ORIGINAL ARTICLE

# Comparison of hemodynamic changes and serum potassium levels in the use of succinylcholine and cisatracurium in electroconvulsive therapy

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**Background:** Electroconvulsive therapy (ECT) is nowadays used commonly as one the most effective treatment methods in psychiatric disorders. In patients undergoing ECT, succinylcholine is usually used. In addition, cisatracurium is occasionally used on a case report basis globally. In this study, we compared the hemodynamic changes and serum potassium levels in the use of succinylcholine and cisatracurium in ECT. **Materials and Methods:** The current crossover clinical trial was performed on 45 patients who were candidates for ECT between 2017 and 2018. The patients were given succinylcholine or cisatracurium randomly on two separate occasions of ECT. The independent *t*-test and Chi square Test were used to compare the data. **Results:** Comparison of mean systolic blood pressure ($P = 0.14$), diastolic blood pressure ($P = 0.33$), and mean arterial pressure ($P = 0.23$) did not show any significant difference between the two groups. The induced seizure duration ($P = 0.002$), return of spontaneous respiratory from seizure ending ($P = 0.001$), and apnea duration ($P = 0.01$) were significantly higher in the cisatracurium group compared to the succinylcholine group. However, the frequency of tachycardia in cisatracurium group was lower than the succinylcholine group ($P < 0.001$). In addition, the serum potassium level had a significant difference ($P < 0.001$) between the two groups. **Conclusion:** Using cisatracurium can be an alternative to succinylcholine during ECT since it causes less elevation in serum potassium and creates a longer duration of induced seizure, more rapid re emergence of spontaneous breathing at the end of seizure ($P = 0.001$), and a lower prevalence of tachycardia compared to succinylcholine ($P < 0.001$).

**Key words:** Cisatracurium, electroconvulsive therapy, hyperkalemia, serum potassium, succinylcholine

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## INTRODUCTION

Electroconvulsive therapy (ECT) is the programmed electrical stimulation of the central nervous system to initiate seizure activity. Electrical stimulation first generates generalized tonic activity for a few seconds and subsequently generalized clonic activity which can last from a few seconds to more than a minute.[1] ECT is an effective treatment in a variety of psychiatric diseases including bipolar disorder, major depression, and acute schizophrenia, catatonia, especially in cases where drug therapy has failed, or it is considered as a selective treatment in patients requiring a rapid response.[2,3]

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According to studies, seizure parameters such as seizure length are important in ECT effectiveness, which appear to be influenced by the type of anesthetic and muscle relaxant drugs.[4,5] Muscle relaxants are divided into two groups of nondepolarizing drugs and depolarizing drugs. Succinylcholine has been found to release large amounts of potassium from skeletal muscle in patients who have burns, muscle trauma, central nervous system trauma, spinal cord injury, peripheral nervous system damage, and muscle changes due to chronic inactivity.[6-13] An increase in potassium levels can cause problems in these patients, including ventricular arrhythmias and cardiac arrest. Cisatracurium and atracurium both act as nondepolarizing neuromuscular blocking agents,



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however, cisatracurium as a muscle relaxant is about three times stronger than atracurium. Cisatracurium is often used in anesthetics to facilitate endotracheal intubation as well as muscle relaxation in maintaining anesthesia in various surgeries, and in addition, it releases less histamine, which is a major complication of atracurium usage.[14-16] Considering the fact that a studies have been performed in anesthesia on cardiovascular changes and increased serum potassium levels in ECT, and the duration of seizure,[17] we compared the hemodynamic changes and serum potassium levels in the use of succinylcholine and cisatracurium in ECT.

## MATERIALS AND METHODS

This current crossover clinical trial study was performed on 45 patients who were candidates for ECT in the psychiatry ward of children and adolescents in Al Zahra Hospital during 2017–2018. After obtaining approval from the Medical Ethics Committee of Isfahan University of Medical Sciences, patients willing to participate in the study were included with informed consent. This clinical trial was registered at www.irct.ir with an identification of IRCT (IRCT20160307026950N14). A Thymatron intravenous device (Somatics, LLC. Lake Bluff, IL, USA) was used for ECT.

