ขนาดของยา Succinylcholine ที่มีประสิทธิภาพในการควบคุม Motor Seizure ในผู้ป่วยที่รับการรักษาด้วย การทำให้ชักด้วยการผ่านกระแสไฟฟ้าในโรงพยาบาลศรีนครินทร์: การศึกษาแบบ Randomized Controlled Trial

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บทคัดย่อ

หลักการและเหตุผล การรักษาด้วยการทำให้ชักด้วยการผ่านกระแสไฟฟ้า (electroconvulsive therapy, ECT) เป็นวิธีการรักษาผู้ป่วยจิตเวชเป็นการทำให้ผู้ป่วยที่ได้รับยาระงับความรู้สึกแบบทั่วไปชักด้วยการผ่านกระแสไฟฟ้า การให้ยาหย่อนกล้ามเนื้อ succinylcholine ก่อนการผ่านกระแสไฟฟ้ามีวัตถุประสงค์เพื่อปรับหรือลดความแรงของการชัก แนวทางของโรงพยาบาลศรีนครินทร์ให้ใช้ยา succinylcholine ขนาด 1.3 มก. /กก. เพื่อพิสูจน์ว่ายา succinylcholine ในขนาดที่น้อยกว่านี้ก็มีประสิทธิภาพ การศึกษานี้จึงเปรียบเทียบความรุนแรงของ motor convulsion ที่ได้จากยา succinylcholine ระหว่างขนาด 1.0 มก./กก. กับ 1.3 มก./กก.

วัตถุประสงค์ เปรียบเทียบ motor seizure modification ใน ECT ที่เกิดจากยา succinylcholine ขนาด 1.0 มก./กก. กับที่เกิดจากขนาด 1.3 มก./กก. การออกแบบการศึกษา เป็นการศึกษาแบบสุ่ม ควบคุม ไปข้างหน้า

วิธีการศึกษา ศึกษาระหว่างเดือนเมษายน พ.ศ.2549 ถึงเดือนมีนาคม พ.ศ.2550 ที่โรงพยาบาลศรีนครินทร์ ผู้ป่วยที่เข้ารับการรักษาด้วย ECT ที่ยินดีและให้คำยินยอมเข้าร่วมกับโครงการวิจัยมี 21 คน ECT แต่ละครั้งจะถูกแบ่งกลุ่มด้วยวิธีสุ่มโดยอาศัยเครื่องคอมพิวเตอร์เป็นสองกลุ่ม กลุ่ม A ได้รับยา succinylcholine ขนาด 1.0 มก./กก. กลุ่ม B 1.3 มก./กก. การประเมินความรุนแรงของ motor seizure อาศัยคะแนน motor seizure modification ซึ่งมี 5 ระดับและได้จากผู้ให้คะแนน 2 คนที่เป็นอิสระแก่กัน ผู้ให้คะแนนให้คะแนนด้วยความเชื่อถือได้ระดับเกือบสมบูรณ์ (kappa = 0.88)

ผลการศึกษา motor seizure modification ในกลุ่ม A และกลุ่ม B อยู่ในระดับดีร้อยละ 74.6 และ 84.6 ของการทำ ECT ตามลำดับ ได้คะแนนระดับแย่ร้อยละ 25.4 และ 15.4 ตามลำดับ ค่า motor seizure modification แตกต่างกันอย่างไม่มีนัยสำคัญ ค่า sodium, potassium, CPK, SGOT, calcium, LDH ในเลือดก่อนและหลังทำ ECTแตกต่างกันระหว่างกลุ่มอย่างไม่มีนัยสำคัญ

สรุป succinylcholine ขนาด 1.0 มก./กก. และ 1.3 มก./กก.ทำให้ความรุนแรงของ motor convulsion intensity ไม่แตกต่างกันอย่างมีนัยสำคัญ ดังนั้นเพื่อลดปริมาณยาที่มากเกินความจำเป็นและลดผลข้างเคียงที่อาจจะตามมา จึงควรเริ่มใช้ยานี้ในขนาด 1.0 มก./กก.

