การแบ่งให้ซัคซินิลโคลีนเพื่อลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน

นายเทวารักษ์ วีระวัฒกานนท์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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SPLIT DOSE OF SUCCINYLCHOLINE FOR MODIFICATION OF SEIZURE DURING MULTIPLE MONITORED ELECTROCONVULSIVE THERAPY

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เทวารักษ์ วีระวัฒเกานนท์: การแบ่งให้ซัคซินิลโคลีนเพื่อลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน (SUCCINYLCHOLINE FOR MODIFICATION OF SEIZURE DURING MULTIPLE MONITORED ELECTROCONVULSIVE THERAPY)
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วัตถุประสงค์ การรักษาด้วยการช็อคไฟฟ้าเป็นทางเลือกหนึ่งในการรักษาโรคจิตที่ดื้อต่อยาหรือมีอาการรุนแรงถึงขั้นทำร้ายตัวเองหรือผู้อื่น ในโรงพยาบาลบางแห่งให้การรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกันในคราวเดียว พบว่าการตอบสนองจะเร็วขึ้นและลดระยะเวลาในการนอนโรงพยาบาลลง ส่วนใหญ่จะลดความรุนแรงของการชักโดยใช้ยาหย่อนกล้ามเนื้อที่มีฤทธิ์สั้นคือซัคซินิลโคลีนเพียงหนึ่งครั้ง บางครั้งฤทธิ์ของยาสั้นเกินไปไม่พอสำหรับการชักครั้งหลังทำให้ชักรุนแรงจนอาจเกิดอันตรายได้ การศึกษานี้เปรียบเทียบการให้ยาซัคซินิลโคลีนหนึ่งครั้งแบบเดิมกับการแบ่งให้ยาแบบสองครั้ง เพื่อค้นหาวิธีการให้ยาหย่อนกล้ามเนื้อที่เหมาะสมสำหรับการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน

รูปแบบการศึกษา เปรียบเทียบในผู้ป่วยคนเดียวกัน คราวแรกจะสุ่มว่าผู้ป่วยจะได้รับยาวิธีใดก่อน การรักษาในคราวต่อไปจะสลับให้ยาอีกวิธีหนึ่ง ผู้ศึกษาและผู้ป่วยไม่ทราบว่าเป็นยาวิธีใด

สถานที่ แผนกจิตเวช โรงพยาบาลจุฬาลงกรณ์

ประชากร ศึกษาในผู้ป่วยโรคจิต 40 รายที่มารับการรักษานี้ที่โรงพยาบาลจุฬาลงกรณ์

วิธีการ ถ้าเป็นวิธีให้ยาครั้งเดียวหลังจากนำสลบแล้วผู้ป่วยจะได้รับยาซัคซินิลโคลีน 1 มก/กก สำหรับการกระตุ้นด้วยไฟฟ้าสองครั้งห่างกัน 3 นาที ถ้าเป็นวิธีแบ่งให้ จะให้ยาซัคซินิลโคลีน 0.75 มก/กก ก่อนการกระตุ้นครั้งแรก และ 0.25 มก/กก ก่อนการกระตุ้นครั้งที่สอง

การประเมินผล เปรียบเทียบการชักของขาสองข้าง ข้างหนึ่งรัดต้นขาไม่ให้ยาซัคซินิลโคลีนเข้าไปได้ ถ้าขาสองข้างชักรุนแรงเท่ากันแสดงว่ายาไม่ได้ผลในการลดความรุนแรงของการชัก

ผลการศึกษา การแบ่งให้ซัคซินิลโคลีนจะลดการชักที่ควบคุมได้ไม่ดีลงจากร้อยละ 43.6 เหลือเพียงร้อยละ 10.3 (p=0.006) โดยที่ระยะเวลาเฉลี่ยในการฟื้นของกล้ามเนื้อยาวนานขึ้นจาก 125 วินาที เป็น 183 วินาที (p=0.001)

สรุป การแบ่งให้ซัคซินิลโคลีนเหมาะสมสำหรับการลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกันแม้ว่าจะทำให้ผู้ป่วยฟื้นจากยาช้าลงเล็กน้อย

หลักสูตร การพัฒนาสุขภาพ ลายมือชื่อนิสิต.....
สาขาวิชา การพัฒนาสุขภาพ ลายมือชื่ออาจารย์ที่ปรึกษา.....
ปีการศึกษา 2544

##4375422030 MAJOR HEALTH DEVELOPMENT
KEYWORD: SUCCINYLCHOLINE/ SPLIT DOSE/ MULTIPLE/ ELECTROCONVULSIVE
THEWARUG WERAWATGANON: SPLIT DOSE OF SUCCINYLCHOLINE FOR MODIFICATION OF SEIZURE DURING MULTIPLE MONITORED ELECTROCONVULSIVE THERAPY
THESIS ADVISOR: ASSOCIATE PROFESSOR ORANUCH KYOKONG, M.D., M.Sc. 63 pp. ISBN 974-03-0725-6

Objective: Electroconvulsive therapy is a treatment for psychiatric patients who fail medical treatment or have severe manifestation. Multiple monitored electroconvulsive therapy, stimulating more than one convulsion in one treatment session, ensures adequate stimulation and results in rapid response**.** Single dose of short acting muscle relaxant is sometimes inadequate for the later stimulation and results in too strong convulsion and injury. We compared succinylcholine dispensed in two divided doses with the usual single dose for modification of convulsion.
Design: Randomized double blind crossover trial.
Setting: Tertiary care public hospital.
Participants: Forty adult psychiatric patients who required multiple monitored electroconvulsive therapy
Intervention: After anesthetized, patients in conventional single dose regimen received 1mg/kg succinylcholine before stimulation then two consecutive electrical stimuli were given in 3 minutes apart. Split dose regimen consisted of 0.75 mg/kg succinylcholine before first stimulation and 0.25 mg/kg before second stimulation. The wash out period was at least 48 hours before switching to another regimen in the next session.
Main outcome measures: Isolated limb with tourniquet and compared the convulsion severity with another side to identify the poor modification of convulsion.
Result: The incident of poor session in single dose regimen was 43.6% compared with 10.3% in split dose regimen (p=0.006). The period effect, sequence effect and carryover effect was not demonstrated. The average time from the end of seizure to 20% muscle twitch height recovery in single dose and split dose were 125 seconds and 183 seconds respectively (p=0.001).
Conclusion: Split dose of succinylcholine is suitable for modification of seizure during multiple monitored electroconvulsive therapy, even though the muscle recovery may be a little bit longer.

Department Health Development Student's signature .....
Field of study Health Development Advisor's signature .....
Acadamic year 2001

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CHAPTER 1

INTRODUCTION

Rationale and Background

Psychiatric disorder is one of the most significant health problems nowadays. Electroconvulsive therapy (ECT) has developed into a widely utilized treatment modality in psychiatric practice (1-3). It has beneficial effects for depressive states, acute schizophrenia and some manic states (4-7). It is effective in the patients who fail medical treatment or have severe manifestation, such as attempting suicide or wanting to hurt surrounding people (8-11). One course of therapy consists of 4-12 sessions depend on the responses (7). A convulsion induced by electrical stimulation is a dangerous intervention given to the innocent psychiatric patients. Unmodified electroconvulsive therapy had been used in the past. It caused psychological and somatic injury and was too cruel to be acceptable. Now we have monitoring for safety and anesthesia for acceptance in the conscious patients (12). Most of all, to attenuate the severity of convulsion and to minimize the injury from the electroconvulsive therapy require the suitable relaxation (13). While the electrical seizure activity in the brain has therapeutic effect on psychiatric symptoms, motor seizure in the body causes only harmful effects on the patients. The stronger

the motor seizure is, the more vulnerable the patient is to get injury from convulsion. From the past, there have been many reports of the injury after electroconvulsive therapy such as vertebral or femoral fracture (14, 15), dental fracture (16, 17), jejunal tear and splenic rupture (18). Currently these complications is decreased by the monitoring and appropriate care during electroconvulsive therapy

Multiple monitored electroconvulsive therapy, which stimulated more than one convulsion in one treatment session, had been recommended to yield better outcome than single therapy (19-23). But several convulsions in one session increase the chance of injury and also extend the time of vulnerable period. There is relatively refractory period following each seizure, which prevents subsequent stimuli from eliciting convulsive activity. Thus the minimum interval between convulsions should be three minutes (19). This causes a problem for appropriate muscle relaxant administration. A single dose of succinylcholine, a short acting muscle relaxant, is usually used and the effect is frequently inadequate to modify the seizure severity of the latter convulsion. The injury might occur even first convulsion is adequately modified but the following one is not. Sometimes supplemental dose of succinylcholine is given with individual judgment when the first convulsion seems to be too violent. We propose that a small dose of succinylcholine should always be given after the first convulsion to lessen the risk of injury from

subsequent convulsion. This is the proposal of split dose administration. The objective of this study is to compare the effect of split dose with the conventional single dose of succinylcholine for modification of motor seizure activity during multiple monitored electroconvulsive therapy.

