Original Article
https://doi.org/10.9758/cpn.2019.17.4.523
Clinical Psychopharmacology and Neuroscience 2019;17(4):523-530

pISSN 1738-1088 / eISSN 2093-4327

Can Propofol Lead to an Increase in Seizure Threshold Over the Course of Electroconvulsive Therapy?

Hande Gurbuz Aytuluk, Tahsin Simsek, Mehmet Yilmaz, Ayse Zeynep Turan, Kemal Tolga Saracoglu

Department of Anesthesiology and Reanimation, University of Health Sciences Derince Training and Research Hospital, Kocaeli, Turkey

Objective: To evaluate the effects of 2 different dose regimens of propofol (low dose: < 1 mg/kg, high dose: ≥ 1 mg/kg) on the duration of the seizures, the required energy for the seizures, and the seizure threshold over the course of electroconvulsive therapy (ECT).
Methods: The electronic medical records of 165 patients receiving 971 sessions of ECT were analyzed retrospectively. Patients were evaluated in two groups according to the according to propofol doses that they had received for ECT. Group LP (n = 91): patients who received low dose propofol (< 1 mg/kg). Group HP (n = 74): patients who received high dose propofol (≥ 1 mg/kg).
Results: The required energy for seizures in Group HP were significantly higher than the Group LP in the 3rd, 4th, 5th, 6th, 7th, 8th, and 9th sessions ($p < 0.05$). The duration of seizures in the Group HP were significantly lower than the Group LP in the 1st, 2nd, 4th, 5th, 7th, and 8th sessions ($p < 0.05$). Higher electrical stimulus was needed to acquire a minimum length of seizure (> 25 sn) during the course of ECT in higher propofol doses. Although there was an increase in the seizure threshold over the course of ECT in both groups, this increase was found to be much more pronounced in the high-dose propofol group according to the low-dose propofol group. Longer duration of seizures was observed in the low-dose propofol group.
Conclusion: Higher doses of propofol in induction of anesthesia can lead to a more progressive rise in seizure threshold than lower doses of propofol.

KEY WORDS: Anesthesia; Electroconvulsive therapy; Propofol; Seizures.

INTRODUCTION

Electroconvulsive therapy (ECT) is a procedure which generalized seizures are induced by transcutaneous electrical stimuli to the brain. The ECT has been used in psychiatry since the early 1930s as an effective treatment of psychiatric disorders [1]. In the 1950s, ECT was receded with the development of antipsychotics and antidepressants. However, in the 1980s, when psychotropic drugs were found to be ineffective in some patients, ECT begun to gain importance again [2]. ECT is a preferred treatment modality in patients with major depression, affective disorders, schizophrenia, and other psychotic disorders, where pharmacological treatment is not adequate, and a rapid clinical response is desired. Several theories were hypothesized about mechanisms of action of ECT-including changes in cerebral blood flow and blood brain barrier, epigenetic modifications, changes in the levels of various hormones, neurotransmitters, and neurotrophic factors, alterations in neuroplasticity, and immune mechanisms [2,3]. In order for ECT to be effective, the required seizure time is > 25 seconds [4,5].

Anesthesia is an important factor for the safety and efficacy of ECT [6,7]. The anesthetic agents should provide rapid induction and recovery, must have fewer side effects, and should not reduce the duration and quality of ECT [8]. Thiopental shortens duration of the seizures, extends recovery, and causes hypotension. Etomidate has

Received: February 20, 2019 / **Revised:** April 22, 2019
Accepted: July 29, 2019
Address for correspondence: Hande Gurbuz Aytuluk
Department of Anesthesiology and Reanimation, University of Health Sciences Derince Training and Research Hospital, Ibni Sina Bulvarı, Derince, Kocaeli 41900, Turkey
E-mail: handegrbz@gmail.com
ORCID: https://orcid.org/0000-0002-3562-9517
*This study was presented as a poster presentation at Euroanaesthesia 2019, Vienna, Austria.

minimal hemodynamic and cardiac adverse effects; on the other hand, it prolongs seizure duration and recovery time. Propofol is the most frequently used hypnotic agent in ECT. It is also known that propofol reduces duration of seizures, however its effect on seizure threshold is controversial. Wang *et al.* [9] emphasized that propofol can induce epileptiform electroencephalogram (EEG) changes after administration of low (< 1 mg/kg) doses, and this epileptiform EEG pattern was attenuated after administration of higher propofol doses.

