The comparison of the effect of repetitive doses of succinylcholine and thiopental sodium on the duration and severity of seizure in Electro convulsive therapy: Randomized clinical trial

Abstract

Background and Aim: Regarding the controversial results on the effects of anesthetics, especially thiopental sodium, on the duration and severity of seizure and the lack of adequate information on the use of doses of anesthetic and paralysing drugs during ECT, this study was designed to determine the effect of repetitive doses of succinylcholine and Thiopental sodium was administered on the duration and severity of seizure during ECT.

Materials and Methods: The present study was a one-blind randomized clinical trial on patients admitted to the psychiatric ward of Dezful Ganjavian Hospital. The research samples were selected after informed consent and entry criteria. Then, the samples were randomly assigned to two groups. In one group, succinylcholine dose was repeated (one third of the initial dose), and in the other group, the dose of thiopental sodium was repeated (one third of the initial dose). In all patients, seizure duration based on EEG monitoring and severity of seizure was determined by the psychiatrist based on the symptoms of the patient during seizure.

Results: There was a significant difference between the quality of seizure in the two treatment groups after the intervention. There was a strong and good seizure in the thiopental sodium group ($p < 0.0001$). There was a significant difference between the variables of seizure status in comparison with the previous shock in the two treatment groups after the intervention ($p < 0.0001$). The duration of seizure was higher in thiopental sodium treatment group, but no significant difference was observed ($p = 0.82$).

Conclusion: The results of this study showed that the duration and quality of seizure was better in patients requiring repetitive doses of hypnotic drugs (Thiopental Sodium), which was used to repeat the dose of muscle relaxant (succinylcholine).

Keywords: Succinylcholine, Thiopental sodium, Seizure, Electroconvulsive therapy

Introduction: Electrotherapy or electroconvulsive therapy (ECT) is an effective strategy in the treatment of various types of psychiatric disorders (1 and 2). ECT is one of the oldest treatments for mental illness (3) and is also a preferred method among all these modern treatments (4). This method was first used in 1938 to create a generalized seizure (5). During this therapeutic procedure, a kind of electrical stimulation of the nervous system is used to initiate the desired seizure activity. This electrical stimulation initially generates tonic activity for 10 seconds and then the activity of the generalized cloning for a few seconds to more than one minute (6-8). Approximately 100,000 patients undergo ectopic treatment every year in the United States (3). According to some studies, the prevalence of mental disorders in Iran is

about 21% (9). This method is used in cases where the patient does not respond to any drug treatment or cannot tolerate drug-induced drug therapy, or in some cases, such as severe symptoms of psychosis, and desire for suicide or intercourse, in cases requiring immediate medical response (10 and 11). In cases such as bipolar disorder, major depression, post-pregnancy psychosis and malignant neuroleptic syndrome were used (14-12). One of the important points that is important in the treatment process with ECT is a generalized seizure that is caused by the device (tonic and colonic) in the patient. In this episode, a seizure has therapeutic properties that at least 20 seconds (15) can be seen as seizures in the electroencephalogram as visible seizures or 35 seconds (16-17).

In a study by Hass and colleagues, the appropriate time for treatment by seizure was obtained between 16 and 120 seconds and did not have seizure time outside of this range or the effects of electro-shock therapy, or the patient had side effects. (15). Following muscle contractions during the procedure, there is a possibility of arthritis and possible fractures (5). Additionally, there may be other side effects such as headache, confusion, delirium, muscle aches, nausea, vomiting and memory loss (18-19). Therefore, in order to reduce these psychological complications (6), during the ECT, the patient normally receives an anesthetic inducing agent, followed by a muscle relaxant (5). Various methods can be used for anesthesia during ECT; But in choosing the agent of anesthesia, we should consider the points that can quickly unconscious the person and immediately there is the possibility of recovery and awakening of the individual, have no hemodynamic side effects and minimize the physical and physiological effects, how it affects the duration or range of seizures, analgesia in the infusion, and, ultimately, the availability and affordability of the drug (20- 23).

These factors can significantly affect seizure induction in the ECT (24-25). There is no drug that has all of these conditions said (22). Therefore, choosing the appropriate anesthetic agent and proper dosage is an essential requirement for shock-induced electrical therapy (24-25).

For many years, Methohexital was the preferred anesthetic agent for ECT (26, 27, and 5), but some restrictions, such as rarely available in some countries, have reduced the use of this drug and increased use of drugs such as propofol and thiopental (5 and 27).