Review of Related Literatures

The need for muscle paralysis was first demonstrated by Dewald et al., who found vertebral fractures in 43% of the men and 14% of the women who underwent ECT without muscle relaxants ("unmodified ECT"). The study showed that these rates decreased to 2% when decamethonium was used for muscle relaxation ("modified ECT") (24). Since then, the use of a muscle relaxant and anesthesia has become widely acceptable.

Succinylcholine was popular for modification of peripheral motor convulsions in electroconvulsive therapy. The recommended dose was between 0.5 to 1.0 mg/kg for both single (25, 26) and multiple electroconvulsive therapy (27). Murali, et al had shown that 1 mg/kg of succinylcholine was more effective in modifying the peripheral convulsion in single therapy (28). For multiple therapy, there was no valid and reliable evidence to support the way to administer succinylcholine. One recommendation, based on traditional experience, was using succinylcholine infusion through out the procedure. It was not popular because of apprehension about

abnormal blockage associated with continuous use of succinylcholine above 3 mg/kg total dosage.

There were some studies using nondepolarizing muscle relaxant for electroconvulsive therapy (29). Atracurium, an intermediate acting nondepolarizer, had been used successfully in multiple electroconvulsive therapy. However the dose of atracurium should be 0.5 mg/kg, instead of 0.3 mg/kg, to obtain effective modification of convulsion (30). The duration of this larger dose was longer. Relaxation of respiratory muscle required assisted ventilation and relaxation of muscles of the upper airway might lead to obstruction or aspiration. Some patients needed a muscle relaxant reversal at the end of the procedure.

A potential replacement for succinylcholine was a short acting, nondepolarizing neuromuscular blocking agent, mivacurium (31, 32). It had fewer side effects and in low dose (0.08 mg/kg) might have no need for any reversal. However the quality of seizure modification was inadequate in 50% of patients receiving mivacurium compared with 12.5% of patients receiving succinylcholine. The study was terminated early because of the objections from the psychiatrists regarding the adequacy of seizure control. Therefore low dose of mivacurium was not recommended as a substitute for succinylcholine during electroconvulsive therapy (33).

CHAPTER 2

RESEARCH METHODOLOGY

1. Research Question

1.1 Primary Research Question

Does split dose of succinylcholine have different effects on modification of seizure severity from single dose during multiple monitored electroconvulsive therapy?

1.2 Secondary Research Question

Does split dose of succinylcholine have different effects on duration of muscle relaxation from single dose after multiple monitored electroconvulsive therapy?

2. Research Objectives

2.1 General Objective

To find the suitable method of succinylcholine administration for multiple monitored electroconvulsive therapy.

2.2 Specific Objective

To compare the method of succinylcholine administration in divided dose with the usual single dose for modification of convulsion severity in psychiatric patients undergoing multiple monitored electroconvulsive therapy.

3. Hypothesis

The proportions of poor modification of convulsion are not different between single dose and split dose of succinylcholine.

H_0: $\theta_{10} + \theta_{11} = \theta_{01} + \theta_{11}$

The proportions of poor modification of convulsion are different between single dose and split dose of succinylcholine.

H_A: $\theta_{10} + \theta_{11} \neq \theta_{01} + \theta_{11}$

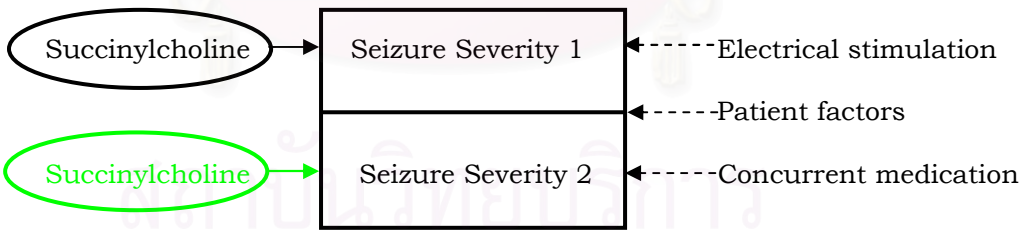
θ_{10} proportions of poor modification of convulsion only in single dose

θ_{11} proportions of poor modification of convulsion in both regimens

θ_{01} proportions of poor modification of convulsion only in split dose

4. Conceptual Framework

Figure 1 Proposed conceptual framework



Succinylcholine is a neuromuscular blocking agent that inhibits motor activity at neuromuscular junction. It has direct motor seizure attenuation in dose dependent fashion without interfering with electrical seizure in the central nervous system because neuromuscular blocking drugs are ionized compounds and, thus,

normally do not cross the blood-brain barrier. However the effect of succinylcholine on motor seizure severity also can be affected by other three major factors (Figure 1).

The electrical stimulation power is the primary determinant whether the stimulation can induce the seizure, which is elicited only when reaching the threshold (34). The electrical stimulation not only directly affects the tonic phase of the seizure but can also stimulate the facial muscles directly.

The next factor is the patient's characteristic. A muscular man can have a strong convulsion and requires more succinylcholine. Some neuromuscular diseases or electrolyte imbalance also influences the patient's response to succinylcholine. Finally, the concurrent medications are the last factor that should be taken into consideration.

5. Study Design

Randomized double blind crossover trial

6. Research Methodology

6.1 Population

6.1.1 Target population

Adult psychiatric patients who required multiple monitored electroconvulsive therapy.

6.1.2 Sampled population

Adult psychiatric patients who were scheduled to receive more than one session of multiple monitored electroconvulsive therapy at Department of Psychiatry, King Chulalongkorn Memorial Hospital.

6.2 Inclusion Criteria

6.2.1 Patients older than 15 years of age

6.2.2 Agreed to participate and obtained informed consent for the study

6.3 Exclusion Criteria

6.3.1 Contraindication to electroconvulsive therapy:

- Recent myocardial infarction, angina pectoris
- Recent cerebrovascular accident
- Intracranial mass lesion
- Congestive heart failure
- Severe pulmonary disease
- Severe osteoporosis
- Major bone fracture
- Glaucoma, Retinal detachment
- Pregnancy

6.3.2 Contraindication to the medication used in this study:

- Thiopental
- Succinylcholine

6.3.3 History of systemic or neuromuscular problems or receiving medication that might interact with the effect of succinylcholine, for example

- Atypical cholinesterase
- Myasthenia gravis

6.4 Sample size estimation

According to the plan to perform statistical analysis by McNemar test for the primary outcome, poor modification of seizure, a two by two table would be constructed as follow (Table 1)

Table 1 Proportion of each outcome between two treatment regimens in crossover trial

		Treatment B	
		0	**1**
Treatment A	**0**	θ_{00}	θ_{01}
	1	θ_{10}	θ_{11}

When θ_{00} was the proportion of patients who had outcome 0 with both treatment A and B. This referred to the proportion of patients who had good modification after both single and split dose succinylcholine. The other proportions were interpreted in the same manner according to the outcome.