In this study, 2 different dose regimens of propofol (low dose: < 1 mg/kg, high dose: ≥ 1 mg/kg) were compared by assessing the effects on duration of the seizures, required energy for the seizures, and seizure threshold over the course of ECT.

METHODS

After approval of the local ethical committee (Decree #14/13, January 4, 2019), the electronic medical records of the patients who received ECT sessions with a standardized protocol of anesthetic drugs (propofol and succinylcholine) between January 2015 and September 2018 were analyzed retrospectively. Patients with missing data, who received drugs that can affect seizures, and who received a different protocol of anesthetic drugs were excluded from the study.

It was observed that there was a significant difference in the regimen of propofol doses due to the different application methods of anesthesia of multiple anesthesiologists. Because of this reason, it was decided to evaluate the patients in 2 groups according to propofol doses. Group LP (n = 91): patients who received low dose propofol (< 1 mg/kg). Group HP (n = 74): patients who received high dose propofol (≥ 1 mg/kg). Propofol doses were calculated by dividing the total amount of propofol administered by the weight of the patient.

Data collection included demographic characteristics, psychiatric diagnosis, overall number of ECT sessions performed, doses and types of anesthetic drugs used, seizure thresholds, seizure durations, complications during the ECT sessions, clinical severity scores on admission and clinical improvement scores following ECT therapy. Before ECT, all patients had preanesthetic evaluation and informed consent was obtained from all patients. Pre-procedural medications of patients were reordered by a psychiatrist. Patients were scheduled for consecutive ECT sessions three times a week (Monday, Wednesday, Friday; except weekends).

In the periprocedural period, patients received no drugs which can affect seizures such as anticonvulsant, benzodiazepine, theophylline or methylphenidate. No premedication was administered to patients. Routine monitorization of non-invasive blood pressure, heart rate, and peripheral oxygen saturation were established. Seizures were monitored with a two-channel EEG. Following preoxygenation with 100% oxygen via face mask, propofol administered intravenously until the patient was unconsciousness, and loss of eyelash reflex. Succinylcholine was then administered for muscle relaxation, and ventilation was assisted. The drug doses for induction of anesthesia in the subsequent sessions were determined based on the previous administered drug doses. Electrical stimulus was delivered via bifrontotemporal electrodes the stimulus with the dosage titration procedure. Seizure threshold was defined as the stimulus dosage that elicited a seizure activity on EEG of at least 25 seconds duration. Duration of the seizure activity on EEG was evaluated by the psychiatrist. No additional anesthetic or muscle relaxant medications were given after the initial bolus. After the procedure, patients were monitored at the recovery room until modified Aldrete scores were 9 or higher.

The scores of the clinical severity of illness on admission and clinical improvement scores following ECT were assessed with Clinical Global Impressions scale (CGI) according to the clinician's judgement, and these data were acquired from the clinical charts. The severity of the illness was rated on the 7-point CGI-Severity (CGI-S) scale from 1 (normal, not at all ill) to 7 (among the most extremely ill patients) [10]. The clinical improvement following ECT therapy was rated on the 7-point CGI-mprovement (CGI-I) scale from 1 (very much improved since the initiation of treatment) to 7 (very much worse since the initiation of treatment) [10]. For evaluation of the response to ECT therapy, we dichotomized patients as responders (CGI-I score of 1, 2, and 3), and non-responders (CGI-I score of 4, 6, and 7).

Statistics

Statistical analyses were performed using computerized statistical software: IBM SPSS, version 24.0 (IBM Corp., Armonk, NY, USA). For intergroup comparisons of

categorical data, Pearson's chi-square test was applied. For continuous variables, the Kolmogorov−Smirnov test was used for the normality of data distribution and followed by the Mann−Whitney U test when a significant difference was found ($p < 0.05$). The correlation of the variables (the required energy for seizures and the duration of seizures) were analyzed using Pearson correlation analysis. Friedman variance analysis was used to evaluate the repeated measures of the required energy for seizures in the consecutive ECT sessions, and *post-hoc* Wilcoxon signed-ranks test was used for paired comparison of these repeated measures. All data were presented as median (min−max) or numbers as appropriate. A $p < 0.05$ was considered to be statistically significant.

