Original Article

Correlation of Seizure Duration to Anesthetic Dosage in Patients Undergoing Electroconvulsive Therapy

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Background: Electroconvulsive therapy (ECT) has been performed under general anesthesia with muscle relaxants in psychotic patients by stimulating the brain with an electrical current.

Objective: To focus on the correlation between the anesthetic dosage and the seizure duration in successive therapeutic course.

Materials and Methods: The present report was a retrospective study. After standard monitoring and pre-oxygenating with 100% oxygen, patients were administered with sodium thiopental 2 to 4 mg/kg and succinylcholine 0.5 to 1.0 mg/kg intravenously. Then psychiatrists discharged an amount of electricity as small as possible to trigger patients up to the therapeutic convulsion. The anesthetic dosage, the electrical current, and the seizure duration were recorded.

Results: One hundred thirty patients were included in the present study. The average dosage of sodium thiopental and succinylcholine in 6-session ECT were 2.6 to 2.7 mg/kg and 0.9 to 1 mg/kg respectively. These anesthetics as well as the electrical current showed significant increase (p=0.001). However, the seizure duration as evidenced by electroencephalogram appeared to decrease significantly (p=0.001) through the electroconvulsive course. Moreover, sodium thiopental showed a negative correlation coefficient that slightly related to the seizure duration; whereas, succinylcholine showed a positive, moderate relationship.

Conclusion: Along the electroconvulsive course, the seizure duration correlated inversely with the anesthetic dosage. The dosages of sodium thiopental and succinylcholine were increased significantly; however, the seizure duration showed clinically decrease.

Keywords: Electroconvulsive therapy, Anesthesia, Anesthetic, Psychiatric patients

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Psychiatric patients have been treated with electroconvulsive therapy (ECT) since 1945. This procedure is usually performed in severe and medication-resistant diseases such as depression and mania, schizophrenia-depression, mood depressive disorder, bipolar disorder, and high risk of suicide[1-3].

In those days, psychotic patients outnumbered medical personnel. As a result, doctors had to use simple methods to treat these patients e.g., plain medicine or ECT without anesthesia (unmodified method). This resulted in pain, discomfort, fear, bad impression, awkward movement, anxiety, as well as physical and psychic trauma[4,5].

To ease these problems, most psychiatrists perform ECT under general anesthesia with muscle relaxants, which is known as modified method. However, this technique requires the cooperation between psychiatrists and anesthetists. Normally, a psychiatrist discharges an amount of electricity as small as possible, known as seizure duration (25 to 60 second) to trigger a patient up to the ideal convulsion while the anesthetist administer the anesthetics as low as possible to control the patient's cardio-pulmonary system and decrease serious side effects such as spine

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fractures[6-9].

At our institute, sodium thiopental and succinylcholine are commonly administered to patients in successive therapeutic course. Interestingly, correlation of the seizure duration and the anesthetic dosage in patients undergoing ECT has rarely been mentioned in the previous studies. Investigators believe that this relationship would indicate the appropriate use of anesthetics in clinical practice. As a result, the objective of the present study was to focus on the correlation between the anesthetic dosage and the seizure duration in successive therapeutic course.

Materials and Methods

This retrospective cohort study had been approved by the Siriraj Institutional Review Board (COA: Si445/2017) and registered via Thai Clinical Trial Registry (TCTR20180810002).

The population was calculated by Poisson distribution:

Mean=variance
Confidence level=95
Appropriate electroencephalogram (EEG)=20%
Rate/1,000=200
Allowable error=1
Average time (per person)=6
Sample size of person time=768
Sample size of subject=128

One hundred thirty patients were enrolled in the present study. The inclusion criteria were both male and female patients, aged between 15 and 65 years, American Society of Anesthesiologists physical status (ASA) I-II, presenting with psychosis, and completely treated with successive ECT (six sessions of 25 to 60 second convulsive duration in each therapeutic course). The exclusion criteria were patients with uncontrolled medical problems, vertebral osteoporosis, or fracture, and repeated ECT in one episode.