Generally, various anesthetic drugs such as Methohexital, Etomidate, ketamine, n-fluorine, propofol and sodium thiopental are used for anesthetics during ECT, but the ideal anesthetic for the ECT method is not yet known (23, 28, 31). A number of centers use Thiopental Sodium (23). Thiopental Sodium is a super-short acting barbiturate with a rapid effect on anesthesia and has a short recovery time. Contrary to these effects, sodium thiopental may cause tachycardia, hypotension, anaphylaxis, facial edema, myocardial depression, and some

other side effects (32). Some studies have shown that propofol and thiopental can reduce the duration of seizures (5 and 33), but propofol is more likely to reduce the duration of seizures compared with thiopental (16, 34-37).

There was no significant difference in the clinical trial study performed by Takahashi and Mishima regarding the effect of propofol and thiopental on the duration of seizure (26). In a study on the duration of seizures in 62 patients undergoing ECT, Bauer and colleagues concluded that the duration of seizures in the thiopental group was shorter than that of propofol (38). Eser and colleagues emphasized during their study that Thiopental Sodium produced longer seizures than propofol, and also indicated that thiopental sodium and propofol were more effective than other anesthetic drugs in their ECT clinical effects (2). Japanese researchers also showed that the duration of seizure in the propofol group is lower than thiopental sodium (39). According to a review of previous studies, there are still many differences in the effects of anesthetic drugs, especially thiopental sodium. The other drug that is given to the patient during an ECT during an ECT are muscle relaxant drugs. What is effective in choosing the type of relaxant drug for ectopic treatment is the mechanism of action, metabolism, and complications of these two groups (40). Succinylcholine is a selective muscle relaxant (a type of depolarizer) in ECT (41). This drug is a short-acting drug and it can be rapidly expelled within 30 to 60 seconds after intravenous injection, which usually lasts 5 to 10 minutes and is very useful in induction of anesthesia (42-44).

Considering the importance of using the appropriate relaxant medications for the ECT and in view of the contradictory results in studies on the effects of anesthetic drugs, especially thiopental sodium, on the duration and severity of seizure and the lack of sufficient information on the use of doses of anesthetic drugs and muscle crippling during ECT, we aimed to study a goal determine the effect of repetitive doses of succinylcholine and thiopental sodium on the duration and severity of seizures in ECT.

Materials and methods:

This study was a tow-group, one-blind, randomized clinical trial. On the one hand, blindness means that only samples are unaware of being placed in any of the groups. The statistical population of this study was all patients admitted to the psychiatric ward of Dezful Ganjavian Hospital who are diagnosed by a psychiatrist under ectopic treatment.

This study was conducted from October 2016 to December 2017 for 14 months in the psychiatric ward of Dezful Ganjavian Hospital in southwestern Iran.
After obtaining necessary permissions and coordinating with the head of the department and cooperation with the psychiatrist, the researcher started to sample according to the criteria of entry.

Criteria for entering the study include the range is between 18 and 60 years old, Satisfaction of the patient's companions to carry out the research, no history of seizure and hypertension and resistance to ECT and having a history of electric shock.

Exit criteria include there is an underlying cardiac disease, including dangerous arrhythmias and ischemia and respiratory diseases, taking anticonvulsants and benzodiazepines, having an anesthetic history with long-term recovery, Dissatisfaction of the patient's companions to continue cooperation in the study and patient's death.

Before the study, patients' records and age, sex, type of disease, number of previous shock sessions and its outcome (in terms of duration and quality of seizure) were recorded. The research samples were selected after informed consent and entry criteria. Then, the samples were randomly assigned to two groups.

The location of the ECT intervention room located in the Department of Psychiatry at Ganjavian Hospital is controlled in terms of light, sound and other environmental stimuli, and is in the same two groups. Also, the date of the last calibration of ECT and anesthetic devices was checked and recorded in two groups.

The process of performing the work was that all patients with the same treatment protocol were under anesthesia for ECT, and the protocol was as follows: Atropine 0.5 mg, Thiopental 3 mg / kg body weight, succinylcholine 0/3 Mg per kilo body weight. All patients were evaluated after induction of anesthesia and before putting ECT dummies. Patients who have not yet taken the usual doses and are not prepared for shock, thus giving an additional dose to these individuals, as follows: In one group, succinylcholine dose was repeated (one third of the initial dose) and in the other group was given a dose of thiopental sodium (one third of the initial dose).

Then the ECT is calibrated using the ECT device in the ECT room (THYMATRON DGX I Type, BF Class with the serial number 3403 of the USA), which on August 3, 2016 for one-year calibration of the device by the hospital's medical engineer and bilaterally Specified energy was given by the doctor.

