

Lidokainin Elektrokonzulzif Tedavi Etkinliği Üzerine Etkisi

The Effect of Lidocaine on The Efficiency of Electroconvulsive Therapy

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ÖZ

GİRİŞ ve AMAÇ: Elektrokonzulzif tedavi psikiyatrik bozuklukların tedavisinde kullanılan en önemli tedavilerden biridir. Tedavinin etkinliği nöbet süresi ile ilişkilidir. Propofol EKT uygulamalarında sıklıkla tercih edilen anestetik ajandır. Propofol indüksiyonu yapılan hastalarda lidokain de adjuvan ajan olarak kullanılmaktadır. EKT için kullanılan anestetik ajanların ve lidokain gibi adjuvan ilaçların da nöbet süresini ve kalitesini etkilememelidir. Bu çalışmada EKT sırasında kullanılan lidokainin nöbet süresi üzerine etkinliğini araştırmayı amaçladık.

YÖNTEM ve GEREÇLER: Bu çalışma randomize kontrollü çift kör olarak dizaynedildi. Hastalar kapalı zarf yöntemiyle randomize edilerek iki gruba ayrıldı; grup P(propofol n=39) ve grup PL (Propofol-lidocaine n=41). P grubundaki hastalara 5 ml SF ve PL grubundaki hastalara 2 ml %2 lidokain+3 ml SF verilmesini takiben propofol indüksiyonu yapıldı. Tüm hastalara bispektral indeks (BIS) değeri 60 olduğunda kas gevşetici olarak 1 ml/kg dozunda süksinilkolin uygulandı.

BULGULAR: Demografik veriler açısından iki grup arasında anlamlı istatistiksel bir fark bulunamadı ($p>0,05$). Toplam propofol dozu ve BIS değerleri açısından anlamlı fark bulunamadı ($p>0,05$). PL grubunda kardiyak aritmi insidansı P grubuna göre anlamlı olarak düşük bulundu ($p>0,036$). Nöbet süresi ise PL grubunda anlamlı derecede yüksek bulundu ($p>0,05$).

TARTIŞMA ve SONUÇ: EKT sırasında adjuvan ajan olarak uygulanan lidokainin nöbet süresini arttırdığı ve tedavi üzerine pozitif etkinliği olduğu kanaatindeyiz. Ek olarak lidokainin EKT sırasında görülen kardiyovasküler istenmeyen etkileri azalttığını düşünüyoruz.

Anahtar Kelimeler: elektrokonzulzif tedavi, lidokain, nöbet süresi

ABSTRACT

INTRODUCTION: Electroconvulsive therapy is the most important therapeutic modality used in psychiatric disorders. The efficiency of the therapy is related to the duration of a seizure. Propofol is frequently chosen anesthetic agent for ECT anesthesia. Intravenous lidocaine is frequently used as an adjuvant agent during propofol induction. Anesthetic agents and also adjuvant agents as lidocaine used for sedation during ECT should not affect duration and quality of the seizure. In this study, we aimed to investigate the effect of lidocaine during electroconvulsive therapy on the length of seizures.

METHODS: Current study designed prospectively randomized controlled double blind trial. Patients were randomly assigned into two groups: Group P (propofol, n=39) or Group PL (propofol-lidocaine, n=41) by sealed envelop method. Patients in Group P were given 5 ml (5 ml SF), patients in Group PL were given 5 ml (2 ml of 2% lidocaine + 3 ml SF) by the researcher, and then propofol induction was performed. All patients in Group P and Group PL were given 1mk/kg of succinylcholine to prevent muscle relaxation when the BIS value was 60.

RESULTS: There was no statistically significant difference between two groups in terms of Demographic information, propofol amounts and bispectral index values ($p>0,05$). The incidence of cardiac arrhythmia was statistically significantly lower in Group PL than Group P ($p=0,036$). Duration of seizure was significantly higher in Group PL compared to Group P ($p<0,05$).

DISCUSSION and CONCLUSION: We concluded that adjuvant lidocaine administration for the ECT procedure prolongs the duration of the seizure and thereby positively impacts treatment. In addition, adding lidocaine decreases procedural adverse cardiovascular effects.