RESULTS

A total of 971 ECT sessions were performed on 165 patients, including 74 males (55%) and 91 female (45%) patients. Three of the female patients underwent ECT because of pregnancy. It was observed that a mean of 1.56 mg/kg (median 1.83 mg/kg [min 1−max 2.56]) propofol was administered to the patients in high dose propofol group, and a mean of 0.67 mg/kg (median 0.6 mg/kg [min 0.4−max 0.89]) propofol was administered to the patients in low dose propofol group. There were no statistically significant differences between the groups in the demographic and clinical characteristics of the patients (Table 1).

There was a statistically significant difference in the required energy for seizures between the two groups. Required energy for seizures in Group HP were significantly higher than the Group LP in the 3rd, 4th, 5th, 6th, 7th, 8th, and 9th sessions ($p < 0.05$) (Table 2). There was a statistically significant difference in the duration of seizures between the two groups. The duration of seizures in the Group HP were significantly lower than the Group LP in the 1st, 2nd, 4th, 5th, 7th, and 8th sessions ($p < 0.05$) (Table 2). The correlation between the duration of seizures and the required energy for seizures showed a negative and statistically significant difference ($p < 0.05$). It was found that shorter duration of seizures correlated higher energy, in the 2nd, 3rd, 4th, 6th, 7th, 8th, and 9th sessions in Group HP, and the 2nd, 3rd, 4th, and 5th sessions in Group LP (Table 3). This means that higher electricity stimulus was needed to acquire a minimum length of seizure (> 25 sn) during the course of ECT in higher propofol doses.

Table 1. Demographic and clinical characteristics of the patients

Variable	Group HP (n = 74)	Group LP (n = 91)	z	χ^2	p value
General characteristics					
Age (yr)	36.7 ± 7.9	36.9 ± 7.4	−0.174		0.862
Weight (kg)	69.4 ± 9.7	72.4 ± 9.7	−0.305		0.721
Succinylcholine (mg/kg)	0.6 ± 0.1	0.5 ± 0.1	−2.737		0.091
Propofol (mg/kg)	1.5 ± 0.4	0.7 ± 0.1	−3.615		<0.001*
Session	6 (1−13)	6 (1−12)	−1.672		0.095
Gender					
Female	46 (62.2)	45 (49.5)		2.666	0.103
Male	28 (37.8)	46 (50.5)			
Severity of the illness					
CGI-S (5/6/7)	22/40/12	26/44/21		1.240	0.538
Clinical response to treatment					
Responders	65 (87.8)	84 (92.3)		0.931	0.335
Diagnoses					
Major depressive disorder	24 (32.4)	17 (18.7)		6.952	0.138
Bipolar disorder	14 (18.9)	14 (15.4)			
Psychotic disorders	17 (23.0)	36 (39.6)			
Schizoaffective disorder	5 (6.8)	7 (7.7)			
Schizophrenia	14 (18.9)	17 (18.7)			

Values are presented as mean±standard deviation, median (min−max), or number (%).
CGI-S, Clinical Global Impressions-Severity scale.
Mann−Whitney U analysis, Pearson's chi-square; *$p < 0.05$.