The equation for sample size calculation for proportion difference between two dependent groups by McNemar test was (35)

$$n = \frac{\psi}{\delta^2}(z_{\alpha/2} + z_{\beta})^2 + \frac{1}{\psi}$$

n = minimum pairs of sample to test the hypothesis

α = 0.05

β = 0.2

$Z_{\alpha/2}$ = 1.96

Z_{β} = 0.84

$\psi = \theta_{10} + \theta_{01}$

$\delta = |\theta_{10} - \theta_{01}|$

From pilot study, 16 pairs of data were obtained. The proportion of outcome in each pair was filled in the table as (Table 2)

Table 2 Proportion of good and poor outcome between two treatment regimens from pilot study in 16 patients

		Split Dose		Total
		good	poor	
Single Dose	good	8/16	1/16	9/16
	poor	6/16	1/16	7/16
Total		14/16	2/16	1

ψ = 6/16 + 1/16 = 7/16

δ = 6/16 - 1/16 = 5/16

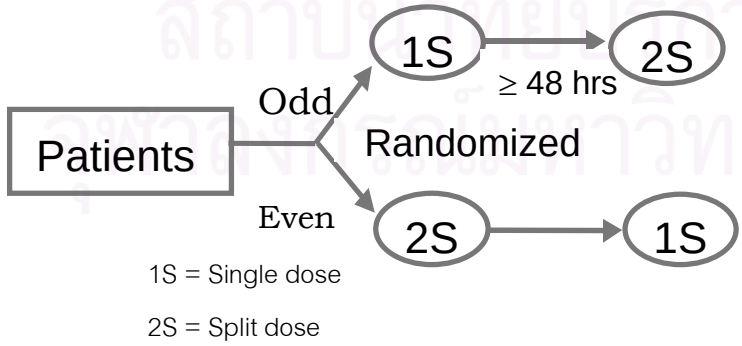
$$n = \frac{7/16}{(5/16)^2}(1.96 + 0.84)^2 + \frac{1}{7/16} = 38.4$$

So, the sample size was n+1 = 40 patients. With full encouragement, telephone and mail contact, each patient should have completed the two sessions of treatment. However if the patient lost follow up after one treatment, the analysis of the data would go on by excluding case and including case with imputing data as worst and best scenario. There was no sample size compensation for patient's loss.

6.5 Randomization

Each patient received one treatment either single dose or split dose in the first session according to randomization. Then he would get another dosage regimen in the next therapy session (Figure 2).

Figure 2 Randomization scheme.



The simple randomization was performed by looking up the computer generated randomized number table in downward direction.

If number was odd, the first session was single dose followed by split dose. Otherwise, in case of even number, the first session would start with split dose then single dose for the second session. For allocation concealment, the numbers was secured in the consecutive sealed opaque envelops. Only one personnel who was the drug dispenser had the right to know each code after having enrolled the patient and beginning the allocation by opening the code from the sealed envelop. The drug dispenser did not involve in any other process of the study.

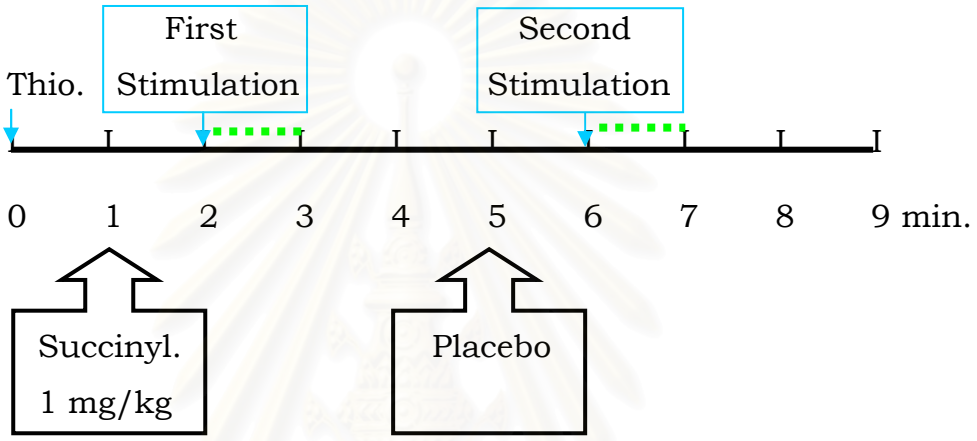
6.6 Intervention

Anesthesia started after preparation for intravenous access and baseline monitoring for EKG, EEG, nerve stimulator, and pulse oximetry. Thiopental 3 mg/kg was given for induction. If the patient was not unconscious after 1 minute, supplemental dose of thiopental was given as necessary and recorded. Then the patient received succinylcholine regimen according to his randomization number

For single dose regimen 1.0 mg/kg of succinylcholine was injected intravenously after the patients were unconscious (Figure 3). One minute later, an electrical stimulation for seizure was given by MECTA SR (MECTRA Corporation, Portland, Ore.). A responsible psychiatrist determined the proper stimulus parameter and tried to keep it constant, if possible, throughout the study. Any change of stimulus between sessions was recorded. Two minutes after termination of the first convulsion, the patient received an

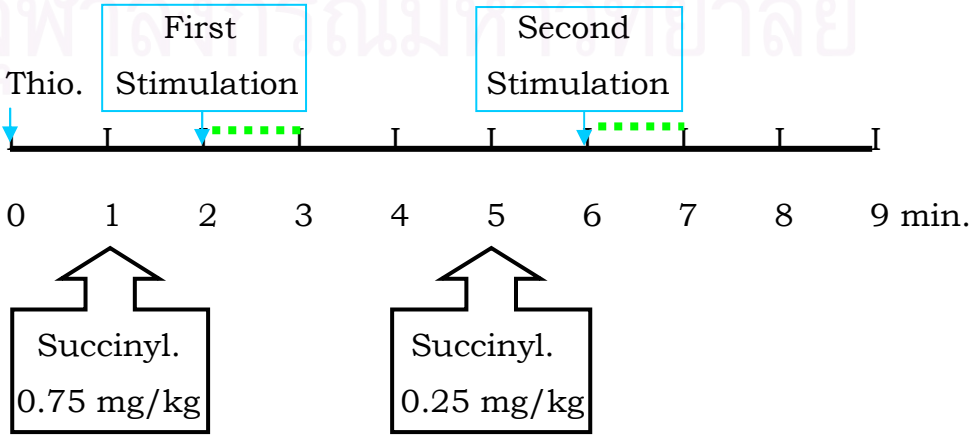
intravenous injection of the placebo. One minute later, the patient would receive the second electrical stimulation. In case of failure to induce seizure, additional electrical stimulus might be given by the psychiatrist's judgment and recorded.

Figure 3 Single dose regimen plan.



For split dose regimen, 0.75 mg/kg of succinylcholine was administered first and then 0.25 mg/kg after the first convulsion instead of placebo (Figure 4). The administration of electrical stimulation was the same as in single dose regimen.

Figure 4 Split dose regimen plan.



The preparation of the study drug in both regimens varied the concentration of medication according to the patient's body weight but it had the same volume, label and characteristic. Nobody could distinguish from its appearance. So everybody, except the drug dispenser, was blind to treatment regimen.

When there were clinical signs of forceful respiration or strong motor movement one minute after administration of the study drug but before any electrical stimulation, inadequate muscle relaxation was possible. Confirmed by muscle twitch height more than 20%, this situation required a rescue dose, 0.5 mg/kg, of open-label succinylcholine. The result was recorded and classified as poor outcome for modification of electroconvulsive therapy.

In the next therapy session, the patients would alternate to another dosage regimen. The interval between therapy sessions was at least 48 hours to ensure that the effect of succinylcholine was washed out completely.

6.7 Observation & Measurement

6.7.1 Instrument and Evaluator for Seizure Modification

The means to evaluate motor seizure severity modification was limb isolation with cuff method (Figure 5). We used a pressure cuff to occlude one extremity so that succinylcholine could not enter that extremity then compared the convulsion with other parts of the body (Table

3). One observer who was blind to treatment assessed grading score for convulsion severity.

Figure 5 Evaluation of motor seizure severity modification by limb isolation with cuff method

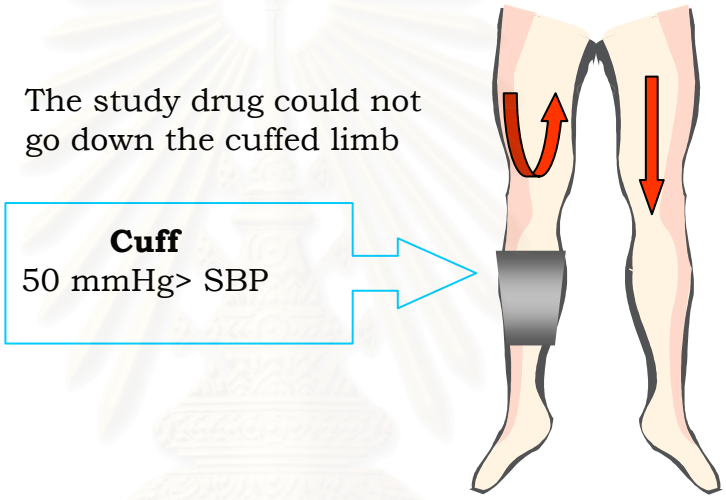


Table 3 Standard of seizure modification score assessment

- Take baseline blood pressure from noninvasive blood pressure monitor (Escort II, USA)
- Select blood pressure cuff with the width more than 2/3 of the diameter of the leg.
- Apply the cuff tightly just below the right knee (Figure 5).
- Raise pressure by 50 mmHg above systolic blood pressure just before the study drug injection.
- Maintain the pressure until the end of assessment.
- Give electrical stimulation 1 minute after succinylcholine injection
- Compare the convulsion between right and left foot at 1 meter distance
- Rate the score as following

Score	Convulsion
1	Violent as unmodified electroconvulsive therapy
2	Bilateral motor convulsions equal intensity both cuffed & uncuffed limbs
3	Bilateral motor convulsions, and the intensity was clearly more in cuffed limb when compared with corresponding uncuffed limb
4	Motor convulsion in cuffed limb and face
5	Motor convulsion only in cuffed limb

The score at 5 meant that succinylcholine was very effective in attenuation of motor convulsion in every part of the body except the limb that we occluded with a pressure cuff. The convulsion could be seen only in the cuffed limb and in the electroencephalogram monitoring brain electrical activity. The score less than 3 indicated poor modification (28, 36) because the limbs that received succinylcholine or not had equal intensity of convulsion. This situation denoted that succinylcholine was not effective.