Process of electroconvulsive therapy

On the day of the procedure, an anesthetist assessed the patient's background, namely medical, and surgical history, anesthesia-related conditions including adverse effects due to induction, inhalational agents or muscle relaxants, anesthetics allergic conditions, as well as indication and contraindication to the procedure.

An anesthetist, then examined each patient's physical conditions such as cardiovascular system (blood pressure, heart rate, and electrocardiogram), respiratory system (adventitious breath sound), oral cavity (dental caries, denture, and loosing teeth), and nervous system (orientation, recent and remote memory, and cognition) as pre-anesthesia baseline values.

In the operating room, the patient was placed on the bed in the supine position without a head support. Jelly pillows were also placed under the patient's scapula and iliac crest while a psychiatrist set up the ECT device and placed a couple of electrodes on both sides of the patient's temple and mastoid area. A nurse anesthetist inserted a cannula No.22 to administer intravenous fluid on either forearm. The electrocardiogram, percutaneous pulse oximetry, and non-invasive blood pressure were applied as standard monitoring. In addition, a tourniquet was wrapped on the calf of either leg to observe muscle contraction during seizure.

After pre-oxygenating the patient with 100% oxygen for two to three minutes, the anesthetist administered sodium thiopental at 2 to 4 mg/kg intravenously until the eyelash reflex disappeared. Then, the nurse anesthetist notified a circulating nurse to inflate the tourniquet and administered succinylcholine at 0.5 to 1.0 mg/kg intravenously until the muscle fasciculation diminished. The anesthetist placed a bite block between the patient's molars and ventilated for a few minutes.

Then the psychiatrist pressed the electricity generator button while the medical personnel hold the patient on his shoulder, wrists, hips, and knees to prevent further convulsive complications.

After seizure, an anesthesiologist took the bite block off, cleared the secretion, and continued to ventilate the patient until consciousness was restored with adequate ventilation. The vital signs were monitored every three to five minutes. The patient, with oxygen cannulation 3 LPM, was placed in the lateral position and moved to the recovery room. Then, the vital signs were monitored every 15 minutes until stable.

The anesthetic dosage, electrical stimulation, and seizure duration were recorded. The data were analyzed by a statistician.

Statistical analysis

Continuous data were presented as mean ± standard deviation and evaluated for statistical significance with the PASW Statistics software, version 18.0 (SPSS Inc., Chicago, Ill, USA).

Comparison and correlation between the anesthetic dosage and the seizure duration in successive therapeutic course were analyzed by

Table 1. Demographic and characteristic data of patients undergoing electroconvulsive therapy (n=130)

Parameters	Total (n=130) n (%)
Sex	
Male	42 (32.3)
Female	88 (67.7)
Age (year); mean±SD	42.6±13.6
Body weight (kg); mean±SD	60.7±13.6
Height (cm); mean±SD	161.9±8.7
Body mass index (kg/m^2); mean±SD	23.1±4.4
Diseases	
Bipolar	23 (17.7)
Schizophrenia	72 (55.4)
Mood depressive disorder	30 (23.1)
Psychotic	5 (3.8)
Electrode positioning	
Right unilateral (male 28:female 72)	100 (76.9)
Bilateral (male 14:female 16)	30 (23.1)

SD=standard deviation

repeated ANOVA with Bonferoni post hoc test and Spearman rank correlation, respectively.

A p-value of less than 0.05 was considered statistically significant difference with a 95% confidence interval.

Results

One hundred thirty patients were included in the present study. The demographic characteristics including gender, age, body weight, height, associated diseases, and electrode positioning are described in Table 1.

The average doses of sodium thiopental and succinylcholine in 6-session ECT were 2.6 to 2.7 mg/kg and 0.9 to 1 mg/kg, respectively. These anesthetics as well as the electrical current showed significant increase (p=0.001). However, the seizure duration as evidenced by EEG appeared to decrease significantly (p=0.001) through the electroconvulsive course (Table 2).