Table 2. Intergroup distribution of the required energy for seizures and the duration of seizures over the course of the electroconvulsive therapy sessions

Session	Required energy for seizures						Duration of seizures					
	Group HP		Group LP		z	*p* value	Group HP		Group LP		z	*p* value
	Number	Median (min−max)	Number	Median (min−max)			Number	Median (min−max)	Number	Median (min−max)		
1	74	26.65 (10.7−71)	91	27 (20−53)	−0.069	0.945	74	24 (0−90)	91	34 (10−90)	−3.240	0.001
2	71	32.5 (11.4−88)	90	31.45 (13.5−57)	−1.778	0.075	71	25 (0−72)	90	30 (10−77)	−2.746	0.006
3	67	35 (17.1−93)	86	31.7 (13.5−59)	−2.516	0.012*	67	28 (10−78)	86	30.5 (10−70)	−1.295	0.195
4	63	40.6 (21−95.1)	79	31.7 (15−60.8)	−3.879	< 0.001*	63	25 (0−56)	79	30 (0−56)	−2.225	0.026
5	57	45.1 (21−93.7)	66	34.7 (22.3−60.8)	−3.907	< 0.001*	57	26 (10−95)	66	32.5 (10−60)	−2.639	0.008
6	46	50 (21−100.2)	50	35.5 (22.5−69.3)	−4.241	< 0.001*	46	25 (10−60)	50	30 (0−55)	−1.627	0.104
7	34	51.95 (25.3−112.6)	28	35.5 (20.7−71.3)	−3.787	< 0.001*	34	26.5 (10−50)	28	33.5 (16−52)	−2.239	0.025
8	25	57.8 (29.7−126.7)	15	35.5 (20.7−69.9)	−3.396	0.001*	25	25 (0−55)	15	32 (20−50)	−2.044	0.041
9	11	61 (29.7−136.9)	6	34.7 (20.7−36.9)	−2.312	0.021*	11	25 (0−50)	6	36 (30−43)	−1.461	0.144
10	4	49.05 (30.4−152)	1	31.7 (31.7−31.7)	< 0.001	1.000	4	37.5 (12−40)	1	30 (30−30)	−0.725	0.468
11	2	49.55 (31−68.1)	1	31 (31−31)	−0.707	0.480	2	35 (35−35)	1	45 (45−45)	−1.414	0.157
12	2	53.85 (31−76.7)	1	34.1 (34.1−34.1)	< 0.001	1.000	2	30 (30−30)	1	40 (40−40)	−1.414	0.157

Mann−Whitney *U* analysis; *$p < 0.05$.

The measurement of the required energy for seizures in the first 6 sessions in Group HP showed a statistically significant difference ($p < 0.005$). All binary pairings were found to be statistically significant with *post-hoc* Wilcoxon signed ranks analysis ($p < 0.005$). The measurement of the required energy for seizures in the first 6 sessions in Group LP also showed a statistically significant difference ($p < 0.005$). All binary pairings−except the 1st session and 9th session pair−were found to be statistically significant with *post-hoc* Wilcoxon signed ranks analysis ($p < 0.005$). There was no statistically significant difference between the low-dose and high-dose propofol groups in duration of seizures with *post-hoc* Wilcoxon signed ranks analysis and Friedman variance analysis ($p > 0.005$) (Table 4).

The correlation of the required energy for seizures and the duration of seizures over the course of the ECT sessions is presented in Figure 1. Although there was an increase in the seizure threshold over the course of ECT in both groups, this increase was found to be much more pronounced in the high-dose propofol group according to the low-dose propofol group. Longer duration of seizures was observed in the low-dose propofol group (Fig. 1).

The clinical response to the treatment according to the propofol doses was assessed with CGI-I scale. The number of responders (the number of patients with CGI-I scores 1, 2, and 3) was 65 in Group-HP, and 84 in Group-LP. This difference was not statistically significant ($\chi^2 = 0.93$, p = 0.33; $p < 0.05$) (Table 1). A brief asystole was observed for once and sinus rhythm was obtained by intervention with atropine. Desaturation (n = 9), arrhythmia (n = 7), bradycardia (n = 5), hypertension (n = 1), self-limited rash (n = 3), and prolonged seizures (n = 3) were the observed complications of ECT. Cognitive dysfunction in 1 patient, amnesia in 2 patients, and prolonged confusion in 2 patients were observed as for the adverse effects of the therapy.

DISCUSSION

The main finding of this study was, although an increase in the seizure threshold was observed in all patients over the course of ECT, this increment was much more pronounced in the high-dose propofol group in comparison with the low-dose propofol group.