We had already evaluated the reliability and validity of this assessment in Thai patients and concluded that the scoring system is useful for our study (Appendix 1).

6.7.2 Neuromuscular function monitoring

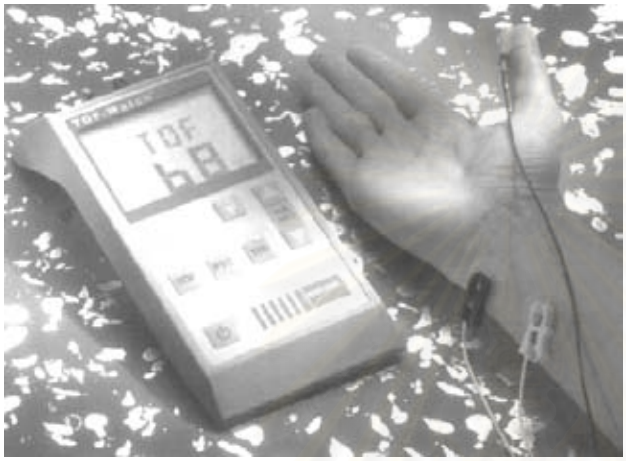
An accelerometer (TOFwatch, Organon, USA) was used for neuromuscular function monitoring from ulnar nerve stimulation. Succinylcholine would block the electrical conduction from ulnar nerve to the adductor pollicis muscle. The contraction of the muscle was assessed by the movement of the thumb with accelerometer transducer (Figure 6). The monitor displayed the twitch height of movement in percentage of baseline contraction. If the muscle is strongly blocked, the twitch height will be 0%. When there is 20% recovery of twitch height, recovery of adequate respiration could be expected.

An investigator assistant performed the neuromuscular function monitoring according to the standard of procedure (Table 4). This assistant would disclose the reading of twitch height to other personnel only if there was clinical sign of inadequate relaxation and twitch height more than 20% before seizure stimulation, which required rescue succinylcholine.

Table 4 Standard of neuromuscular function monitoring

1. Use the extremity that is not applied blood pressure cuff.
2. Locate ulnar nerve by palpation for ulnar arterial pulse and flexor carpi ulnaris tendon.
3. Fix two red dot electrodes just above the wrist and one inch apart along the ulnar nerve.
4. Adhere acceleration receptor at ipsilateral thumb.
5. Ensure free movement of the thumb and acceleration receptor.
6. Setup electrode with TOFwatch.
7. After induction of anesthesia, calibrate for supramaximal stimulation and record baseline muscle twitch height from muscle contraction when stimulated.
8. Set the frequency of stimulation at 0.1 Hz throughout the study.
9. Record the time from the end of convulsion until recovery of muscle twitch is at least 20% by using a stopwatch.

Figure 6 Neuromuscular monitoring by accelerometer attached at right hand.



6.8 Data Collection

The patient chart was the source of demographic and concurrent medication data. The investigator acquired the data of electrical stimulation and seizure outcome from observation during electroconvulsive therapy at outpatient department of psychiatry. We recorded all the data first in a case record form and then transferred to digital data files for analysis. Verification between case record form and digital data files was performed before statistical analysis.

Main outcome:

- Number of patients who had poor modification of convulsion during first and second convulsion categorized by grading score for convulsion severity

Secondary outcome:

- Time to 20% muscle twitch height recovery

Confounding factor

- Electrical stimulation: current, frequency, duration
- Patients' characteristics: age, weight, height, gender
- Concurrent medication

6.9 Data Analysis

We commenced data analysis at the end of the study without any interim analysis. First, we constructed the frequency table for outcome from each patient and then considered the period effect, sequence effect, and carry-over effect from this table (37). After that the statistical analysis aimed at difference of outcome from the treatment effects in paired subject, using SPSS version 7.5 software. We used the level of statistical significance at $p<0.05$ and performed the following statistical hypothesis test.

- McNemar test: for dichotomous outcomes, seizure modification status (good/poor)
- Paired t test: time taken for at least 20% neuromuscular twitch height recovery

Although the data were time data type and trend to be skew, there are no censor data. The assumption of normality would be checked by histogram, normal plot, and Shapiro-Wilk test. In case of assumption not fulfill, nonparametric test, Wilcoxon signed rank test, would be more suitable.

6.10 Data Presentation

The primary outcome was presented as percentage of poor modification in single and split dose. The difference in these two proportions and 95% confidence interval was shown. A table of baseline patient characteristics and one table for detail of outcome comparing two treatments would be displayed.

6.11 Ethical Consideration

The ethical committee at Faculty of Medicine, Chulalongkorn University had reviewed and approved the study protocol. The study embarked on obtaining consent from the committee and patients, or their responsible relatives. The patients could withdraw from the study at any time without any interference on their further standard treatment. All the data was used for study purpose only and was confidential.

There was a data safety monitoring board arranged to guard for the patient well-being. During the study, all equipment for resuscitation was prepared. Any adverse effects, that might occur,

were treated until recovery and any serious one would be reported to the ethic committee and the data safety monitoring board within 24 hours.

CHAPTER 3

RESULT

There were forty patients enrolled in the study (Table 5). It was necessary to exclude one female patient after first session of split dose therapy with good modification of seizure because she got amnesia side effect after the therapy. So the later session for her was changed to single ECT stimulation. In 39 eligible patients, there were 17 sessions (43.6%) of poor modification outcome from single dose regimen compared with 4 sessions (10.3%) in split dose regimen. Nineteen patients had good results in both regimens whereas one patient had poor result in both regimens (Table 6). The intrasubject comparison with McNemar test (Table 7) showed statistically significant difference between the result from the two regimens (χ_c^2 = 7.58, 1 df, p = 0.006). Absolute risk reduction for poor modification of seizure by using split dose regimen was 33.3%, with 95% confidence interval from 14.1% to 52.6%. So the number needed to treat was 3, with 95% confidence interval from 1.9 to 7.1.

Table 5 Patients' characteristics and ECT information; mean (SD) where applicable

Patients' Data		
Age (yr)	36.0 (11.9)	
Male/female	19/21	
Weight (kg)	61.0 (14.8)	
Height (cm)	161.0 (9.4)	
Regimen	Single Dose	Split Dose
Thiopental (mg)	184.7 (44.7)	184.7 (44.7)
First Stimulation		
- Frequency (Hz)	66.9 (7.7)	66.5 (7.4)
- Current (amp)	0.8 (0)	0.8 (0)
- Duration (sec)	1.3 (0.3)	1.3 (0.3)
- Muscle twitch before stimulation (%)	5.4 (7.0)	7.6 (8.8)
- Seizure duration (sec)	42.1 (17.0)	41.5 (17.1)
Second Stimulation		
- Frequency (Hz)	67.4 (8.5)	66.5 (7.4)
- Current (amp)	0.8 (0)	0.8 (0)
- Duration (sec)	1.3 (0.4)	1.3 (0.3)
- Muscle twitch before stimulation (%)	7.0 (19.8)	3.2 (6.3)
- Seizure duration (sec)	47.7 (20.0)	45.1 (19.3)
Muscle recovery time (sec)	125 (93)	183 (131)*

* p=0.001, Wilcoxon signed rank test

Table 6 Outcome in each sequence of treatment.