In all patients, prior to anesthetic induction, an EEG (Electro Encephalogram) monitoring was established performed by the ECT and the device was switched on just before the ECT pads were placed on the patient's skull and until the EEG seizure was resolved, this monitoring continued. After improving respiration and relative alertness, the patient was transferred to recovery, and oxygen was given to him with a mask, and he was kept under care until complete vigilance and the possibility of discharge from recovery.

In all patients, seizure duration based on EEG monitoring and severity of seizure was determined by the psychiatrist based on the symptoms of the patient during seizure.

Blood pressure and pulse rate were measured and recorded in both groups before and after intervention. The interval between ECT and patient's alertness (adequate respiratory rest and open eyes or obedience) were determined and recorded in all patients. Since ECC patients undergo several ECT sessions, it is easy to conclude by comparing the duration of seizures in the previous series with the result after repeated dosing.

Finally, the data were analyzed using SPSS software version 22. To test the relationship between qualitative variables, Chi-square test (Fisher's exact test) and independent t-test were used to compare quantitative variables between two groups. The significance level of the above tests was considered < 0.05.

Results:

In this study, 120 patients with an average age of 34.39 ± 28.9 years were included in the study. Of these, 62 (51.7%) were in the Succinylcholine group and 58 (48.3%) were in the thiopental sodium group. Also, 84 (70%) were female and the rest were male. There was no statistically significant difference between two groups in terms of demographic characteristics (p> 0.05). Demographic indicators are presented in Table 1.

The most common disorder in these people was depression and O.C.D was 19.2%. In general, 54.2% of the seizures were good and strong and the rest were poor. The mean seizure duration in all patients was 29.22 ± 7.86 seconds and 10.2% of seizures were better than before.

Table 1. Distribution of demographic variables divided to two groups of treatment in patients undergoing ECT

Demographic characteristics	Thiopental sodium group N = 58	Succinylcholine group N = 62	P-value
Age (years) Mean ± Std	34/41 ± 9/05	± 9/58 34/41	0/98
Weight(Kilograms) Mean ± Std	69/75 ±6/44	±6/82 69/33	0/73
Gender			0/16
Male	36/2	24/2	
Female	63/8	75/8	
Type of disease (frequency)			0/91
bipolar	13/8	11/3	
Major Depression	17/2	21	
Manic Depression	3/4	9/7	
Postpartum Psychosis	1/7	3/2	
Catatonic schizophrenia	5/2	3/2	
post maternal psychosis	6/9	6/5	
Schizophrenia	6/9	8/1	
Catatonic	3/4	4/8	
O.C.D	22/4	16/1	
Depression	8/6	3/2	
Acute Psychosis	5/2	8/1	
	5/2	4/8	

psychosis

Chi-square test showed that there was a significant difference in seizure quality in the two treatment groups after intervention. There were potent and good seizures in the thiopental sodium group ($p < 0.0001$) (Figure 1).
Chi-Square-Pearson test showed that there was a significant difference between the seizure status in comparison with the previous shock in the two treatment groups after intervention ($p < 0.0001$) and in the thiopental-sodium group, 21.1% of the seizures compared previous shock were better but in the succinylcholine group this variable was zero (Figure 2).
Independent T-test showed that the duration of seizure was higher in thiopental sodium group, but no significant difference was observed ($p = 0.82$) (Fig. 3).

Figure 1. Comparison of the frequency of seizure quality in two treatment groups in terms of weak or potent of seizure