In many clinical trials, possible determinants for initial

Table 3. Correlation of the required energy for seizures and the duration of seizures

Session	Group HP			Group LP		
	Number	r	*p* value	Number	r	*p* value
1	74	−0.227	0.052	91	−0.165	0.118
2	71	−0.319	0.007*	90	−0.264	0.012*
3	67	−0.370	0.002*	86	−0.314	0.003*
4	63	−0.378	0.002*	79	−0.370	0.001*
5	57	−0.218	0.104	66	−0.447	< 0.001*
6	46	−0.552	< 0.001*	50	−0.173	0.230
7	34	−0.445	0.008*	28	−0.147	0.455
8	25	−0.557	0.004*	15	−0.215	0.441
9	11	−0.631	0.037*	6	−0.022	0.966
10	4	−0.912	0.088	1		
11	2			1		
12	2			1		

Pearson correlation; *$p < 0.05$.

Table 4. The variance of the required energy for seizures in the first 6 sessions

Session	Group HP			Group LP		
	χ^2	Z	*p* value	χ^2	Z	*p* value
Required energy for seizures						
Friedman test	167.983		0.000*	114.097		0.000*
Wilcoxon signed ranks						
Session 2−1		−5.963	0.000*		−4.738	0.000*
Session 3−1		−6.603	0.000*		−5.535	0.000*
Session 4−1		−6.580	0.000*		−6.066	0.000*
Session 5−1		−6.368	0.000*		−6.102	0.000*
Session 6−1		−5.742	0.000*		−5.069	0.000*
Session 7−1		−5.012	0.000*		−4.106	0.000*
Session 8−1		−4.286	0.000*		−3.111	0.002*
Session 9−1		−2.803	0.005*		−1.753	0.080
Session 3−2		−5.715	0.000*		−4.667	0.000*
Session 4−2		−6.190	0.000*		−5.032	0.000*
Session 5−2		−6.175	0.000*		−5.252	0.000*
Session 6−2		−5.590	0.000*		−4.462	0.000*
Session 4−3		−5.774	0.000*		−4.178	0.000*
Session 5−3		−6.058	0.000*		−4.678	0.000*
Session 6−3		−5.615	0.000*		−4.146	0.000*
Session 5−4		−5.862	0.000*		−4.119	0.000*
Session 6−4		−5.373	0.000*		−3.449	0.001*
Session 6−5		−3.960	0.000*		−2.555	0.011*
Duration of seizures						
Friedman test	1.416		0.923	6.179		0.289

Friedman variance analysis and *post-hoc* Wilcoxon signed ranks analysis; *$p < 0.05$.

seizure thresholds [11], changes in the seizure thresholds, and the duration of seizures in ECT have been researched widely [12]. It is well-established that changes in the seizure threshold occur during the course of ECT [12,13]. Sex, age, electrode placement, and the cumulative number of treatments are associated with an increase in seizure threshold which is attributed to anticonvulsant effect of ECT [14]. Although, anesthetic drugs are known to have effect on seizure thresholds, the role of propofol on the seizure threshold during the course of ECT is uncertain.

Propofol is a frequently used anesthetic agent for both sedation and hypnosis. Propofol can inhibit seizure activ-

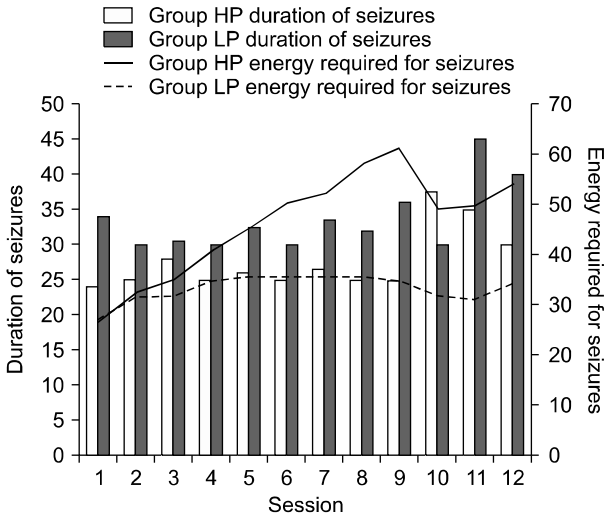

Fig. 1. Correlation of the required energy for seizures and the duration of seizures over the course of the electroconvulsive therapy sessions.