Outcome	(Good, Good)	(Good, Poor)	(Poor, Good)	(Poor, Poor)
Single-Split Sequence	10	1	8	1
Split-Single Sequence	9	8	2	0

Table 7 Number of patients grouped by seizure modification status after single dose and split dose of succinylcholine

		Split Dose		Total
		good	poor	
Single Dose	good	19	3	22
	poor	16	1	17*
Total		35	4	39

* χ_c^2 = 7.58, 1df, p=0.006, McNemar test

When tabulating the number of poor outcome session by treatment sequence and session period (Table 8), the period effect, sequence effect, and carryover effect could be evaluated. A comparison of the two row marginals (11 sessions in the first period compared with 10 sessions in the second period) did not show any period effect because the difference was very small. A comparison of the column marginals (11 sessions in single-split sequence compared with 10 sessions in split-single sequence) also did not show any

sequence effect. The median time between sessions for wash out period in single-split sequence group was 3 days (range 2-42 days). The median time between sessions for wash out period in split-single sequence group was 3 days (range 2-21 days).

Table 8 Poor outcome session tabulated by period and sequence of treatment.

Poor Outcome Session	Single-Split Sequence	Split-Single Sequence	Total
Period 1	9 in 20	2 in 19	11 in 39
Period 2	2 in 20	8 in 19	10 in 39
Total	11 in 40	10 in 38	21 in 78

Six patients during single dose required a rescue dose of open-label succinylcholine because of clinical sign of inadequate muscle relaxation immediately before electrical stimulation whereas three patients in split dose regimen needed the rescue. After the rescue the convulsion showed good modification of seizure.

When excluding the patients who received a rescue dose of succinylcholine, there still were 11 sessions of poor modification outcome from single dose regimen compared with 1 session in split dose regimen (Table 9). The difference was statistically significant (χ_c^2 = 6.75, 1 df, p=0.009).

Table 9 Number of patients grouped by seizure modification status after single dose and split dose excluding the patients who received a rescue dose of succinylcholine.

		Split Dose		Total
		good	poor	
Single Dose	good	19	1	20
	poor	11	0	11*
Total		30	1	31

* χ_c^2 = 6.75, 1 df, p=0.009, McNemar test

The average time from the end of seizure to 20% muscle twitch height recovery in single dose and split dose were 125 seconds and 183 seconds respectively (Table 5). The difference was statistically significant (p=0.001, Wilcoxon signed rank test).

Six patients had slow onset of muscle relaxation both during single dose and split dose session. One minute after succinylcholine administration, the patients had muscle tone and muscle twitch height was still high but decreasing. In these cases, the first stimulation was delayed for another half minute until muscle twitch height came below 20%. Another four patients had this slow onset of muscle relaxation, which required the same management, only during split dose of succinylcholine. There were 2 patients in single dose regimen and 1 patient in split dose regimen who had poor modification of the first convulsion.

One patient had tooth injury and bleeding per gum after convulsion during single dose session in spite of protection with silicone tooth guard. Other adverse effect of multiple monitored electroconvulsive therapy found in the study was amnesia in six patients. Two of these were after single dose and four after split dose. These patients were converted to single electroconvulsive therapy protocol, which stimulated the patient only once per one session. The change in therapy protocol was made after both sessions of the study in five patients because the symptom occurred after they completed the trial. The amnesia was not alleviated by this management but did not progress. Hypertension, blood pressure above 160/110 mmHg, was found in 7 patients. Four of them had history of hypertension and received antihypertensive medication beforehand. There were three patients who had significant myalgia that required analgesics. One patient had nausea and vomiting. No other serious adverse effect was found.

CHAPTER 4

DISCUSSION

By using split dose regimen, we could reduce the risk of poor modification of seizure from 43.6% to 10.3%. The patients might have average muscle recovery time extended from 125 seconds to 183 seconds. However this was an acceptable trade off. The mean of recovery time difference was less than one minute which was not clinically significant.

Poor modification of seizure could result in morbidity or mortality as had been reported in unmodified electroconvulsive therapy. Even though these outcomes were rare especially in the new trend of modified electroconvulsive therapy and difficult to demonstrate the difference from muscle relaxant administration regimen (38, 39), the strong convulsion itself was an unfavorable outcome for the patients. The inadequacy of the relaxation and violent seizure might lead to objection and misunderstanding from the psychiatrists (33).

The problems of period effect, sequence effect, and carryover effect were the major obstacle to interpret the outcome from any crossover trial (37). The period effect was the change of responses due to the difference between the first and second period of

observation because each patient was observed twice. The sequence effect occurred whenever the order in which treatments were given produced a difference in the response. The carryover effect was the persistence of the effect of the first treatment extending beyond its period of application to influence the action of a subsequent treatment. The primary solution to overcome these problems was selection of appropriate situation that should have no such an effect by the nature of diseases, intervention and outcomes in the study. We had reasons to believe that our study complied with these criteria. The response of our patients to electrical stimuli or succinylcholine and the short action of succinylcholine compared with the duration of washout period between sessions were all proper for the crossover study. The elimination half-life of succinylcholine was only 4 minutes (40, 41) while the washout period was at least 48 hours. For clinical duration of action, there was considerable inter-individual variation. In randomly chosen genotypically normal adult surgical patients, reported values ranged from 8.1 to 21.0 min for the time to 90% recovery after succinylcholine 1 mg/kg (42-44). The second period of treatment should be free of residual effect from previous treatment by our washout period.

In addition, when the data were classified by the period and the sequence of treatment, the effect of these two factors could be estimated. If there was uniformed carryover effect, affecting both

treatments equally, it would appear as a period effect and would not bias the estimate of treatment differences. If the carryover was not uniform, affecting the two treatments differently, then there would be a sequence effect, obscuring the true treatment differences (37). Because the data did not demonstrate any period effect and sequence effect (Table 8), the assumption of no carryover effect was not violated. However, we did not do the statistical pre-testing, i.e. carrying out preliminary tests of assumption before further statistical analysis, for all of these effects because this so-called two-stage procedure (45) was not the recommended approach now and had many disadvantages. Usually the statistical test for carryover effect is not powerful. The test for significance frequently ends up with nonsignificant result and wide confidence interval of effect extending across zero (46).

For the only one drop out patient, there was no need to impute the result of convulsion with the worst and best case scenario. By excluding this case should not affect the main outcome.

Murali, et al (28) had shown that 1 mg/kg of succinylcholine was more effective in modifying the peripheral convulsion in single therapy than 0.5 mg/kg while our study use 0.75 mg/kg in the first portion of the split dose. This might slow onset of succinylcholine down and cause delay of the first stimulation about 30 seconds in some patients, but it was adequate for modification of the first convulsion in most patients. If 1 mg/kg was used instead of 0.75

mg/kg, the muscle relaxation might be a little bit better and sooner but the recovery time would be longer. Our study also showed that 0.75 mg/kg of succinylcholine was effective in modifying the peripheral convulsion in first convulsion, so it could be used in single therapy as well as 1 mg/kg.

There were some practice to administer the supplemental dose of succinylcholine depended on the result of the first convulsion and also on the clinical sign of inadequate muscle relaxation. Infrequently, a neuromuscular monitoring was used in guiding for succinylcholine administration. While these practices might rescue some patients, the remained patients still had high risk of poor modification of convulsion (Table 9). Although neuromuscular monitoring might have some value in some patients, the discrepancy of relaxation of muscle in different part of the body produced the problem when relying too much on the monitoring. Some patients had recovery of respiration but the muscle twitch was zero. In this case the stimulation might be done with good outcome. In contrast, quite a number of patients who had twitch height below 20% before the stimulation had poor modification of seizure.

The issue of rescue dose was one limitation to show more difference of effect between the two regimens. If there was no rescue, the incidence of poor convulsion would increase, but it was not ethical and not practical. In real clinical practice, anesthesiologists would

give some more relaxant, if there were any clinical signs of inadequate muscle relaxation.

There was another clinical practice that gave only one dose of succinylcholine for two electrical stimulations. By inducing the second stimulation earlier, 45 seconds after the first convulsion, the second convulsion might occur within the duration of action of single dose succinylcholine. With this practice one needed to increase the electrical current because the stimulation would fall on the relative refractory period. This meant that there was more electrical current reaching the brain and it might do more harms to the brain. In addition, the failure rate of stimulation increased, and in this situation, another stimulation with higher level of current to the brain was retried until the adequate seizure occurred (34). We suggested that the stimulation should be done in the appropriate period, beyond 3 minutes after the first stimulation, with the same setting of electrical stimulation as the first stimulation. The stimulation could be done without concerning about inadequate duration of muscle relaxation by using split dose regimen.