Keywords: electroconvulsive therapy, lidocaine, duration of seizure

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INTRODUCTION

Electroconvulsive therapy (ECT) is the most important therapeutic modality used in psychiatric disorders.^{1,2} The efficiency of the therapy is related to the duration of a seizure.³ A 25-second seizure duration is accepted as efficient (appropriate), and durations of less than 25 seconds have been reported to negatively affect the clinical results⁽⁴⁾.

The hypnotic agents used during ECT should have a short half-life and should not affect the duration and quality of a seizure⁽⁵⁾. Thereby propofol is frequently chosen anesthetic agent for ECT anesthesia. The most important advantages of propofol are short-term loss of consciousness and a relatively more stable cardiovascular response with the use of this drug ⁽⁶⁾.

Intravenous lidocaine is frequently used as an adjuvant agent during propofol induction.^{7,8} Anesthetic agents and also adjuvant agents as lidocaine used for sedation during ECT should not affect duration and quality of the seizure. Some published literature states that the use of lidocaine has both a reducing and enhancing effect on seizure duration ^(9,10).

In this study, we aimed to investigate the effect of lidocaine which is an adjuvant agent during anesthesia for electroconvulsive therapy procedures on the length of seizures.

METHODS

Current study designed prospectively randomized controlled double blind trial. After Local ethics committee approval, informed consent obtained from patients or their first-degree relatives for ECT. The ASA status I-II one hundred patients were included in the evaluation. Five patients were excluded because of cardiac disease, 13 patients were excluded from the study because they took psychotropic medications (antidepressants, antipsychotics, benzodiazepines, antiepileptics, or antihistaminics) for the last month, and 2 patients were excluded because of known neurological disease. As a result, the study was completed with 80 patients.

Premedication was not given to any of the patients. Venous catheterization was done on patients' right hands with a 20-gauge angiocath in the ECT room. Standard monitorizations of

electrocardiogram (ECG), noninvasive arterial pressure, oxygen saturation levels, and bispectral index (BIS) monitorization were performed.

Patients were randomly assigned into two groups: Group P (propofol, n=39) or Group PL (propofol-lidocaine, n=41) by sealed envelop method.

Patients in Group P were given 5 ml (5 ml SF) by a researcher who did not know the contents of the clear drug mix; propofol induction was then performed. Patients in Group PL were given 5 ml (2 ml of 2% lidocaine + 3 ml SF) by the researcher, who did not know the contents of the clear drug mix in, and then propofol induction was performed. All patients in Group P and Group PL were given 1mk/kg of succinylcholine to enable muscle relaxation when the BIS value was 60.

ECT was performed with maximum stimulant output at a rate of 65–100 % following the end of fasciculations due to succinylcholine. Electrographic seizure times were noted. Patients with no seizure activity or seizure activity of less than 25 seconds were re-stimulated. During the procedure, all ECG changes were recorded as rhythm problems, and if SpO₂ fell below 90%, respiratory distress was noted. The patients were observed until the modified aldrete scores were 10. Each patient underwent 5 ECT sessions. A total of 400 ECT sessions was recorded.

Statistical Analysis

When the findings obtained in the study were evaluated, statistical analyses were reviewed using IBM SPSS Statistics 13.0. The Mann-Whitney U test was used for numeric data not matching normal distribution, and the results were given as mean ± standard deviation. The Chi-square test was used to analyze the intermittent variables, and the results were given as frequency (percentage). The one-way ANOVA/post-hoc test was used in the analysis of repeated measurements, and the Wilcoxon test was used in the binary comparison of recurrent measurements. The Minitab 17-Power and Sample size test was used to examine the power of the study and sample size. The results were evaluated with a 95% confidence interval and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Eighty patients between the ages of 22 and 59 years (38.8 ± 7.34) were included in the study. Thirty-six (45%) of the patients were female, and 44 (55%) were male. The standard effect size of our study with 40 patients in each group with a 95% confidence interval was 64%, and the power was 81%.

The demographic information and laboratory values of the patients are summarized in **Table 1**. There was no statistically significant difference between the two groups in terms of mean age, sex, height, weight, and preoperative serum albumin values ($p > 0.05$).