คำสำคัญ electroconvulsive therapy, succinylcholine, motor seizure modification, muscle injury

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Effective Dosage of Succinylcholine in Controlling Motor Seizure in Patients Undergoing Modified Electroconvulsive Therapy at Srinagarind Hospital: A Randomized Controlled Trial

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Abstract

Background: Electroconvulsive therapy (ECT), a psychiatric treatment, electrically induces seizures in anesthetized patients for therapeutic effect. Administering succinylcholine immediately before the electrical discharging aims at modification or reduction of the intensity of motor convulsion. The Srinagarind Hospital guideline for routine practice prescribes 1.3 mg/kg succinylcholine. In order to demonstrate that a lower dosage is as effective, the authors compared the intensity of motor convulsion resulting from succinylcholine at 1.0 and 1.3 mg/kg.

Objective: To compare motor seizure modification during ECT after muscular relaxation by succinylcholine at 1.0 mg/kg vs. 1.3 mg/kg.

Design: Prospective randomized controlled trial.

Methods: The study period was between May 2006 and March 2007 at Srinagarind Hospital. Twenty-one patients undergoing ECT participated in the study on a volunteer basis after giving informed consent. Consecutive ECT sessions were computerized randomized so that the patient received either 1.0 mg/kg (group A) or 1.3 mg/kg (group B) of succinylcholine. Motor seizure intensity was rated by two blinded independent raters using the five-point Motor Seizure Modification Scale (Kappa = 0.88). The inter-rater reliability was almost perfect.

Results: Motor seizure modification in group A and B was graded **'**good**'** in 74.6% and 84.6% of ECT sessions vs. **'**poor**'** in 25.4% and 15.4%, respectively. There was no significant statistical difference in the motor seizure modification between the two groups. There was also no statistical difference between the pre- and post-ECT serum sodium, potassium, CPK, SGOT, calcium or LDH concentration between groups.

Conclusion: The effect of 1 or 1.3 mg/kg of succinylcholine on motor convulsion intensity in ECT was not statistically different. In order, therefore, to reduce an unnecessarily high dosage and contingent effects, succinylcholine in ECT should begin at 1.0 mg/kg.

Keywords: electroconvulsive therapy, succinylcholine, motor seizure modification, muscle injury

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Introduction

Electroconvulsive therapy (ECT) is a common treatment for psychiatric conditions. Normally ECT is done under general anesthesia and a muscle relaxant is administered to prevent violent muscle contractions[1-2]. The muscle relaxant used in ECT in the authors' hospital is succinylcholine, a short-acting neuromuscular blocking agent (NMBA). Succinylcholine binds competitively to nicotinic cholinergic receptors, depolarizing the neuromuscular junction, leading to uncoordinated and weak contractions of striated muscle fibers. Latha *et al.* found that a dose of succinylcholine ranging between 0.45 and 1.3 mg/kg (mean 5$\pm$0.78 mg) failed to provide good modification in about one-fourth of patients[3]. A recent anecdotal report suggested a relatively larger dose (1.2-1.58 mg/kg)[4]. The Guidelines of the Royal College of Psychiatrists[5] recommend 0.5-1 mg/kg, but these are not based on empirical evidence, which is a concern because a dosage of succinylcholine as low as 0.5 to 1.0 mg/kg can cause severe muscle contractions, leading to increased muscle enzyme[6-9].

The usual ECT protocol in Srinagarind Hospital was bilateral type, using Thymatron™ System IV ECT machine. The percent energy of the electrical discharge for each ECT session was set to approximate one-half of the patient's age (e.g., 25% for a 50 year-old). Both bilateral electrical stimulation and the half-age formula for electrical intensity during ECT can cause vigorous seizures so that a high dosage of succinylcholine is needed to suppress the muscle contractions.