The study showed high incidence of amnesia in both regimens. This might due to the way that multiple monitored electroconvulsive therapy given in our hospital. We used bilateral frontal stimulation, which might cause more memory loss than unilateral stimulation (47).

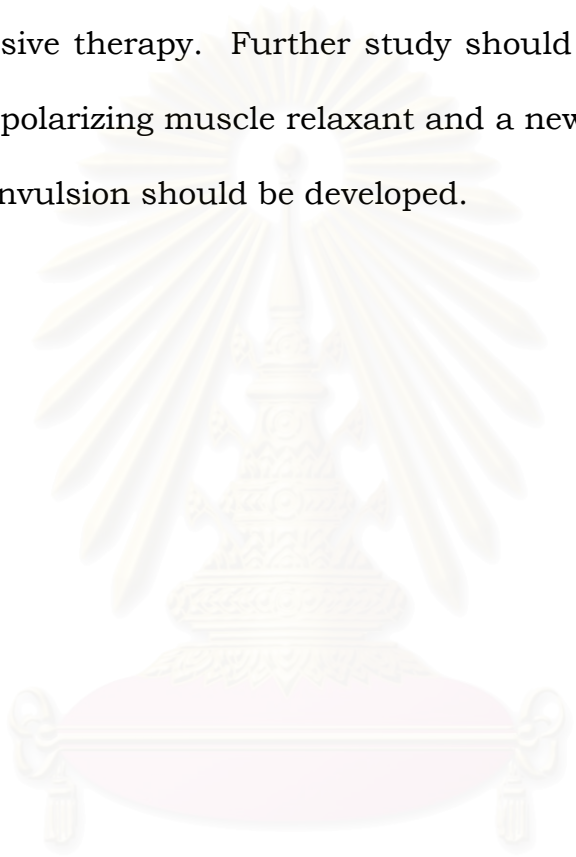
A frequent schedule, on every other day so that the response was rapid to shorten hospital stay, might be another factor (7).

Cheam EW, et al used other grading system to assess the seizure modification for the efficacy of muscle relaxant (33). This grading, based on subjective opinion, had questionable reliability because of low agreement between observers. It was not sensitive to change, especially in the middle range. The seizure modification score that we used was more objective and reliable. The validity could also be demonstrated to some extent (Appendix 1) but we still doubt about its discriminating power. Sometimes patients who had the same score appeared to have different seizure severity at some degrees. We suggest that a new scale should be developed and it should be a continuous scale.

In the past, continuous succinylcholine infusion had been recommended for multiple monitored electroconvulsive therapy but it is not popular now (48). We need intermittent adequate relaxation just before each convulsion, so intermittent dose would be more appropriate. With high dose of infused succinylcholine to achieve intense relaxation throughout the procedure would result in complication such as abnormal phase II blockage. Another possible consideration for multiple monitored electroconvulsive therapy was using nondepolarizing muscle relaxant (29). But until now the study

in both single and multiple electroconvulsive therapy did not have satisfactory results (30, 33).

In conclusion, we recommend that split dose of succinylcholine is suitable for modification of seizure during multiple monitored electroconvulsive therapy. Further study should be done to compare it with nondepolarizing muscle relaxant and a new scale for assess the severity of convulsion should be developed.



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APPENDICES

APPENDIX 1

The Validity and Reliability of Seizure Modification Score in Thai Patients

Rationale and Background

There were many grading scores to describe the severity of motor seizure during electroconvulsive therapy such as

0 no seizure

1+ mild

2+ moderate

3+ strong

4+ violent as unmodified

Another scoring system to assess seizure modification was proposed by Cheam EW, et al as (1)

0 No seizure: no detectable motor activity

1 Over modified: seizure activity barely visible

2 Desired level: well defined, but modified, seizure activity

3 Under modified: excessive seizure activity making the patient difficult to manage

4 Full seizure: full seizure activity with high risk of patient injury

All of these scoring systems were base on subjective opinion. They were not sensitive to change, especially in the middle range, and

the reliability of them was questionable because they were not stable between observers.

Latha V, et al used a scale to measure motor seizure modification during electroconvulsive therapy with a cuff method (2). It looked more objective. The validity and reliability of the scale had been test in foreign patients. The scale seemed to be suitable for our next study and we would appraise it for Thai patients.

Research Question

Is seizure modification score valid and reliable for Thai patients?

Study Design

Prospective descriptive study

Research Methodology

Population

Target population

Adult psychiatric patients who required modified electroconvulsive therapy.

Sampled population

Adult psychiatric patients who were scheduled to received modified electroconvulsive therapy at Department of Psychiatry, King Chulalongkorn Memorial Hospital

Inclusion Criteria

– Patients older than 15 years of age

– Agreed to participate

Exclusion Criteria

1. Contraindication to electroconvulsive therapy
2. Contraindication to the medication used in this study
3. History of systemic or neuromuscular problems or receiving medication that may interact with the effect of succinylcholine.

Instrumental Design

Motor seizure modification during electroconvulsive therapy was assessed with the cuff method (fig 1). We used a pressure cuff to occlude one extremity so that succinylcholine could not enter that extremity then compared the convulsion with other parts of the body. Two observers who were blind to treatment separately assessed grading score for convulsion severity according to table 1

Fig 1 Cuff method to prevent succinylcholine from entering the right leg

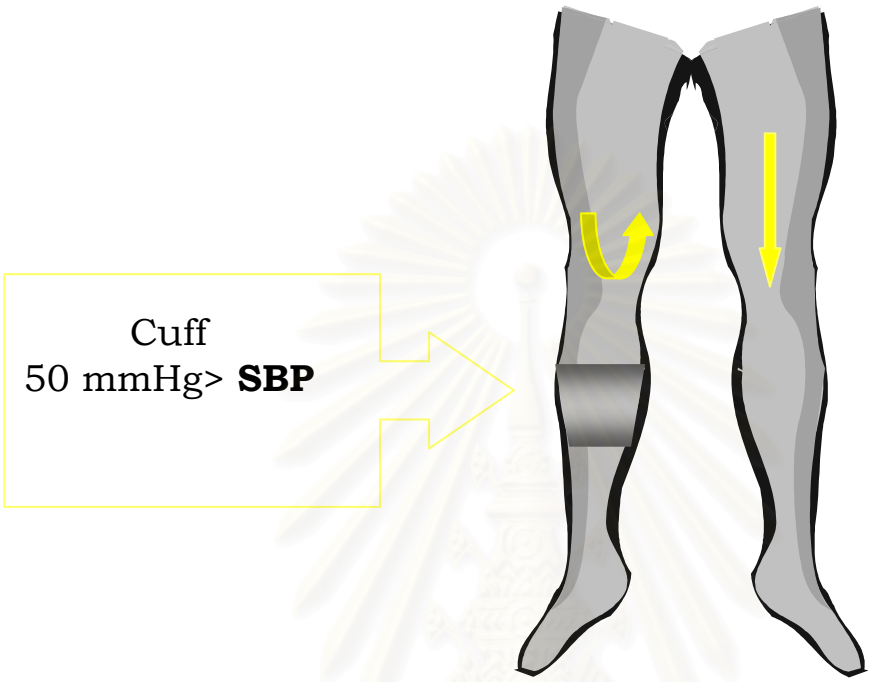

Table 1 Seizure Modification Score

Score	Convulsion
1	Violent as unmodified electroconvulsive therapy, strong convulsion in all part of the body
2	Bilateral motor convulsions equal intensity both cuffed & uncuffed limbs
3	Bilateral motor convulsions, and the intensity was clearly more in cuffed limb when compared with corresponding uncuffed limb
4	Motor convulsion only in cuffed limb and face
5	Motor convulsion only in cuffed limb

Score = 5 meant that succinylcholine was very effective in attenuation of motor convulsion in every part of the body except the limb that we occluded with a pressure cuff. The convulsion could be seen only in the cuffed limb and electroencephalogram that monitored brain electrical activity.

Score < 3 indicated poor modification because the limbs that received succinylcholine or not had equal intensity of convulsion (3).