Table 1. Demographic characteristics of groups			
	Group P (n=39)	Group PL (n=41)	p
Male (n)	22	22	0,982 [†]
Female (n)	17	19	
Age (year) (mean \pm SD)	37,9 \pm 7,62	39,6 \pm 7,05	0,364*
Weight (kg) (mean \pm SD)	68,2 \pm 11,38	70,3 \pm 9,69	0,327 [†]
Height (cm) (mean \pm SD)	170,05 \pm 6,70	168,53 \pm 6,93	0,161 [†]
Serum Albumin (mg/dl) (mean \pm SD)	3,99 \pm 0,38	4,15 \pm 0,48	0,231 [†]

*Ki-square test, [†]Mann Whitney U test

Patient respiratory problems, arrhythmias, and re-stimulation data are summarized in **Table 2**. There was no statistically significant difference between the two groups in terms of respiratory problems ($p=0.636$) and re-stimulation rates ($p=0.713$). There was a statistically significant difference in the rates ($p=0.036$) of arrhythmias when we compared the two groups in the study.

Table 2. Complication characteristics of the groups

	Group P (n=195)	Group PL (n=205)	p
Respiratory depression (n)	4	2	0,636
Arrhythmia (n)	16	6	0,036*
Re-stimulation (n)	8	6	0,713

Ki-square test, * $p < 0,05$

The BIS monitoring values of the patients are summarized in **Table 3**. There was no statistically significant difference between the two groups in terms of BIS monitorization values ($p > 0.05$) in the study.

Table 3. BIS values of groups

	Group P (n=39)	Group PL (n=41)	p
1. Session of BIS values (n) (mean \pm SD)	59,38 \pm 1,38	59,51 \pm 0,81	0,868
2. Session of BIS values (n) (mean \pm SD)	59,64 \pm 1,08	59,51 \pm 1,02	0,826
3. Session of BIS values (n) (mean \pm SD)	59,89 \pm 1,61	58,87 \pm 2,11	0,127
4. Session of BIS values (n) (mean \pm SD)	59,33 \pm 1,38	59,12 \pm 1,18	0,458
5. Session of BIS values (n) (mean \pm SD)	59,53 \pm 1,57	59,17 \pm 1,39	0,581

Mann Whitney U test

The amounts of propofol used in patients are summarized in **Table 4**. There was no statistically significant difference between the two groups in terms of propofol amounts ($p > 0.05$) in the study.

Table 4. Propofol values of the groups

	Group P (n=39)	Group PL (n=41)	p
1.session Propofol (mg) (mean ± SD)	89,48±41,09	76,34±18,40	0,308
2. session Propofol (mg) (mean ± SD)	89,74±36,38	77,31±19,87	0,270
3. session Propofol (mg) (mean ± SD)	76,15±13,10	74,39±18,98	0,175
4. session Propofol (mg) (mean ± SD)	81,53±18,10	77,31±18,97	0,232
5. session Propofol (mg) (mean ± SD)	89,74±29,94	77,92±17,49	0,126
<i>Mann Whitney U test</i>			

The seizure durations of the patients are summarized in **Table 5**. Both groups in the study were compared in terms of seizure duration. Duration of seizure was significantly higher in Group PL compared to Group P ($p<0,05$).

In the evaluation of the seizure times measured in the different ECT sessions of the groups, it was observed that the measurements in at least one time period in both groups were statistically significantly different from other time periods (**Table 6, figure 1**).

Table 5. Seizure durations of the groups

	Group P (n=39)	Group PL (n=41)	p
1.session Seizure duration (sn) (mean ± SD)	34,33±3,79	40,09±11,39	0,031*
2. session Seizure duration (sn) (mean ± SD)	31,33±3,04	36,04±9,02	0,023*
3. session Seizure duration (sn) (mean ± SD)	30,53±3,58	33,60±4,99	0,009*
4. session Seizure duration (sn) (mean ± SD)	29,46±3,07	31,92±4,22	0,013*
5. session Seizure duration (sn) (mean ± SD)	26,74±2,30	28,60±3,46	0,017*
<i>Mann Whitney U test, * p<0,05</i>			

In Group P, there was a statistically significant difference between the first and second seizure durations and between the fourth and fifth seizure durations. There was a statistical similarity between other seizure durations.

In Group PL, there was a statistically significant difference between the second and third seizure durations and between the fourth and fifth seizure durations. There was statistical similarity between other seizure durations.