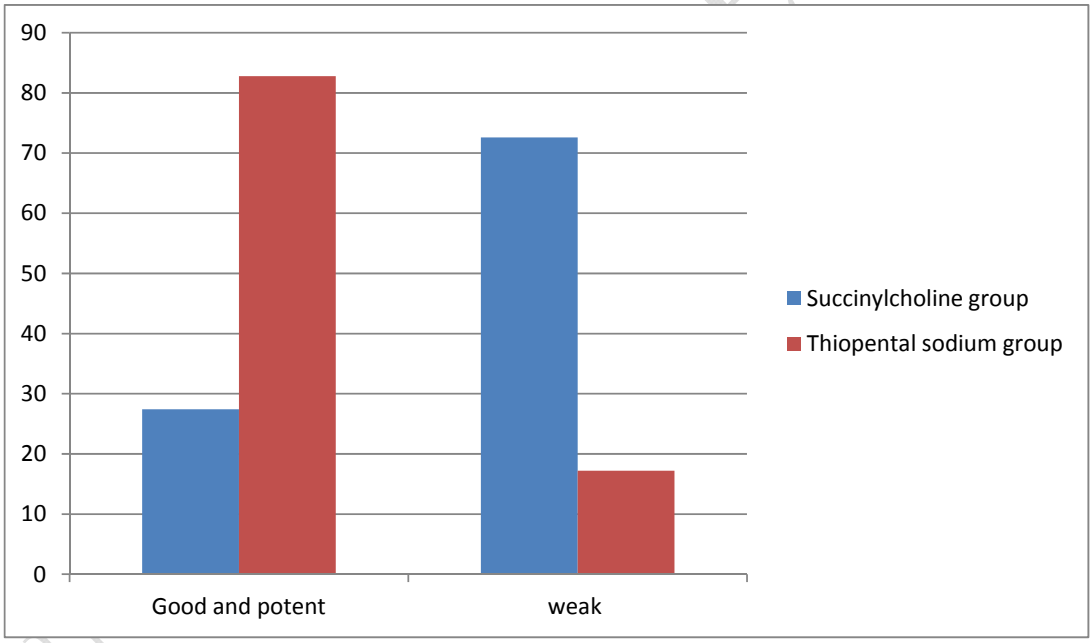


Figure 2. Comparison of the frequency of seizure status compared with the previous shock in the two treatment groups in terms of getting better, weakening or unchanged seizure

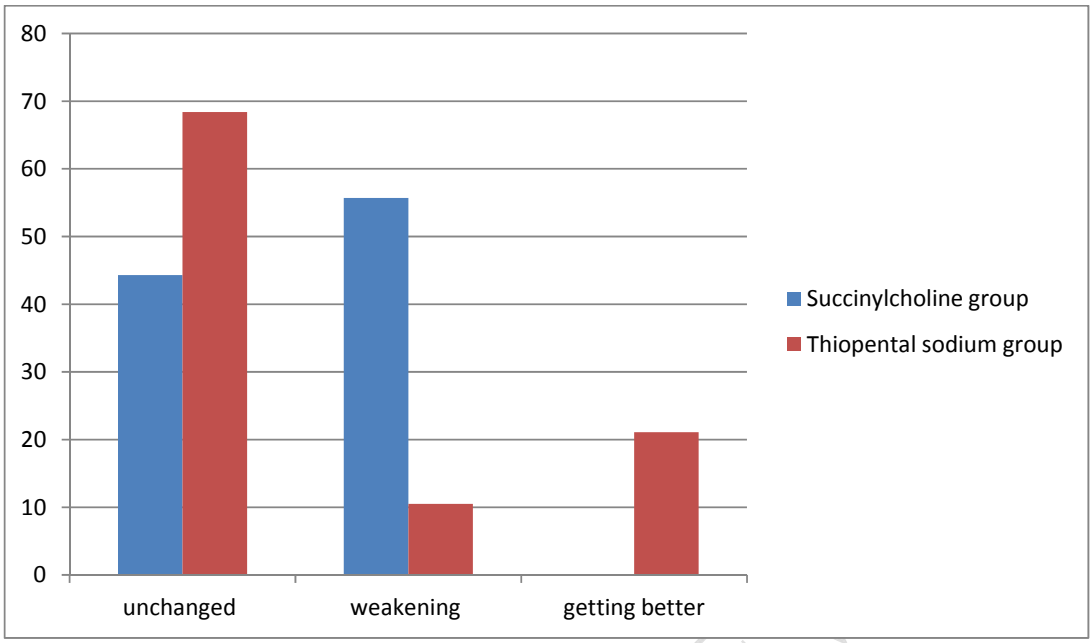
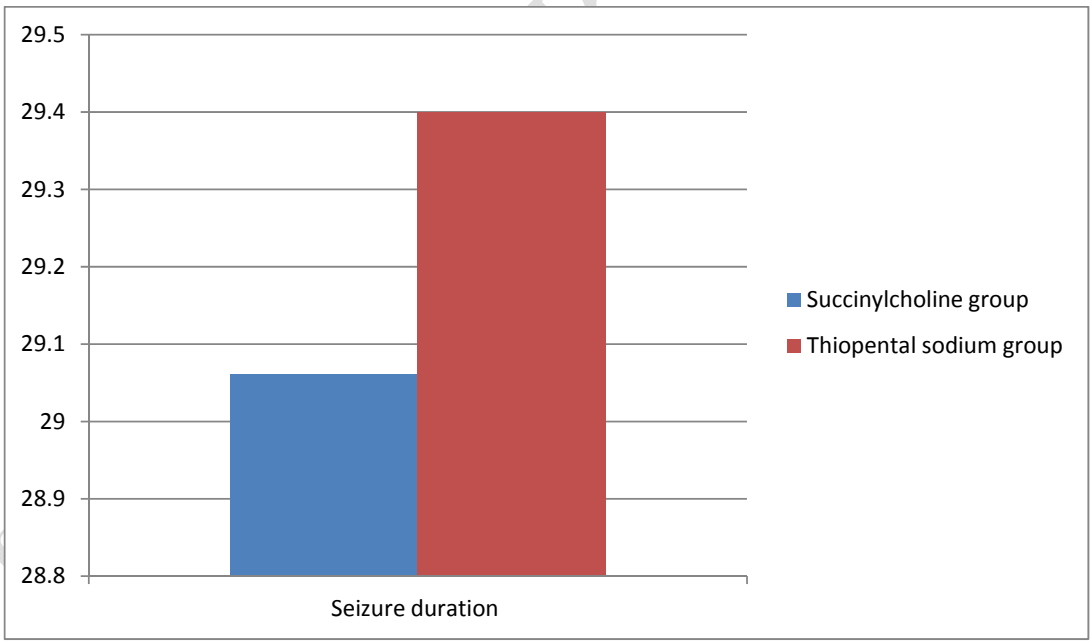