Data Gathering Technique

Motor seizure modification was assessed by two independent raters who did not know the results of each other. The standard process of measurement was

1. Take baseline blood pressure from noninvasive blood pressure monitor (Escort II, USA)
2. Use blood pressure cuff with the width more than 2/3 of the diameter of the leg.
3. Apply the cuff tightly just below the right knee.
4. Raise pressure by 50 mmHg above systolic blood pressure just before the succinylcholine injection.
5. The pressure will be maintained until the end of assessment.
6. Give electrical stimulation 1 minute after succinylcholine administration
7. Grading convulsion according to table 1.

Statistical test

The statistics for ordinal outcome from two raters were weighted kappa to measure the agreement beyond chance. For relation between score and other factor, Pearson's correlation coefficient was used. The analysis was done by Stata 6.0 statistical software with statistical significant level at $p<0.05$.

Result

We obtained the data from measurement in 34 convulsions to test for reliability of the scale (Table 2).

Table 2 Weighted kappa for interrater agreement

```
. kap Rater1 Rater2, tab wgt(w)

           |               Rater2
    Rater1 |         2          3          4 |     Total
-----------+---------------------------------+----------
         2 |         9          1          0 |        10
         3 |         4         16          0 |        20
         4 |         0          0          4 |         4
-----------+---------------------------------+----------
     Total |        13         17          4 |        34


Ratings weighted by:
   1.0000   0.5000   0.0000
   0.5000   1.0000   0.5000
   0.0000   0.5000   1.0000

             Expected
Agreement    Agreement     Kappa   Std. Err.         Z        Pr>Z
------------------------------------------------------------------
  92.65%     67.04%     0.7769     0.1305      5.95      0.0000
```

Pearson's correlation coefficient was calculated to show the relationship of grading score from both raters and other variables that seemed to be logically related (Table 3)

Table 3 Pearson's correlation coefficient of seizure modification score and other succinylcholine dosage and muscle twitch height from neuromuscular monitor before electrical stimulation

	Rater 1		**Rater 2**	
	Correlation	p	Correlation	p
Succinylcholine dose	.365	.034	.376	.028
Twitch height	-.496	.003	-.417	.014

Interpretation

All 34 convulsions were rated from 2 to 4. There were 29 convulsions that had perfect agreement by both observers. The data show that there was 92.65% of agreement between two raters. The expected agreement by chance was 67.04%. From calculation, we obtained kappa = 0.7769, so we could conclude that the level of agreement was very substantial.

There was statistically significant correlation between the seizure modification score and the variable that, in biological sense, should be related to the score ($p<0.05$).

When the dose of succinylcholine was high, the patient was supposed to be relaxed and had high seizure modification score (4). The level of muscle relaxation was assessed by accelerometer. If there was good relaxation, stimulation of ulnar nerve would result in a low twitch height and the patient should have high seizure modification score (5). According to these reasons, positive correlation between the

seizure modification score and the dose of succinylcholine used were shown. Negative correlation with the twitch height just before convulsion was also obtained. However the correlation was not strong.

Discussion

We had appraised a scale to measure motor seizure modification during electroconvulsive therapy with a cuff method in Thai patients. The test showed good interrater reliability. Then intrarater reliability could be assessed in the same manner with two copies of video record of the convulsion.

For validity assessment, expert opinions were come from three anesthesiologists, one psychiatrist, and two nurses. All of the experts had been involved in ECT for more than five years and they agreed on face validity.

Even though some conventional grading scores for convulsion were concurrently recorded with the seizure modification score, they were not used as a gold standard to test the criterion validity of the seizure modification score because they were not unequivocally valid enough to be gold standard measurement for seizure severity.

In another way, we recorded the variables that logically related with the seizure modification score such as succinylcholine dose and twitch height before the seizure. Some correlation with these

variables was shown but not high. When two measurements were compared, the maximum correlation between them was the square root of the product of their reliabilities. We also found no statistically significant correlation to other variables that were not logically related to the score such as age and body weight.

In conclusion, the scoring system is useful for our further study. Nevertheless, we will try to enhance the accuracy before used by standardizing the measurement method in an operations manual, training the rater and blinding the observer to the intervention.

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APPENDIX 2

Patient Information Sheet

&

Consent Form

ข้อมูลสำหรับผู้ป่วย (Patient Information)

ชื่อโครงการวิจัย การแบ่งให้ซัคซินิลโคลีนเพื่อลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน

สถานที่ทำการวิจัย คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ผู้ทำการวิจัย นพ.เทวารักษ์ วีระวัฒกานนท์

เรียน ผู้ป่วยทุกท่าน

ท่านเป็นผู้ได้รับเชิญจากแพทย์ให้เข้าร่วมการศึกษาทางคลินิกในการแบ่งให้ยาหย่อนกล้ามเนื้อเพื่อลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน ก่อนที่จะตกลงเข้าร่วมการศึกษาดังกล่าว ขอเรียนให้ท่านและญาติทราบถึงเหตุผลและรายละเอียดของการศึกษาวิจัยในครั้งนี้

ในการรักษาด้วยการช็อคด้วยไฟฟ้าแบบหลายครั้งติดต่อกันซึ่งผู้ป่วยได้รับอยู่นั้น ผู้ป่วยจะได้รับการกระตุ้นด้วยไฟฟ้าอย่างน้อยสองครั้งเพื่อให้เกิดการชักขึ้น ยาหย่อนกล้ามเนื้อจะช่วยลดความรุนแรงของการชักและป้องกันการบาดเจ็บที่เกิดจากการชักที่รุนแรงเกินไป ยาหย่อนกล้ามเนื้อที่ใช้อยู่เดิมคือซัคซินิลโคลีนเพียงหนึ่งครั้งนั้นมีฤทธิ์สั้นประมาณ 5 นาที อาจไม่ครอบคลุมถึงการชักครั้งหลัง

การศึกษานี้จะเปรียบเทียบการให้ยาซัคซินิลโคลีนหนึ่งครั้งแบบที่ทำกันอยู่เดิมกับการแบ่งให้ยาแบบสองครั้งในผู้ป่วยคนเดียวกัน เพื่อค้นหาวิธีการให้ยาหย่อนกล้ามเนื้อที่เหมาะสมสำหรับลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน การรักษาในครั้งแรกจะมีการสุ่มว่าผู้ป่วยจะได้รับยาแบบใดก่อน ผู้ป่วยที่ได้รับยาแบบหนึ่งครั้งในการรักษาครั้งแรกจะได้รับการยาแบบแบ่งให้สองครั้งเมื่อมารักษาในวันต่อไป ส่วนผู้ป่วยที่ได้รับยาแบบแบ่งให้สองครั้งในการรักษาครั้งแรกจะได้รับการยาแบบหนึ่งครั้งเมื่อมารักษาในวันต่อไป ดังนั้นระยะเวลาที่ผู้ป่วยเกี่ยวข้องกับการวิจัยจะเท่ากับช่วงระยะที่ผู้ป่วยมารับการรักษาด้วยไฟฟ้าสองครั้งด้วยกัน จำนวนผู้ป่วยที่จะร่วมในการวิจัยประมาณ 40 ท่าน

เมื่อเสร็จสิ้นการศึกษาผู้ทำการศึกษาจะนำผลในผู้ป่วยแต่ละรายมาเป็นแนวทางในการให้ยาหย่อนกล้ามเนื้อที่เหมาะสมต่อไป

หากท่านตกลงที่จะเข้าร่วมการศึกษาวิจัยนี้ จะมีข้อปฏิบัติร่วมดังต่อไปนี้

- ท่านไม่ต้องเสียค่าใช้จ่ายในการรักษาเพิ่มขึ้นจากการศึกษานี้ ดังนั้นขอให้ท่านกลับไปพบแพทย์ตามนัดเพื่อรับการรักษาต่อไปอีก
- ก่อนเริ่มต้นการศึกษาและการพบแพทย์แต่ละครั้ง แพทย์จะตรวจร่างกาย ตรวจวัดความดันโลหิต, ชีพจรและน้ำหนักเพื่อความปลอดภัยในการรักษา
- ระหว่างที่ศึกษา ขอความร่วมมือจากท่านให้มารักษาตามปกติที่แพทย์นัดโดยไม่ขาด

อาการข้างเคียงที่เกิดจากยาดังกล่าว จะเกิดขึ้นเพียงเล็กน้อย และมีโอกาสจะเกิดพอกันไม่ว่าจะให้ยาซัคซินิลโคลีนแบบหนึ่งครั้งหรือสองครั้ง ซึ่งแพทย์จะเป็นผู้อธิบายรายละเอียดต่างๆของผลข้างเคียง แพทย์จะแจ้งให้ท่านทราบ และยินดีตอบคำถามต่างๆ ที่ท่านสงสัยโดยละเอียด