ity, but it can also have a proconvulsant impact. It was specified in a study that, propofol can act as a pro or anticonvulsant agent in a dose-depended fashion [9]. Regarding to that study, a low dose of propofol (0.5 to 1 mg/kg) was associated with epileptiform patterns on EEG, on the contrary a large dose of propofol (2 to 2.5 mg/kg) attenuated the amplitudes of all EEG waves [9]. This result was also concluded in animal studies [15,16].

Several studies have compared the effects of propofol and different hypnotic agents in ECT. Propofol was shown to shorten the duration of seizures, however, it was thought that it had no effect on seizure threshold during the ECT treatment [17,18]. On the contrary, it was found in a study comparing the effects of etomidate and propofol that, the patients who had received propofol necessitated significantly higher amounts of electrical stimulus over the course of ECT [19]. Similar to all of these findings, in this study patients who were administered larger doses of propofol (1 to 2.56 mg/kg) required significantly increasing doses of electrical stimuli for seizures on the course of ECT therapy. Higher doses of propofol were associated with significantly shorter seizures.

Mechanism of action of propofol is to increase the inhibitory tonus in the cranial nervous system, by increasing gamma-aminobutyric acid (GABA) which is the principal inhibitory neurotransmitter. It has also been shown that electroconvulsive shock results in increased GABA concentrations in several neural regions [20,21]. Anticonvulsant effect of ECT was attributed to enhancement of GABAergic or endogenous opiate neurotransmission, which in turn could lead to a progressive rise in seizure threshold [13]. The significant increase in the seizure threshold over the course of ECT in high-dose propofol group may be the result of the additive effect of both higher doses of propofol and the anticonvulsant effect of ECT on GABA concentrations. At this point, randomized controlled trials are needed to explain the relation between propofol doses and seizure thresholds.

Some of the previous authors have suggested that rise in the seizure threshold was directly related with the clinical efficacy [22]. In contrast to these findings, following studies have failed to support this hypothesis [20,23]. Accordingly, clinical outcomes of this study were not affected by the magnitude of the rise in the seizure threshold.

ECT is related to some complications such as bone and soft tissue injury, sustained seizure activity, significant changes in autonomic function, facial flush, respiratory distress and oxygen desaturation [24,25]. Bradycardia, hypotension, and cardiac pause or a brief asystole can be caused by parasympathetic response [26]. Tachycardia and hypertension are related to sympathetic activation [27]. Postprocedural headache and myalgia (due to muscle fasciculations with succinylcholine) can be reduced with rocuronium and sugammadex [28]. The prevalence of the complications that we observed in this study was consistent with the literature.

1. The strengths of this study are, despite the lack of randomization, the two groups were well matched in terms of demographic and clinical characteristics. The standard type of anesthetic agents that were used for ECT allowed us to compare the different induction regimens of individual anesthesiologists. In many studies, anesthetic agents were tended to be switched in a single course of ECT, however, in this study the anesthetic drug doses in the subsequent sessions were determined based on the previous administered drug doses. Additionally, the large number of patients in comparison with other studies is another strength of this study.

First limitation of this study is that it is a retrospective analysis and it cannot be generalized yet. In the daily clinical practice of anesthesia, like many anesthetics, propofol is administered by titration until a desired clinical effect is achieved [29]. Although, a propofol dose between

1 to 2 mg/kg is adequate for induction of anesthesia in most cases, propofol requirement can be influenced by several factors which can affect pharmacodynamics and pharmacokinetics, such as degree of anxiety, speed of injection, cardiac output, lean body mass, drug interactions, etc. [30,31]. Because of the retrospective nature of the study, we could not be able to standardize these variables, nor study the effects of a fixed dose of propofol. Thus, we observed different propofol dosing regimens individualized for patients.