Then, they were selected using the Random Allocation software (Department of Anaesthesiology and Critical Care, Isfahan, Iran). The inclusion criteria for this study included those under the age of 18 years and the American Society of Anesthesiologists physical status classifications I and II.[18]Furthermore, exclusion criteria included obesity (a body mass index equal to or >30), history of asthma, allergies, myocardial infarction in the last 6 months, stroke in the past 6 weeks, cardiac fibrillation and flutter, ECT repeated at the same session, and diseases such as hypertension and hyperactivity. The patients were excluded if they underwent a seizure <20 s, a seizure of more than 90 s, needed cardiopulmonary resuscitation, or if we could not withdraw enough blood for sampling.

The data obtained were analyzed by SPSS-24 software (IBM, USA) after they were entered into the computer. The statistical tests used to analyze the data were Chi-square, paired *t*-tests, and Fisher's exact if needed. The method was done so that patients were randomly assigned to two groups: one group with packet (A) and a second group with packet (B) under electroconvulsive. Package (A) contained 1.5 mg/kg ketamine and 0.5 mg succinylcholine and package (B) contained 1.5 mg ketamine and 50 μg/kg cisatracurium. The person who administered the medication and the person who recorded the vital signs were separate and were unaware of the contents of the packets. Syringes of the same shape and size were used. Patients were fasted for at least 6 h, and two peripheral venous lines were prepared with 18 gauge catheters and blood samples were taken from the right arm at these times: before the anesthetic drug injection (base time), before induction of ECT (after drug prescription), after the seizure, and 20 min after induction of anesthesia. Before inducing anesthesia, patients were provided with a simple oxygen mask and given 4–6 L of oxygen flow for a period of 3 min. Monitoring included electrocardiogram and heart rate, pulse oximetry, and noninvasive blood pressure carried out for all patients. Heart rate, average arterial blood pressure, diastolic blood pressure and systolic blood pressure, and hemoglobin saturation by oxygen were measured at these times.

## RESULTS

Based on the relatively small sample size in each group, and the lack of establishment of the normal hypothesis (based on the Kolmogorov–Simonov test), the mean values of age, weight, and height were assessed using the nonparametric Mann–Whitney test in both the groups. The results showed that values of age, weight, and height did not show any significant differences between the two groups. The demographic data are shown in Table 1.

Therefore, the multivariate test was used to analyze the data. According to the results of all of the multivariate tests, the effect of time was significant for all of the six variables, but the interaction of time and group was significant for only systolic blood pressure (SBP) ($P = 0.03$), potassium levels ($P < 0.001$), and mean arterial pressure (MAP) ($P = 0.04$).

In addition, these results demonstrated that the variation of trends was not significant among the groups except for changes in potassium levels (F [1.88] =32.26; [$P < 0.001$]).

The data regarding the means and standard deviation of each of the SBP, diastolic blood pressure (DBP), hazard ratio (HR), potassium levels, SaO2, and MAP are noted in Table 2. The fluctuation trends for SBP, DBP, and MAP indicates that the mean of these values prior to drug administration was the least and at the second time (after drug injection) and the most at the third time (after seizure abatement), again descending after the fourth time (20 min after anesthesia induction) [Table 2].

**Table 1: Mean age, weight, and height in two groups**

| Variable | CIS (*n*=45) | SUC (*n*=45) | *P* |
|---|---|---|---|
| Age (years) | 14.4±1.1 | 14.3±1.2 | 0.93 |
| Weight (kg) | 57.8±8.8 | 57.3±9.2 | 0.79 |
| Height (cm) | 159.2±6.9 | 159.4±7.4 | 0.91 |

Values are mean SD or median (IQR). CIS=Cisatracurium; SUC=Succinylcholine; SD=Standard deviation; IQR=Interquartile range

In regard to the three variables mentioned above, except for the baseline period which had a higher means in the succinylcholine group compared to cisatracurium, in the three other periods, the means in the cisatracurium group were higher than the succinylcholine group. HR also increased with time but showed a reduction in the fourth time. However, the changing patterns with $SaO_2$ were more different than other variables; such that $SaO_2$ was highest before drug injection, with the lowest during the second (after drug use) and third (after seizure ending) times but increasing during the fourth period.