การเข้าร่วมการศึกษานี้ เป็นไปโดยสมัครใจ ท่านอาจจะปฏิเสธที่จะเข้าร่วม หรือถอนตัวจากการศึกษานี้ได้ทุกเมื่อ โดยไม่กระทบต่อการดูแลรักษาที่จะได้รับจากแพทย์

ประการสำคัญที่ท่านควรทราบคือ

ผลของการศึกษานี้ จะใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น โดยข้อมูลต่างๆ จะถูกเก็บไว้ในคอมพิวเตอร์ และไม่มีการแพร่งพรายสู่สาธารณชน ขอรับรองว่าจะไม่มีการเปิดเผยชื่อผู้ป่วยตามกฎหมาย

หากท่านมีปัญหา หรือข้อสงสัยประการใด กรุณาติดต่อ นพ.เทวารักษ์ วีระวัฒกานนท์ ใบประกอบวิชาชีพเวชกรรมเลขที่ 12345 แผนกวิสัญญี ตึกสิรินธร ชั้น 4 โรงพยาบาลจุฬาลงกรณ์ โทร 256-4215 ซึ่งยินดีให้คำตอบแก่ท่านทุกเมื่อ

ขอขอบคุณในความร่วมมือของท่านมา ณ ที่นี้

ใบยินยอมเข้าร่วมการวิจัย (Consent form)

ชื่อโครงการวิจัย การแบ่งให้ซัคซินิลโคลีนเพื่อลดความรุนแรงของการชักจากการรักษาด้วยการช็อคไฟฟ้าแบบหลายครั้งติดต่อกัน

ผู้ทำการวิจัย นพ.เทวารักษ์ วีระวัฒกานนท์
ใบประกอบวิชาชีพเวชกรรมเลขที่ 12345 หมายเลขโทรศัพท์ 256-4215

ข้าพเจ้า……..ผู้แทน/ผู้ปกครอง/ญาติ ของผู้ป่วยชื่อ…….ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้ ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยถึงวัตถุประสงค์ของการวิจัย วิธีการวิจัย อันตราย หรืออาการที่อาจเกิดขึ้นจากการวิจัย หรือจากยาที่ใช้รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยรับรองว่าจะตอบคำถามต่างๆ ที่ข้าพเจ้าสงสัยด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าพอใจ

ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยนี้เมื่อใดก็ได้ และเข้าร่วมโครงการวิจัยนี้ โดยสมัครใจ และการบอกเลิกการเข้าร่วมการวิจัยนี้ จะไม่มีผลต่อการรักษาโรคที่จะพึงได้รับต่อไป

ผู้วิจัยรับรองว่าจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวผู้ป่วยเป็นความลับ และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวผู้ป่วยต่อหน่วยงานต่าง ๆ ที่เกี่ยวข้องกระทำได้เฉพาะกรณีจำเป็น ด้วยเหตุผลทางวิชาการเท่านั้นตามกรอบที่กฎหมาย และกฎระเบียบได้อนุญาตไว้โดยไม่ล่วงละเมิดเอกสิทธิ์ในการปิดบังข้อมูลของผู้ป่วย

ผู้วิจัยรับรองว่าหากเกิดอันตรายใดๆ จากการวิจัยดังกล่าว ผู้ป่วยจะได้รับการรักษาพยาบาล โดยไม่คิดมูลค่า และจะได้รับการชดเชยรายได้ที่สูญเสียไประหว่าง การรักษาพยาบาลดังกล่าว ตลอดจนเงินทดแทนความพิการที่อาจเกิดขึ้นตามความเหมาะสม

ข้าพเจ้าได้อ่านข้อความข้างต้นแล้ว และมีความเข้าใจดีทุกประการ และได้ลงนามในใบยินยอมนี้ด้วยความเต็มใจ

ลงนาม……..ผู้แทน/ผู้ปกครอง/ญาติ
(……..) วันที่……../……../……
ลงนาม……พยาน
(……..) วันที่……../……../……
ลงนาม……..ผู้ทำวิจัย
(……..) วันที่……../……../……

APPENDIX 3

Case Record Form

CASE RECORD FORM

Split Dose Of Succinylcholine For Modification Of Seizure
During Multiple Monitored Electroconvulsive Therapy

Address_____
_____
Telephone_____
HN_____

Sex: Male ☐ Female ☐
Age: _____ years
Weight: _____ kg Height: _____ cm

Diagnosis
_____
_____

Associated Disease:
_____
_____
_____

Remark
_____

Name_____ Case Number ☐☐☐ 61

Date: ___/___/___ ECT session ☐☐☐

Concurrent Medication:

_____

_____

_____

Medication:

Thiopental _____ mg Supplement _____ mg

Succinyl rescue dose _____ mg

First Electrical Stimulation:

Frequency_____Hz Duration_____sec

Current (0.8) _____Amp Pulse width (1.4)_____

Twitch height before sitmulation _____%

First Convulsion:

Duration_____ sec

Convulsion grading____+

Seizure Modification Score

Score	Convulsion
1	Violent as unmodified
2	Bilateral convulsion, equal intensity both cuffed & uncuffed limb
3	Bilateral convulsion, intensity is clearly more in cuffed limb
4	Motor convulsion in cuffed limb and face
5	Motor convulsion only in cuffed limb

Second Electrical Stimulation:

Frequency_____Hz Duration_____sec

Current (0.8) _____Amp Pulse width (1.4)_____

Twitch height before sitmulation _____%

Second Convulsion:

Duration_____ sec

Convulsion grading____+

Seizure Modification Score

Score	Convulsion
1	Violent as unmodified
2	Bilateral convulsion, equal intensity both cuffed & uncuffed limb
3	Bilateral convulsion, intensity is clearly more in cuffed limb
4	Motor convulsion in cuffed limb and face
5	Motor convulsion only in cuffed limb

Time to at least 20% twitch height recovery _____ sec

Number of fail stimulation_____

Complication

_____

Remark

_____

Name_____ Case Number ☐☐☐ 62

Date: ___/___/___ ECT session ☐☐☐

Concurrent Medication:

_____

_____

_____

Medication:

Thiopental _____ mg Supplement _____ mg

Succinyl rescue dose _____ mg

First Electrical Stimulation:

Frequency_____Hz Duration_____sec

Current (0.8) _____Amp Pulse width (1.4)_____

Twitch height before sitmulation _____%

First Convulsion:

Duration_____ sec

Convulsion grading____+

Seizure Modification Score

Score	Convulsion
1	Violent as unmodified
2	Bilateral convulsion, equal intensity both cuffed & uncuffed limb
3	Bilateral convulsion, intensity is clearly more in cuffed limb
4	Motor convulsion in cuffed limb and face
5	Motor convulsion only in cuffed limb

Second Electrical Stimulation:

Frequency_____Hz Duration_____sec

Current (0.8) _____Amp Pulse width (1.4)_____

Twitch height before sitmulation _____%

Second Convulsion:

Duration_____ sec

Convulsion grading____+

Seizure Modification Score

Score	Convulsion
1	Violent as unmodified
2	Bilateral convulsion, equal intensity both cuffed & uncuffed limb
3	Bilateral convulsion, intensity is clearly more in cuffed limb
4	Motor convulsion in cuffed limb and face
5	Motor convulsion only in cuffed limb

Time to at least 20% twitch height recovery _____ sec

Number of fail stimulation_____

Complication

_____

Remark

_____

VITAE

Thewarug Werawatganon was born on October 30, 1961 in Bangkok, Thailand. He graduated from the Faculty of Medicine, Chulalongkorn University in 1985. Then he was appointed from the Ministry of Public Health as a general practice doctor at a district hospital in Ayuthaya province. Meanwhile, he received a Bachelor Degree of Art (Politics) from Ramkumhaeng University in 1988. From 1988 to 1990, He underwent a residency training program at Chulalongkorn Memorial Hospital and obtained a Thai Board of Anesthesiologist from the Medical Council of Thailand in 1990. He has been working as an instructor at the Department of Anesthesiology, Chulalongkorn University since then.

In 1996, he obtained a scholarship from Japanese Council of Medical Training to be a fellow at Department of Anesthesia, Toranomon Hospital, Tokyo, Japan. In the year 2000, he received a fund from Ministry of University to study for a Master Degree of Science, Major Health Development, which was a course organized by Thai CERTC in conjunction with Chulalongkorn University.