In conclusion, although an increase in the seizure threshold can be observed in all patients over the course of ECT, higher propofol doses (≥ 1 mg/kg) in induction of anesthesia can lead to a more progressive rise in seizure threshold over the course of ECT. Larger propofol doses according to lower doses are associated with shorter duration of seizures. Thus, when propofol doses remained below 1 mg/kg, it may be beneficial for inducing longer duration of seizures without a significant contribution to the rise of seizure threshold.

■ **Acknowledgments**

Special thanks to Dr. H. İmer Aras from Derince Training and Research Hospital, Department of Psychiatry.

■ **Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

■ **Author Contributions**

Conceptualization: Hande Gurbuz Aytuluk, Tahsin Simsek, Mehmet Yilmaz, Ayse Zeynep Turan, Kemal Tolga Saracoglu. Data acquisition: Hande Gurbuz Aytuluk, Tahsin Simsek, Mehmet Yilmaz. Formal analysis: Hande Gurbuz Aytuluk, Tahsin Simsek, Mehmet Yilmaz, Ayse Zeynep Turan, Kemal Tolga Saracoglu. Writing — original draft: Hande Gurbuz Aytuluk. Review & editing: Hande Gurbuz Aytuluk, Tahsin Simsek, Mehmet Yilmaz, Ayse Zeynep Turan, Kemal Tolga Saracoglu.

■ **ORCID**

Hande Gurbuz Aytuluk https://orcid.org/0000-0002-3562-9517
Tahsin Simsek https://orcid.org/0000-0002-3068-4998
Mehmet Yilmaz https://orcid.org/0000-0002-5353-9996
Ayse Zeynep Turan https://orcid.org/0000-0001-8548-8364
Kemal Tolga Saracoglu https://orcid.org/0000-0001-9470-7418

REFERENCES

1. von Meduna LJ. *Anticonvulsant therapy of schizophrenia. Halle:Marhold Verlagsbuchhandlung;1937.*
2. Singh A, Kar SK. *How electroconvulsive therapy works?: understanding the neurobiological mechanisms. Clin Psychopharmacol Neurosci 2017;15:210-221.*
3. Şenyurt M, Aybek H, Herken H, Kaptanoglu B, Korkmaz A. *Evaluation of oxidative status in patients treated with electroconvulsive Therapy. Clin Psychopharmacol Neurosci 2017; 15:40-46.*
4. Ding Z, White PF. *Anesthesia for electroconvulsive therapy. Anesth Analg 2002;94:1351-1364.*
5. American Psychiatric Association. *Task Force on Electroconvulsive Therapy. The practice of ECT: recommendations for treatment, training and privileging. Convuls Ther 1990;6:85-120.*
6. Canbek O, Ipekcıoglu D, Menges OO, Atagun MI, Karamustafalıoglu N, Cetinkaya OZ, *et al. Comparison of propofol, etomidate, and thiopental in anesthesia for electroconvulsive therapy: a randomized, double-blind clinical trial. J ECT 2015;31:91-97.*
7. Taş N, Demir EY. *Rocuronium-sugammadex in anesthesia for electroconvulsive therapy. Curr Approach Psychiatry 2015;8: 76-84.*
8. Mayo C, Kaye AD, Conrad E, Baluch A, Frost E. *Update on anesthesia considerations for electroconvulsive therapy. Middle East J Anaesthesiol 2010;20:493-498.*
9. Wang B, Bai Q, Jiao X, Wang E, White PF. *Effect of sedative and hypnotic doses of propofol on the EEG activity of patients with or without a history of seizure disorders. J Neurosurg Anesthesiol 1997;9:335-340.*
10. Busner J, Targum SD. *The clinical global impressions scale: applying a research tool in clinical practice. Psychiatry (Edgmont) 2007;4:28-37.*
11. van Waarde JA, Verwey B, van der Mast RC. *Meta-analysis of initial seizure thresholds in electroconvulsive therapy. Eur Arch Psychiatry Clin Neurosci 2009;259:467-474.*
12. Fink M, Petrides G, Kellner C, Mueller M, Knapp R, Husain MM, *et al*; CORE Group. *Change in seizure threshold during electroconvulsive therapy. J ECT 2008;24:114-116.*
13. Coffey CE, Lucke J, Weiner RD, Krystal AD, Aque M. *Seizure threshold in electroconvulsive therapy (ECT) II. The anticonvulsant effect of ECT. Biol Psychiatry 1995;37:777-788.*
14. Sackeim H, Decina P, Prohovnik I, Malitz S. *Seizure threshold in electroconvulsive therapy. Effects of sex, age, electrode placement, and number of treatments. Arch Gen Psychiatry 1987;44:355-360.*
15. Lee VC, Moscicki JC, DiFazio CA. *Propofol sedation produces dose-dependent suppression of lidocaine-induced seizures in rats. Anesth Analg 1998;86:652-657.*
16. Hartung J, Ying H, Weinberger J, Cottrell JE. *Propofol prevents or elevates the threshold for lidocaine-induced seizures in rats. J Neurosurg Anesthesiol 1994;6:254-259.*