Moreover, sodium thiopental showed a negative correlation coefficient that slightly related to the seizure duration; whereas, succinylcholine showed a positive, moderate relationship (Table 3).

Discussion

In the present study, psychiatrists performed ECT under general anesthesia with muscle relaxants.

Table 2. Anesthetics dosage and seizure duration of patients undergoing electroconvulsive therapy (n=130)

Episode	Anesthetics; mean±SD	
	Thiopental (mg) (mg/kg)	Succinylcholine (mg) (mg/kg)
1	156.0±45.6 (2.6±0.7)	54.7±18.2 (0.9±0.2)
2	157.1±46.0 (2.6±0.7)	57.6±18.0 (1.0±0.2)
3	156.4±48.7 (2.6±0.7)	58.8±19.0 (1.0±0.3)
4	159.6±52.9 (2.6±0.7)	59.7±20.9 (1.0±0.3)
5	162.9±57.6 (2.7±0.8)	60.1±21.8 (1.0±0.3)
6	162.2±56.0 (2.7±0.8)	60.0±21.7 (1.0±0.3)
p-value	0.001	0.001

	Seizure duration; mean±SD	
	Electrical current (mC)	Electroencephalogram (second)
1	327.6±166.6	41.5±15.3
2	323.9±167.1	40.1±14.2
3	337.0±176.6	37.1±12.0
4	346.7±185.6	36.1±13.0
5	356.6±201.9	37.3±16.3
6	364.2±199.5	36.1±12.8
p-value	0.001	0.001

SD=standard deviation

p<0.05 is significant difference

Table 3. Correlation coefficient between anesthetics dosage and seizure duration

	Correlation coefficient; rs (p-value)	
	Sodium thiopental/EEG	Succinyl choline/EEG
1	–0.004 (0.966)	–0.018 (0.838)
2	–0.068 (0.439)	0.110 (0.212)
3	0.082 (0.354)	0.263 (0.003)
4	–0.092 (0.300)	0.165 (0.061)
5	–0.072 (0.417)	0.181 (0.040)
6	–0.033 (0.714)	0.154 (0.036)

EEG= electroencephalogram

The dosage of sodium thiopental and succinylcholine as well as electrical current showed significantly increases through the electroconvulsive course.

The average doses of sodium thiopental and succinylcholine were 2.6 to 2.7 mg/kg and 0.9 to 1 mg/kg, respectively. By comparison, the American Psychiatric Association[10] and Kaplan and Sandock[11] recommended figures of sodium thiopental and succinylcholine as 2 to 4 mg/kg and 0.5 to 1.25 mg/kg and, 1.5 to 2.5 mg/kg and 0.75 to 1.5 mg/kg, respectively.

Both anesthetics appeared to increase sharply throughout the treatment. This might be because most anesthetics particularly sodium thiopental was metabolized by enzyme cytochrome P-450 and repetitive drugs administration apparently enhanced the enzyme activity, resulting in increased anesthetics requirement[12]. This was confirmed by Muir, in his handbook on drug interactions, analgesic protocols and their consequences, and analgesic drug antagonism. He mentioned that drug tolerance could occur when increasing drug doses were required over time to maintain a desired effect. This was attributed to pharmacokinetic changes (e.g., liver enzyme induction and increased clearance) or pharmacodynamic changes (altered cellular responses and reduced drug effects)[13].

Additionally, Odhiambo et al in a study on effects of phenobarbital and carbon tetrachloride on liver enzymes, confirmed that an administration of barbiturates needed continuous adjustment and regulation of dosage by an attending physician. As thiopental generally caused induction of liver microsomal enzymes involved in drug metabolism, drugs administered after the body was exposed to barbiturates were expected to metabolize faster due to an increase in the levels of drugs metabolizing enzyme[14].