In the data from between January and November 2005, the average dosage of succinylcholine used for each ECT session was 1.3 mg/kg which is high enough to cause muscle injury. Lowering the dosage but having enough to allow an ECT without muscle injury would be ideal. The aim of the present study is to compare the efficacy of succinylcholine 1.0 mg/kg vs. 1.3 mg/kg in inducing smooth convulsions without muscle injury.

Methods

The present research was a randomized double blind controlled trial. The Khon Kaen University Research Ethics Committee approved the study. The study period was between May 2006 and March 2007. The participants were in-patients receiving ECT at the Psychiatry Ward of Srinagarind Hospital. The participants were required to given written informed consent before participating in the study. If the patient was a minor or incapacitated, informed consent was needed from the parents or spouse or principal care-taker of the patient.

The psychiatric diagnoses in the ECT patients included schizophrenia, severe major depressive disorder with/without psychotic features, severe bipolar depression with/without psychotic features and bipolar mania. Computerized randomization helped divide each ECT session into two groups and both groups would get the same ECT parameters except that the respective dosage of succinylcholine in group A and B was 1.0 and 1.3 mg/kg. Patients who were taking lithium, having liver disease, allergic to the anesthetic agents, having a history of malignant hyperthermia, neuroleptic malignant syndrome, and organophosphate poisoning were excluded from the study. Normally ECT service was done on alternative days except on weekends.

The sample size was calculated as a discrete variable for good motor modification. Murali *et al*. stated

that about 16% of ECT with succinylcholine 1.0 mg/kg would have poor motor modification then $p = 0.02$, $\alpha = 0.05$ and $\beta = 0.2$ (two-sided)[5]. Therefore, the sample size which is the number of ECT session in the study equals 64 per group. The primary outcome of the study was the degree of motor seizure modification (*i.e.*, using a five-point scale as in Table 1 based on Latha *et al*.)[6].

Table 1 Scoring the extent of motor seizure modification[6]

Score	Location and intensity of convulsions
1	Violent convulsions as in unmodified electroconvulsive therapy
2	Bilateral motor convulsions and they are equal in intensity in both the cuffed and uncuffed limbs
3	Bilateral motor convulsions and the intensity is more in the cuffed limb than the uncuffed limb
4	Motor convulsions in the cuffed limb and face
5	Motor convulsions only in the cuffed limb

Getting a score of 2 or less indicated poor motor seizure modification, and greater than that number indicated good motor seizure modification. Rater(s) of the motor seizure modification during ECT were the in-charge 3rd year psychiatry residents. The psychiatry residents attended motor seizure modification scoring practice sessions until their inter-rater agreement reached Kappa 0.88.

In order to control the confounding factors, several conditions were strictly followed when delivering the ECT service, including: (1) educating the patient on ECT and getting their informed consent; (2) refraining from anticonvulsants and benzodiazepine at least 5 days before ECT except for emergency treatment; (3) common antipsychotics, antidepressants were allowed; (4) nothing per oral was allowed since midnight the night before ECT until recovery; (5) an intravenous line was opened 2 hours before the ECT session; (6) vital signs were monitored including NIBP, SpO_2, EKG; preoxygenation with 100% oxygen using the Bain circuit; (7) inducing patient unconsciousness with 5 mg/kg thiopental; (8) ventilation was assisted via manual mask ventilation; (9) the blood pressure cuff was inflated around the left calf immediately before injecting succinylcholine for observe muscle contraction after electrical discharging; and, (10) discharging the electricity immediately after the termination of succinylcholine induced fibrillation.

The ECT machine used was a Thymatron System IV and the Percent Energy of the electrical discharge intensity was half of the patient's age. Thiopental 5 mg/kg and succinylcholine in a fixed 3 ml solution (both 1.0 mg/kg and 1.3 mg/kg) were prepared and delivered to the patient by an anesthesiologist or a nurse anesthetist. Both the patients and rater of motor seizure reduction were blinded to the concentration of succinylcholine.

