciculations in Group S was not measured. Due to that limitation, we couldn't analyze statistically the covariate effects of that difference in timing of electrical stimulus between the groups.

In both groups, duration of motor seizures was in clinically effective ranges. Although the available literature is inconsistent regarding duration of clinically effective, electrically induced seizure activity, Sackeim et al [14] have suggested motor and electroencephalographic (EEG) seizure activity of 20 to 30 seconds for successful ECT [18-20]. O'Connell [21] reported that seizure duration of less than 30 seconds was not clinically effective. Considering these reports, a neuromuscular relaxant agent lengthening seizure duration would indeed be advantageous.

In this study, no recall phenomena was observed. This finding is not surprising given the use of bilateral ECT in this study. It is known that when unilateral, nondominant ECT is administered, cognitive adverse effects are few, and recall of pre-ECT phenomena is common [22]. In contrast, when bilateral ECT is administered, there is usually a loss of memory for events just preceding the ECT. Even if awareness during anesthesia occurs in the context of bilateral ECT, the patient is unlikely to remember it after the treatment [23-26].

There are some limitations with this study. First, we did not attempt to assess neuromuscular function using a nerve stimulator because of possible discomfort to the patients. Second, we did not analyze duration of EEG seizure activity in patients undergoing ECT treatments.

Rocuronium, when used in conjunction with a reversal agent, is an adequate alternative neuromuscular blocker to succinylcholine for ECT.

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