Moreover, barbiturates had anticonvulsant effects via regulation of gamma-aminobutyric acid (GABA) transmission resulting in the elevating seizure threshold (ST)[15]. Thus, psychiatrists by necessity increased the electrical current and the thiopental dosage as the session progressed. This agreed with Chi et al in a study on the effects of psychotropic drugs on ST during ECT. They mentioned the link between anticonvulsant effects and an increase in GABA concentration[16].

On the other hand, succinylcholine is normally rapidly hydrolyzed by butyrylcholinesterase (BChE) in plasma[17]. The higher drug requirement might result from increased BChE activity, potentially decreasing the amount of succinylcholine reaching the neuromuscular endplate. This was confirmed by Ammundsen et al in the editorials on succinylcholine resistance. They summarized that despite the reasons for this increased enzyme activity remained unknown (inherited or acquired), it had been described in many conditions such as alcoholism, anxiety states, and schizophrenia. Thus, along the ECT session, increased succinylcholine dosage become necessary for excellent muscle relaxation[18].

Though an optimal electrical stimulus was critical for inducing therapeutic seizures and energy levels exceeding ST were crucial for proper therapeutic effects, patients having antipsychotics and antidepressants prior to the treatment affected the increase of ST and psychiatrists consequently had to use higher electrical energy[16]. This was consistent with Chi et al who claimed that higher doses of antipsychotics and antidepressants that affected ST during ECT might demand higher electrical levels[16].

However, Chiao et al in a study on psychotropic medication effects on ST and seizure duration during ECT, believed that psychotropic drugs might have negligible effects on these matters[19]. In addition, Okazaki et al in a study regarding antipsychotic drugs increasing seizure frequency in epilepsy patients, found that patients taking antipsychotic agents tended to have fewer seizure incidents than controls[20].

Furthermore, high electrical currents could increase pain sensitivity and EEG would also differ. This noxious stimuli urged anesthesia personnel to increase the anesthetic dosage and the seizure duration as evidenced by EEG, which was gradually suppressed. Murrell et al in a study on rats[21] and Mcllhone et al in a study on anesthetized chickens[22] confirmed the effects of noxious stimuli on the EEG. Additionally, Saab, in a study on visualizing the complex brain dynamics of chronic pain, revealed that electroencephalography reflected the electrical brain activity and was related to structural and functional components of the pain experience and followed pain attenuation after drug administration[23]. As a result, electroencephalography might help clinicians to optimize pain treatment by selection of individual optimal analgesics.

Conclusion

Along the successive electroconvulsive course, seizure duration correlated inversely with anesthetic dosage. The dosage of 2.6 to 2.7 mg/kg sodium thiopental and 0.9 to 1 mg/kg succinylcholine showed significant rises; however, the seizure duration appeared to decrease significantly.

What is already known on this topic?

ECT has been performed for therapeutic effects in psychotic patients by electrically stimulating the brain. Minimal currents are needed to induce generalized seizures under general anesthesia with muscle relaxants known as modified technique. Thiopental and succinylcholine are commonly administered in patients with successive treatment. These help to improve effectiveness and decrease

serious side effects. However, the correlation between anesthetic dosage and seizure manifestation has rarely been mentioned.

What this study adds?