Some operational definitions in the present study follow. EEG seizure duration was the period of time (in seconds) since delivering the electrical stimulus until postictal EEG suppression. Motor seizure duration was the period of time since delivering the electrical stimulus until cessation of clonic activity in the cuffed limb. Time to emergence from anesthesia was the period of time since falling unconscious from the pentothal sodium until the patient opened his/her eyes.

Immediately before and after anesthesia 4 ml of the patient's blood was drawn for assessment of the concentration of: sodium, potassium, creatinine phosphokinase (CPK), serum glutamate-oxalase transaminase (SGOT), calcium and lactate dehydrogenase (LDH).

Statistics analysis

The comparison of motor seizure modification between the two doses of succinylcholine was done using Pearson Chi-Square. The comparisons between age, sex, electrical stimulation, muscle contraction and the before and after ECT values for blood chemistry was done using the Independent Samples Test (t-test for Equality of Means, Levene's Test for Equality of Variances). SPSS 11.0 was the statistical software used.

Results

During the study period there were 21 psychiatric in-patients undergoing ECT, 12 (57%) of whom had paranoid schizophrenia, 3 (14%) major depressive disorder, 2 (9.5%) bipolar mania, 1 (4.7%) catatonia and 1 (4.7%) other psychosis. The total number of ECT sessions was 128, and the average per patient was 6. The age range was between 14 and 69 years. The American Society of Anesthesiologists (ASA) physical status class ranged between I and II. Group A (succinylcholine 1.0 mg/kg) and group B (succinylcholine 1.3 mg/kg) underwent 63 and 65 ECT sessions, respectively.

The motor seizure modification in group A was poor for 16 (25.4%) ECT sessions and good for 47 (74.6%); in Group B there were 10 (15.4%) poor sessions and 55 (84.6%) good ones. Both groups tended to generate good motor seizure modification and no significant statistical difference was found (p = 0.159, χ^2 =1.98) (Table 2).

The mean (and SD) percent energy in group A was 21.61 (7.5) and group B was 22.1 (7.28) units. Both groups achieved a satisfactory ECT result and there was no significant difference in the percent energy of ECT stimulation (p = 0.707) between groups. The mean (and SD) EEG seizure duration in group A was 44.32 (17.5) seconds vs. 45.09 (20.8) seconds in group B (p = 0.824). The motor seizure duration inspected from EMG in group A was 32.04 (10.85) seconds vs. 28.03 (9.88) seconds in group B. Group B had significantly shorter EMG seizures than group A (p = 0.031, 95% CI of the difference = 0.36-7.67) (Table 3).

Table 2 Motor seizure modification between groups

Motor modification score	GROUP		
	A	B	total
Poor($\leq$2)	16(25.4)	10(15.4)	26(20.3)
Good(>2)	47(74.6)	55(84.6)	102(79.7)
Total	63(100)	65(100)	128(100)

Value as number of ECT sessions (percent), A = succinylcholine 1.0 mg/kg, B = succinylcholine 1.3 mg/kg, χ^2=1.98, p-value = 0.159

Table 3 ECT parameters comparison between groups

Parameter	Group		p-value	95% CI of the Difference
	A	B		
Percent energy21.61(7.50)	22.10(7.28)	0.707	-3.10-2.11	
EEG seizure duration (sec)	44.32(17.50)	45.09(20.80)	0.824	-7.56-6.03
Motor seizure duration (sec)	32.04(10.85)	28.03(9.88)	0.031*	0.36-7.67