Table 6: Seizure durations for each ECT sessions of groups		df	F	p
1.Group	Between Groups	4	29,017	0,000*
	Within Groups	190		
	Total	194		
2.Group	Between Groups	4	28,416	0,000*
	Within Groups	200		
	Total	204		
ANOVA				

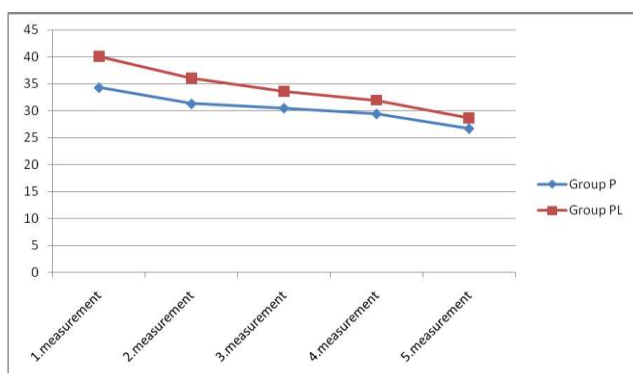


Figure 1. Seizure durations for each ECT sessions of groups

DISCUSSION

In this study, we sought to find the effect of lidocaine on the duration of seizures. The main finding of our study was that lidocaine has an enhancing effect on the duration of seizures during ECT.

The lidocaine administered prior to propofol injection decreased the hemodynamic response to intubation and propofol injection pain.^{11,12} The current study addresses the effect of lidocaine while performing ECT on seizure duration.

In the literature, ECT was said to be used more frequently in patients between the ages of 45 and 64.¹³ In contrast, another study mentioned a more

frequent use of ECT in patients between the ages of 25 and 44.¹⁴ Parallel with these, the mean age of the patients in our study was $38.8(\pm 7.34)$ years.

Lidocaine using as an adjuvant drug is an amide structured, rapid-acting local anesthetic agent, with its medium length of duration. Complications, including convulsions, respiratory depression, and local anesthetic toxicity may occur while overdose administration of lidocaine.¹⁵ Even with lower blood concentrations, local anesthetic agents like lidocaine are known to cause systemic toxicity in patients with low serum albumin levels (16).

Because it is a reliable therapeutic modality, ECT may result in side effects, such as arrhythmia and respiratory depression (17). In this study, we found the incidence of respiratory depression to be similar between the groups. However, the incidence of arrhythmia was statistically significantly lower in Group PL. There were also similarities in the preoperative serum albumin levels of the groups.

We think that the use of lidocaine as an adjuvant agent during the ECT procedure decreases arrhythmia incidence due to the antiarrhythmic effect of lidocaine. In addition to lidocaine has no enhancing effect on respiratory depression incidence.

Some studies state there is no relationship between the duration of a seizure and the patient's response to therapy during the ECT period.^{3,18} However, some studies show a relationship between the length of a seizure and the therapy response during ECT (19).

Seizure activity of less than 25 seconds observed with EEG is considered insufficient for therapeutic efficiency (4). Kuşçu et al. reported in their study, which compared ketamine, thiopental, and a ketamine-thiopental combination, that seizure duration was shorter in the group of patients who were given the ketamine-thiopental combination. This effect was described as a result of the combination of two different anesthetic agents without dose reduction and deeper anaesthesia (20).

For this reason, we provided the depth of anesthesia as follows: To standardize the depth of anaesthesia, propofol induction was given to the patients until their BIS levels reached approximately 60. The BIS levels and the propofol doses used in these groups were found statistically similar. This condition was interpreted to mean there was no effect of the depth of anesthesia on the duration of the status.

Some studies searched for the effects of lidocaine uses during ECT procedures. In a study conducted by Wajima et al. on 25 patients, it was reported that use of 1.5 mg/kg lidocaine for an ECT procedure resulted in more stable hemodynamics and a reduced duration of seizures(9). In addition, Abedinzadeh et al. reported that, in a study of 72 patients, use of 1.5 mg/kg lidocaine was more stable hemodynamically and increased the duration of seizures(10). These two studies indicate that the use of lidocaine has different effects on seizure duration. However, the common feature of both studies is that anesthesia depth monitoring has not been done. We regarded this as the limit of our work.

Contrary to these studies, our study involved the use of 40 mg of lidocaine and BIS monitoring for anesthesia depth standardization.

We concluded that adjuvant lidocaine administration for the ECT procedure prolongs the duration of the seizure and thereby positively impacts treatment. In addition, adding lidocaine decreases procedural adverse cardiovascular effects.