17. Gábor G, Judit T, Zsolt I. *Comparison of propofol and etomidate regarding impact on seizure threshold during electroconvulsive therapy in patients with schizophrenia. Neuropsychopharmacol Hung 2007;9:125-130.*
18. Gazdag G, Kocsis N, Tolna J, Iványi Z. *Etomidate versus propofol for electroconvulsive therapy in patients with schizophrenia. J ECT 2004;20:225-229.*
19. Patel AS, Gorst-Unsworth C, Venn RM, Kelley K, Jacob Y. *Anesthesia and electroconvulsive therapy: a retrospective study comparing etomidate and propofol. J ECT 2006;22:179-183.*
20. Krystal AD, Coffey CE, Weiner RD, Holsinger T. *Changes in seizure threshold over the course of electroconvulsive therapy affect therapeutic response and are detected by ictal EEG ratings. J Neuropsychiatry Clin Neurosci 1998;10:178-186.*
21. Sackeim HA, Decina P, Prohovnik I, Malitz S, Resor SR. *Anticonvulsant and antidepressant properties of electroconvulsive therapy: a proposed mechanism of action. Biol Psychiatry 1983;18:1301-1310.*
22. Sackeim HA. *The anticonvulsant hypothesis of the mechanisms of action of ECT: current status. J ECT 1999;15:5-26.*
23. Duthie AC, Perrin JS, Bennett DM, Currie J, Reid IC. *Anticonvulsant mechanisms of electroconvulsive therapy and relation to therapeutic efficacy. J ECT 2015;31:173-178.*
24. Mirzakhani H, Welch CA, Eikermann M, Nozari A. *Neuromuscular blocking agents for electroconvulsive therapy: a systematic review. Acta Anaesthesiol Scand 2012;56:3-16.*
25. Narayanan A, Lal C, Al-Sinawi H. *General anaesthesia protocols for patients undergoing electroconvulsive therapy: retrospective analysis of 504 sessions over a five-year period at a tertiary care hospital in Oman. Sultan Qaboos Univ Med J 2017;17:e43-e49.*
26. Bryson EO, Aloysi AS, Farber KG, Kellner CH. *Individualized anesthetic management for patients undergoing electroconvulsive therapy: a review of current practice. Anesth Analg 2017;124:1943-1956.*
27. Saito S. *Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. J Anesth 2005;19:142-149.*
28. Saricicek V, Sahin L, Bulbul F, Ucar S, Sahin M. *Does rocuronium-sugammadex reduce myalgia and headache after electroconvulsive therapy in patients with major depression? J ECT 2014;30:30-34.*
29. van den Berg JP, Vereecke HE, Proost JH, Eleveld DJ, Wietasch JK, Absalom AR, *et al. Pharmacokinetic and pharmacodynamic interactions in anaesthesia. A review of current knowledge and how it can be used to optimize anaesthetic drug administration. Br J Anaesth 2017;118:44-57.*
30. Schnider TW, Minto CF, Gambus PL, Andresen C, Goodale DB, Shafer SL, *et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. Anesthesiology 1998;88:1170-1182.*
31. Wilson ES, McKinlay S, Crawford JM, Robb HM. *The influence of esmolol on the dose of propofol required for induction of anaesthesia. Anaesthesia 2004;59:122-126.*