Value as mean (SD), * p<0.05

Table 4 Pre and Post ECT session blood chemistry mean value comparison

Variables		Group		p-value	95% CI of the Difference
		A	B		
Sodium	Pre-ECT	139.31(2.84)	139.52(2.72)	0.677	-1.17-0.76
(mEq/L)	Post-ECT	136.88(8.05)	137.86(7.07)	0.469	-3.62-1.67
Potassium	Pre-ECT	4.68(4.03)	4.21(0.50)	0.353	-0.52-1.46
(mEq/L)	Post-ECT	4.21(0.72)	4.25(0.74)	0.770	-0.29-0.21
Calcium	Pre- ECT	9.02(0.48)	9.07(0.56)	0.581	-0.23-0.13
(mEq/L)	Post-ECT	8.65(1.33)	8.72(1.14)	0.753	-0.50-0.36
LDH	Pre- ECT	190.60(61.45)	208.92(67.81)	0.112	-40.97-4.33
(IU/L)	Post-ECT	181.62(99.14)	173.33(59.05)	0.571	-20.61-37.19
SGOT	Pre- ECT	30.44(18.86)	33.73(22.22)	0.368	-10.51-3.92
(IU/L)	Post-ECT	33.41(23.66)	33.30(29.43)	0.982	-9.25-9.46
SGPT	Pre-ECT	34.69(35.98)	38.16(42.21)	0.618	-17.21-10.27
(IU/L)	Post-ECT	38.00(34.95)	44.07(53.00)	0.447	-21.83-9.67
CPK	Pre- ECT	326.73(371.93)	328.80(358.35)	0.974	-129.81-125.67
(IU/L)	Post-ECT	264.92(459.85)	180.36(205.32)	0.185	-41.27-210.37

Muscle injury from ECT based on the difference between the before and after mean values for serum sodium, potassium, CPK, SGOT, calcium, LDH indicated no statistically significant difference between groups (Table 4).

Discussion

Normally therapeutic ECT results in a cerebral seizure of at least 25 seconds. The present study revealed that therapeutic ECT could be achieved with nearly the same magnitude of electrical stimulus (percent energy) with either 1.0 or 1.3 mg/kg succinylcholine; in other words there was no statistically significant difference in the cerebral seizure duration. The motor seizure duration in the 1.0 mg/kg group was, however, significantly longer than in the 1.3 mg/kg group.

Either 1.0 or 1.3 mg/kg of succinylcholine did not result in any significant difference in the motor seizure modification score. However 1.0 mg/kg tended to produce more poor motor seizure durations albeit the difference was statistically significant. This result accords with Murali *et al.* who reported that succinylcholine at 1.0 mg/kg would result in good motor seizure modification in almost 80% of ECT sessions. When contemplating the risk for both neuroleptic malignant syndrome (NMS), Saito reported that the dosage of succinylcholine in ECT could be as low as 0.5-1 mg/kg and still have a 75-85% chance of good motor seizure modification[8].

Muscle injuries during ECT vis-à-vis the blood concentration values of CPK, sodium, potassium, SGOT, calcium, and LDH both before and after ECT were compared. The authors found that succinylcholine 1.0 and 1.3 mg/kg resulted in no statistically significant difference in these values. Murali *et al.* found that succinylcholine 1.0 mg/kg caused the concentration of serum potassium, SGOT, and LDH to be significantly higher than with 0.5 mg/kg[6]. This result differs from the present study. Importantly, the hyperkalemia did not reach cardiotoxic levels in the present study but Cooper *et al.* did report the unexpected occurrence of hyperkalemia[11]. Much more injury to muscle during muscle relaxation with succinylcholine 1.0 mg/kg can be found in general patients than in ECT-treated schizophrenia[7]. The previous study suggested that lidocaine can reduce succinylcholine induced post-operative myalgia[10].

The present study had some limitations such as the authors did not follow myoglobin concentration as a means of monitoring muscle injury because of the expense of the test. In addition, the sample size was small. Notwithstanding, in order to reduce an unnecessary high dosage and contingent effects, succinylcholine in ECT should therefore begin at 1.0 mg/kg.

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