Unlike SBP, DBP, HR, and MAP, the mean values for $SaO_2$ levels were more elevated in the cisatracurium group compared to the succinylcholine group at the baseline time but higher in the succinylcholine group at the other three intervals. The changing patterns of the two groups regarding all six variables using the analysis of the profile are shown in Figure 1.

For further evaluation of the dual results (difference of the results in two), the Bonferroni correction was used. In the case of SBP, the highest difference of means was at the first and third intervals which meant that the mean SBP after seizure was higher than the baseline interval ($P > 0.001$).

Furthermore, the mean DBP after drug use and after the ending of seizure was 10 units above the baseline interval (before drug use) ($P < 0.001$). The mean MAP after drug administration and after ending of seizure was higher than the baseline time ($P < 0.001$). The highest difference for HR was between the 1st and 2nd measurement periods. Such that; the mean HR after drug injection was higher than the baseline interval ($P < 0.001$). In addition, the mean $SaO_2$ after drug use was more than the baseline interval (before drug use) ($P < 00.1$).

Furthermore, the independent *t*-test showed that the time of seizure ($P = 0.002$) and return of spontaneous respiration from seizure ending ($P = 0.001$) in the cisatracurium group were significantly higher than the succinylcholine group, but the mean duration of seizure ending to start of verbal response ($P = 0.33$), complete consciousness ($P = 0.75$), and length of stay in recovery ($P = 0.65$) was not significantly different between the two groups [Table 3].

Chi-square test also showed that the frequency of cough in the succinylcholine group was significantly higher than the cisatracurium group ($P = 0.004$), but the frequency of tachycardia in the succinylcholine group was higher than cisatracurium group ($P < 0.001$). Fisher's exact test showed that the frequency of laryngospasm, nausea, muscular pain, and bradycardia was not significantly different between the two groups ($P > 0.05$) [Table 4].

**Table 2: Mean systolic blood pressure, diastolic blood pressure, mean arterial pressure, potassium serum levels, and heart rate in two groups at different times**

| Variable | Time | Group, mean±SD | | $P^a$ | $P^b$ |
|---|---|---|---|---|---|
| | | CIS (*n*=45) | SUC (*n*=45) | | |
| SBP | 0 | 112.2±13.6 | 113.9±13.1 | *F*=39.92 | *F*=2.17 |
| | 1 | 131.04±17.3 | 124.8±20.9 | <0.001 | 0.145 |
| | 2 | 133.02±15.2 | 125.6±23.2 | | |
| | 3 | 122.8±14.3 | 117.6±14.6 | | |
| DBP | 0 | 67.2±10.2 | 68.9±10.4 | *F*=27.36 | *F*=0.924 |
| | 1 | 80.3±12.9 | 76.5±17.2 | <0.001 | 0.339 |
| | 2 | 80.5±12.9 | 76.5±17.2 | | |
| | 3 | 74.9±13.03 | 71.7±14.3 | | |
| MAP | 0 | 67.2±10.2 | 83.9±10.6 | *F*=35.39 | *F*= 1.45 |
| | 1 | 80.3±12.9 | 92.6±17.9 | <0.001 | 0.232 |
| | 2 | 80.5±12.9 | 92.7±20.1 | | |
| | 3 | 74.9±13.03 | 87.01±13.8 | | |
| K | 0 | 4.06±0.18 | 4.03±0.17 | *F*=28.39 | *F*=32.26 |
| | 1 | 4.10±0.17 | 4.56±0.3 | <0.001 | <0.001 |
| | 2 | 4.31±0.16 | 4.81±0.30 | | |
| | 3 | 4.09±0.13 | 4.11±0,19 | | |
| HR | 0 | 92.2±14.2 | 93.6±19.2 | *F*= 18.41 | *F*=0.260 |
| | 1 | 102.7±17.3 | 103.4±21.1 | <0.001 | 0.612 |
| | 2 | 100.2±14.1 | 100.2±18.01 | | |
| | 3 | 88.7±11.01 | 91.8±16.3 | | |
| SaO2 | 0 | 97.2±1.7 | 96.8±4.2 | *F*= 16.45 | *F*=2.70 |
| | 1 | 93.9±3.4 | 95.8±4.9 | <0.001 | 0.107 |
| | 2 | 94.6±4.2 | 95.9±5.1 | | |
| | 3 | 96.8±2.2 | 98.5±6.3 | | |