Figure 3. Comparison of mean seizure duration in two treatment groups in seconds



Discussion: In each session of shock therapy, the duration and quality of seizure resulting from shock is a therapeutic criterion, and the longer the quality of the seizure is better, the better the outcome. On the other hand, anesthetic drugs that are prescribed and occasionally repeated before the end of the shock, affect the duration and quality of seizures. Therefore, in this study, we tried to use drugs that would improve the outcome of shock therapy, which means that the seizure obtained from shock therapy is better and takes longer. The aim of this study was to determine the effect of repeated doses of succinylcholine and thiopental sodium

on the duration and severity of seizure during ECT. There was no statistically significant difference between two groups in terms of demographic characteristics ($p > 0.05$).

The results of this study showed that there is a significant difference between the seizure status in comparison with the previous shock in the two treatment groups after the intervention ($p < 0.0001$) and in the thiopental-sodium group, 21.1% of the seizures compared to the Previous shock, they were better, but in the succinylcholine group, this variable was zero.

Also, the duration of seizure was higher in thiopental sodium treatment group, but no significant difference was found ($p = 0.82$). This finding was not consistent with the study by Bauer et al., Who performed on the duration of seizure in 62 patients undergoing ECT. Their study showed that the duration of seizure in the thiopental group was shorter than that of propofol (38). Also, Dew et al showed that shorter seizures were observed with thiopental sodium, which is not consistent with the present study (25). But Eser and colleagues showed that Thiopental Sodium produced longer seizures than propofol, and also indicated that thiopental sodium and propofol were more effective than other anesthetic drugs in relation to their clinical effects in ECT (2), which is consistent with the results of this study. Regarding the controversial results, it seems that supplementary studies with the comparison of propofol, thiopental sodium and succinylcholine on the duration, quality and severity of seizure following ECT seem necessary.

In the present study, there was a significant difference between the quality of seizure in the two treatment groups after the intervention, and there was a strong and good seizure in the thiopental sodium group ($p < 0.0001$), but in the succinylcholine group 55.7% The seizures became weaker with the study of Holmberg and his colleague to determine the effect of succinylcholine as a muscle relaxant in ECT. They showed that the powerful and short-term effect of succinylcholine can reduce seizures (reduced seizure quality) (41). In the study, vertebral fractures were also observed after succinylcholine treatment.

Therefore, considering the results of this study and previous studies, thiopental sodium seems to be more appropriate than succinylcholine for duplicate doses in ECT, although some studies have been shown to have a negative effect on it. It is suggested that other studies comparing different anesthetic drugs and muscle relaxant.

Conclusion:

The results of this study showed that the duration and quality of seizure was better in patients who needed to repeat the dose of hypnotic drugs (thiopental sodium), which was used to repeat the dose of muscle relaxant (succinylcholine), however, only the difference in seizure

duration between the two treatment groups was not statistically significant but clinically meaningful.

Also, in the thiopental sodium group, 21.1% of the seizures were better than the previous one, but in the Succinylcholine group, this variable was zero. In order to use the results of this study in the clinic, further studies are considered necessary.

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