REFERENCES

1. Adams Jr HP1, Kendell RE. The present status of electroconvulsive therapy. *Br. J. Psychiatry* 1981;139:265–83.
2. Kocaçya MH, Savaş HA, Selek S. Case Report: Four Depression Patients were Treated by Maintenance Electroconvulsive Therapy. *Bulletin of Clinical Psychopharmacology* 2008;18:113-8.
3. Sackeim HA, Prudic J, Devanand DP, Kiersky JE, Fitzsimons L, Moody BJ, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *N. Engl. J. Med* 1993;328:839–46.

4. Sackeim HA. The anticonvulsant hypothesis of the mechanisms of action of ECT: current status. *J. ECT* 1999;15:5–26.

5. Folk JW, Kellner CH, Beale MD, Conroy JM, Duc TA.. Anesthesia for electroconvulsive therapy: a review. *J. ECT* 2000;16:157–70.

6. Fredman B, d'Etienne J, Smith I, Husain MM, White PF. Anesthesia for electroconvulsive therapy: effects of propofol and methohexital on seizure activity and recovery. *Anesth. Analg* 1994;79:75–9.

7. Canbay O, Celebi N, Arun O, Karagöz AH, Sarıcaoğlu F, Özgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. *Br. J. Anaesth* 2008;100:95–8.

8. Aouad MT, Siddik-Sayyid SM, Al-Alami AA, Baraka AS. Multimodal analgesia to prevent propofol-induced pain: pretreatment with remifentanyl and lidocaine versus remifentanyl or lidocaine alone. *Anesth. Analg* 2007;104:1540-4.

9. Wajima Z, Yoshikawa T, Ogura A, Imanaga K, Shiga T, Inoue T, et al. Intravenous verapamil blunts hyperdynamic responses during electroconvulsive therapy without altering seizure activity. *Anesth Analg* 2002;95:400–2.

10. Abedinzadeh M, Noorian K, Mozafari S. Effect of lidocaine on duration of seizure and hemodynamic alterations in electroconvulsive therapy. *J. Gorgan Univ. Med. Sci* 2013;15:1-5.

11. Euasobhon P, Dej-arkom S, Siriussawakul A, Muangman S, Sriraj W, Pattanittum P, et al. Lidocaine for reducing propofol-induced pain on induction of anaesthesia in adults. *The Cochrane Library* 2016;18:CD007874

12. Yilmaz VK, Yilmaz M, Özyurt A, Canik S. Effectiveness of Magnesium Sulphate and Lidocaine on Hemodynamic Responses Caused By Laryngoscopy and Endotracheal Intubation. *Journal of Kartal Training & Research Hospital* 2015;26:237-42.

13. Minhas H, Ostroff R. Practice of electroconvulsive therapy in a tertiary care hospital in Pakistan. *The Journal of ECT* 2012;28:7-9.

14. Chanpattana W, Kunigiri G, Kramer B. Survey of the practice of electroconvulsive therapy in teaching hospitals in India. *The Journal of ECT* 2005;21:100-4.

15. Celik M, Uysal Soyer Ö, Şekerel BE. Allergy

and Toxicity Related to Lidocaine. Asthma Allergy Immunol 2008;6:22-4.

16. Berde CB. Local Anesthetics In: Miller RD, Miller's Anesthesia. Philadelphia, PA: Churchill Livingstone; 2000:491–521.

17. Rice E, Sombrotto L. Cardiovascular morbidity in high-risk patients during ECT. American Journal of Psychiatry 1994;151:1637-41.

18. Gangadhar B, Subbakrishna D. Post-seizure EEG fractal dimension of first ECT predicts antidepressant response at two weeks. J. Affective

Disorders 1999;52:235-8.

19. Kho KH, Blansjaar BA, Vothknecht S, Cornelissen NMP, Koomen E, Zwinderman AH, et al. A study into predictors for the speed of response to electroconvulsive therapy. The Journal of ECT 2004;20:154-9.

20. Kuşçu ÖÖ, Karacaer F, Biricik E, Güleç E, Tamam L, Güneş Y. Effect of Ketamine, Thiopental, Ketamine- Thiopental Combination on Depression at Electroconvulsive Therapy Anesthesia Turk J Anaesth Reanim 2015;43:313–7.