[a]Time effect, [b]Group effect. 0=Before administering anesthetic drug; 1=After the administration of the drug (before induction); 2=After the end of seizure; 3=20 min after induction. Values are mean SD or median (IQR). CIS=Cisatracurium; SUC=Succinylcholine: SBP=Systolic blood pressure; DBP=Diastolic blood pressure: MAP=Mean arterial pressure; K=Potassium serum levels; HR=Heart rate; $SaO_2$=Oxygen saturation; SD=Standard deviation; IQR=Interquartile range

**Table 3: The mean of different quantitative variables in the two groups**

| Variable | Unit | Mean±SD | | *P* |
|---|---|---|---|---|
| | | Group (CIS) | Group (SUC) | |
| Induced seizure time | Sec | 38.5±6.9 | 33.1±9.3 | 0.001 |
| End of seizure until the verbal response | Min | 19.8±4.9 | 21.0±5.9 | 0.02 |
| Apnea duration | Sec | 117.6±9.8 | 69.6±10.1 | 0.01 |
| Full consciousness after seizure | Min | 29.68±13.8 | 30.3±6.6 | 0.001 |
| Recovery duration | Min | 27.9±4.7 | 28.8±12.1 | 0.68 |

*Independent *t*-test. Values are mean SD or median (IQR). CIS = Cisatracurium; SUC = Succinylcholine; Sec = Second; Min = Minute ; SD = Standard deviation; IQR = Interquartile range

## DISCUSSION

With the arrival of the ECT in the psychiatric arena, many treatment-resistant cases were successfully treated.[19] However, the challenge that still continues to be scrutinized by the researchers is the use of an appropriate anesthetic with a short half-life, minimal complications and hemodynamic