Seizure durations correlated inversely with anesthetic dosage. The dosage of sodium thiopental (2.6 to 2.7 mg/kg) and succinylcholine (0.9 to 1 mg/kg) showed significant increases, however, seizure durations showed clinical decreases through the electroconvulsive course.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Bschor T, Bauer M, Adli M. Chronic and treatment resistant depression: diagnosis and stepwise therapy. Dtsch Arztebl Int 2014;111:766-75.
2. Kellner CH, Greenberg RM, Murrough JW, Bryson EO, Briggs MC, Pasculli RM. ECT in treatment-resistant depression. Am J Psychiatry 2012;169:1238-44.
3. Grover S, Chakrabarti S, Hazari N, Avasthi A. Effectiveness of electroconvulsive therapy in patients with treatment resistant schizophrenia: A retrospective study. Psychiatry Res 2017;249:349-53.
4. Andrade C, Rele K, Sutharshan R, Nilesh S. Musculoskeletal morbidity with unmodified ect may be less than earlier believed. Indian J Psychiatry 2000;42:156-62.
5. Jirakulsawat A, Siriussawakul A, Triyasunant N. Incidence of oral injury and risk factor associated with oral injury in psychiatric patients undergoing electroconvulsive therapy in Siriraj hotpital. Siriraj Med J 2012;64:145-8.
6. Watts BV, Groft A, Bagian JP, Mills PD. An examination of mortality and other adverse events related to electroconvulsive therapy using a national adverse event report system. J ECT 2011;27:105-8.
7. Uppal V, Dourish J, Macfarlane A. Anesthesia for electroconvulsive therapy. Continuing education in anesthesia, critical care & pain. BJA Educ 2010;10:192-6.
8. Richard A. Electroconvulsive therapy. 5th ed. New York: Oxford University Press; 2002.
9. Kadiyala PK, Kadiyala LD. Anaesthesia for electroconvulsive therapy: An overview with an update on its role in potentiating electroconvulsive therapy. Indian J Anaesth 2017;61:373-80.
10. American Psychiatric Association. The practice of ECT: recommendations for treatment, training, and privileging. Washington, DC: American Psychiatric Press;1990.
11. Isenberg KE, Zorumski CF. Electroconvulsive therapy. In: Sandock BJ, Sandock VA, editors. Kaplan & Sandock's comprehensive textbook of psychiatry. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2000. p. 2503-15.
12. Bokoch MP and Eilers H. Intravenous anesthetics. In: Pardo MC, Miller RD, editors. Basics of anesthesia. 7th ed. Philadelphia: Elsevier; 2018. p. 104-22.
13. Muir WW 3rd. Drug interactions, analgesic protocols and their consequences, and analgesic drug antagonism. In: Gaynor JS, Muir WW 3rd, editors. 2015. 335-55.
14. Odhiambo F, Chek JBL, Moro JO. Effects of phenobarbital and carbon tetrachloride on liver enzymes. J Appl Biosci 2012;56:4097-107.
15. Frey HH, Popp C, Loscher W. Influence of inhibitors of the high affinity GABA uptake on seizure thresholds in mice. Neuropharmacology 1979;18:581-90.
16. Chi SH, Jeong HG, Lee S, Oh SY, Kim SH. Effects of psychotropic drugs on seizure threshold during electroconvulsive therapy. Psychiatry Investig 2017;14:647-55.
17. Viby-Mogensen J. Correlation of succinylcholine duration of action with plasma cholinesterase activity in subjects with the genotypically normal enzyme. Anesthesiology 1980;53:517-20.
18. Ammundsen HB, Sorensen MK, Gatke MR. Succinylcholine resistance. Br J Anaesth 2015;115:818-21.
19. Chiao S, Isenberg K, North CS. Psychotropic medication effects on seizure threshold and seizure duration during electroconvulsive therapy stimulus titration. J ECT 2019.
20. Okazaki M, Adachi N, Akanuma N, Hara K, Ito M, Kato M, et al. Do antipsychotic drugs increase seizure frequency in epilepsy patients? Eur Neuropsychopharmacol 2014;24:1738-44.
21. Murrell JC, Mitchinson SL, Waters D, Johnson CB. Comparative effect of thermal, mechanical, and electrical noxious stimuli on the electroencephalogram of the rat. Br J Anaesth 2007;98:366-71.
22. McIlhone AE, Beausoleil NJ, Kells NJ, Mellor DJ, Johnson CB. Effects of noxious stimuli on the electroencephalogram of anaesthetised chickens (Gallus gallus domesticus). PLoS One 2018;13:e0196454.
23. Saab C. Visualizing the complex brain dynamics of chronic pain. J Neuroimmune Pharmacol 2013;8:510-7.