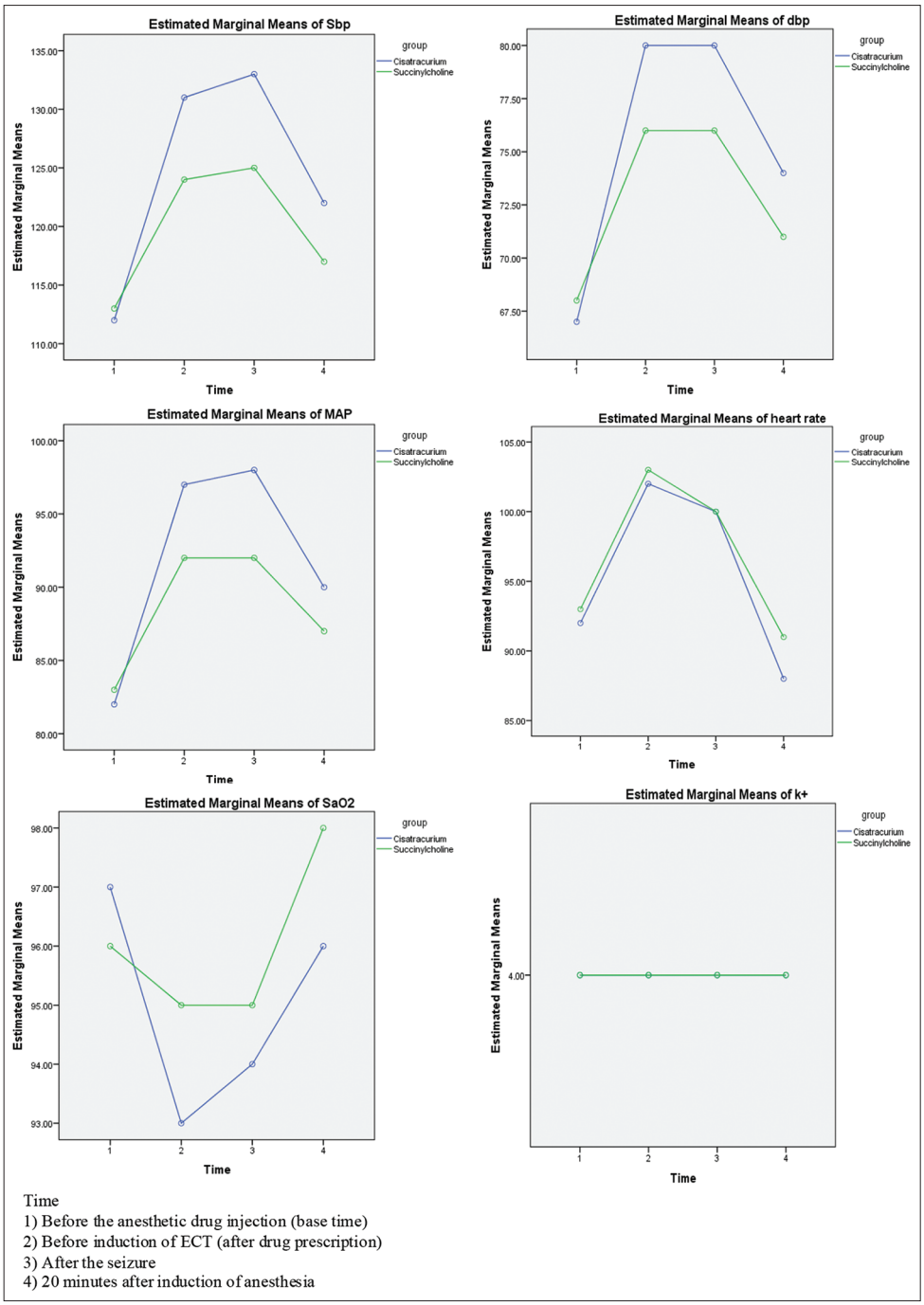


**Figure 1:** Trend changes in two drug groups at four measurement times

**Table 4: Frequency of drug complications used in the two groups**

| Complications | CIS, *n* (%) | SUC, *n* (%) | $\chi^2$ | df | *P* |
|---|---|---|---|---|---|
| Cough | 2 (4.5) | 12 (26.7) | 8.21 | 1 | 0.004 ($\chi^2$) |
| Laryngospasm | 0 | 1 (2.2) | - | - | 0.5* |
| Nausea | 0 | 1 (2.2) | - | - | 0.5* |
| Muscular pain | 0 | 2 (4.4) | - | - | 0.25* |
| Bradycardia | 1 (2.2) | 0 | - | - | 0.5* |
| Tachycardia | 26 (57.8) | 40 (90.9) | 12.74 | 1 | <0.001 ($\chi^2$) |

$\chi^2$=Chi-square test,*Fisher's exact test. CIS=Cisatracurium; SUC=Succinylcholine; df=Degrees of freedom

stability that can provide the suitable time and quality for seizure during the ECT.[20]

Our findings showed that systolic, diastolic, mean blood pressure, and heart rate and arterial oxygen saturation level were not significantly different between the two groups. However, the level of potassium increased significantly during the time and decreased again at the last time, and these changes were significantly higher in the succinylcholine group than that of the cisatracurium group.

Furthermore, the duration of induction seizure and return of the spontaneous respiration was significantly higher in cisatracurium group than that of the succinylcholine group. The duration of the seizure ending until the verbal response, duration of the seizure ending until the complete consciousness, and duration of stay in the recovery were less in the cisatracurium group, but there was no significant difference between the two groups. In terms of the complications, the frequency of cough in the succinylcholine group was also significantly higher than that of the cisatracurium group, and the frequency of tachycardia in the succinylcholine group was greater than that of the cisatracurium group. However, despite the fact that the number of laryngospasm, nausea, muscular pain, and tachycardia was higher in succinylcholine group, there was no significant difference between the two groups.

In a study by Schultz *et al*., who have been studying changes in heart rate before and after the treatment with ECT in depressed patients, it has been suggested that depression may be accompanied by a reduction in parasympathetic activity. ECT relatively increases the vagus (parasympathetic), and the cardiac activity increases as a result. A change in the effects of respiratory syncope in respiratory sinus arrhythmia is an indication of parasympathetic activation of the heart and heart rate changes which is one of these symptoms as the Hamilton Depression Rating Scale scores, which significantly reduced parasympathetic activity in depression.[21] In our article, the frequency of tachycardia in the succinylcholine group was greater than that of the cisatracurium group, which is consistent with the two above-mentioned studies.

Disorders in conduction pathways of the heart are observed at a potassium level >6.5 mg/L, but serum potassium levels may be increasing rapidly.[22]

Many factors may increase potassium before performing ECT, such as anxiety[23] beta agonists[24] antagonists,[25] increased CO2 concentration,[26] and anesthetic drugs.[27]

Effect of the anesthesia induction drugs on the serum potassium concentration was determined and the changes in serum potassium caused by propofol are very similar to the induction of anesthesia with barbiturates.[27]

In Fogarty's study, which was performed on 37 patients who were divided into two groups of propofol and propofol plus succinylcholine, potassium was significantly increased in the first group compared to the second group.[27]

In a comparison between succinylcholine and rocuronium through a cross-sectional study carried out by Turkkal *et al*., the duration of seizure and return of spontaneous respiration in the rocuronium group was significantly longer than that of succinylcholine and there was no significant difference between the two groups in terms of the mean, systolic, diastolic blood pressure, and arterial blood oxygen saturation[28] which was consistent with our study, which was consistent with our study, but the difference was that in our study cisatracurium was used instead of rocuronium. In Bali's study, 60 patients divided into 3 groups (A, B, C) receiving ECT and one control group without ECT, in which the first group (methohexital 80–100 mg, succinylcholine 30–40 mg) and the second group (methohexital 1.6 mg/kg, succinylcholine 1 mg/kg) received two different doses of methohexital and succinylcholine, and in the third and fifth groups (thiopental sodium 5 mg/kg, succinylcholine 1 mg/kg), blood samples were taken for measuring serum potassium levels just before anesthesia induction (baseline time), inmediately prior to electroshock therapy (after anesthesia induction), after seizure cessation, and 20 minutes after induction. The results of this study indicate that ECT increases potassium levels,[29] which is consistent with our study on the potassium increase. In a study consistent with our paper by Aggarwal *et al*. on 120 patients, increases in the serum potassium were significant in all three groups and the author of the article found these findings due to the contraction of muscle containing blood by potassium concentration increase, following succinylcholine. Patients with hyperkalemia may be also at high risk of hyperkalemia by using succinylcholine after an ECT.[30]

In conclusion, among nondepolarizing muscle relaxants used instead of succinylcholine in special cases, rocuronium can be also recommended, but it must be used to protect the airways in the use of reverse rocuronium[28] and since cisatracurium has a moderate effect on muscle relaxants in terms of duration of effect, and use of low doses of which does not require reverse[29] and compared with rocuronium, the use of low-dose cisatracurium is economical since it does not require reverse; therefore, cisatracurium is preferred among nondepolarizing muscle relaxants. On the other hand, not only it has not had any restriction compared to succinylcholine in ECT, it may even be a more appropriate substitute.[31] On the other hand, if the duration of the seizure is < 20 s, we will not have a more effective ECT; therefore, the use of atracurium as a muscle relaxant seems to have better therapeutic effects with less complications due to increased seizure duration, compared with succinylcholine in ECT.[32]

## CONCLUSION

Using succinylcholine relaxant in people with high potassium levels in serum is not recommended to perform ECT. Furthermore, in patients with hyperkalemia, using succinylcholine should be prevented from receiving the emergency ECT.

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## Conflicts of interest

There are no conflicts of interest.

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