



The Effect Of Levetiracetam Therapy On Electrocardiography Parameters

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INTRODUCTION

Epilepsy is a frequently seen neurological disease characterized by seizures. The basic aim of treatment is the suppression of seizures, the reduction of their frequency, and improvement of the patient's quality of life, with antiepileptic agents being employed for this purpose (1)

Some antiepileptic drugs are reported to be capable of causing cardiac arrhythmias and affecting cardiac excitability and conduction, thus further exacerbating the disease's impaired autonomic cardiac effect (1,2).

Levetiracetam is an antiepileptic drug (AED) used in the treatment of children and adults. It is employed in mono-and polytherapy in adult and pediatric patients with focal and generalized secondary seizures, primary generalized tonic clonic seizures, and myoclonic seizures (3,4).

Levetiracetam is also capable of inhibiting potassium ion channels. It can therefore result in cardiac arrhythmias during use, with the potential to prolong the QT interval at ECG. The adverse effects and potential mechanisms of action of levetiracetam in terms of cardiac conduction modulation have not to date been elucidated in the literature.

OBJECTIVES

The purpose of this study was to compare the ECG parameters before and at the sixth month of treatment of patients diagnosed with epilepsy and started on levetiracetam therapy.

Table 1 Demographic and laboratory characteristics of patients using levetiracetam

Age	10.93±3.74 (4-17) years
Sex n (%)	
Male	16 (53.33%)
Female	14 (46.7%)
Seizure type n (%)	
Focal	13 (43.3%)
Generalised	17 (56.7%)
EEG n (%)	
Normal	6 (20 %)
Abnormal	0 (0%)
Focal epileptiform discharges	13 (43.3%)
Generalised epileptiform discharges	11 (36.7%)
Cranial magnetic resonans imaging n (%)	
Normal	25 (83.3%)
Abnormal	5 (16.7%)

Table 2 Comparison of ECG parameters before and after treatment with levetiracetam

	Pretreatment Mean±SD (Min–Max)	Posttreatment 6.months Mean±SD (Min–Max)	P value
PR interval (sec.)	0.136±0.019 (0.11-0.18)	0.131±0.015 (0.12-0.16)	0.271
QTc (sec.)	0.411±0.023 (0.4-0.5)	0.402±0.022 (0.35-0.45)	0.127
Heart rate (beat/min.)	94.87±12.12 (60-115)	92.27±9 (71-107)	0.257

MATERIALS AND METHODS

The files of 30 patients diagnosed with epilepsy based on ILAE criteria at the Balıkesir University Medical Faculty pediatric neurology clinic, Turkey, between 01 August 2019 and 01 February 2021 and started on levetiracetam therapy were examined in this study.

Patients with additional chronic disease (such as hypertension, diabetes mellitus, congenital or acquired heart disease, or chronic lung disease), with different drug use histories (macrolides, antipsychotics, antidepressants, antihistaminics, or anti-arrhythmic drugs), or receiving polytherapy were excluded.

Cases' clinical findings, electroencephalography (EEG), cranial magnetic resonance imaging (MRI) and electrocardiography data before and at the sixth month of treatment were recorded.

ECGs were performed by the same clinician using a 12-lead device set to 25 mm/sec and 10 mm/mV amplitude, PR interval, QTc, and peak heart rate were recorded.

Corrected QT (QTc) was calculated using the Bazett formula. Interval lengths were averaged over all leads using the modified Fridericia' formula in order to determine the QTc interval (QTc: QT/RR).

RESULTS

Thirty patients diagnosed with epilepsy and started on levetiracetam therapy were included in the study. The patients' mean age was 10.93±3.74 (4-17) years. Sixteen (53.33%) patients were boys and 14 (46.7%) were girls. Thirteen (43.3%) were found to experience focal seizures, and 17 (56.7%) generalized epilepsy-type seizures. EEG was normal in six cases (20%), focal epileptiform in 13 (43.3%) cases, and generalized epileptiform in character in 11 (36.7%). Cranial MRI was normal in 25 (83.3%) cases, but was interpreted as abnormal in five (16.7%). Twenty-eight (93.3%) patients were started on levetiracetam at 20 mg/kg, and two (6.7%) at 25 mg/kg (Table 1).

The mean PR interval at ECG before patients started on levetiracetam was 0.136±0.019 (0.11-0.18) msn, the QTc interval was 0.411±0.023 (0.4-0.5) msn, and the mean peak heart rate was 94.87±12.12/min (60-115). At the sixth month of levetiracetam therapy, the mean PR interval was 0.131±0.015 (0.12-0.16), the mean QTc interval was 0.402±0.022 (0.35-0.45) msn, and the mean peak heart rate was 92.27±9/min (71-107). Comparison of the ECG parameters (PR interval, QTc, and peak heart rate) revealed a shortening in the PR interval and QTc values at the sixth month of treatment and a decrease in the peak heart rate, although the changes were not statistically significant (Table 2).

No significant gender difference was observed between the ECG parameters before treatment and at the sixth month. No significant difference was also determined in terms of epilepsy types and ECG parameters before and at the sixth month of treatment (P>0.005) (Table 3, Table 4).

Table 3 Comparison of ECG parameters before and after treatment with levetiracetam between genders

Sex	Pretreatment Mean±SD (Min–Max)			Posttreatment 6.months Mean±SD (Min–Max)		
	Female	Male	P value (Pre)	Female	Male	P value (Post)
PR interval (sec.)	0.130±0.015 (0.12-0.16)	0.140±0.022 (0.11-0.18)	0.225	0.137±0.0149 (0.12-0.16)	0.131±0.015 (0.12-0.16)	0.963
QTc (sec.)	0.41±0.024 (0.4-0.5)	0.408±0.023 (0.4-0.5)	0.702	0.403±0.018 (0.38-0.44)	0.40±0.025 (0.35-0.45)	0.815
Heart rate (beat/min.)	96.57±10.7 (80-115)	93.37±13.4 (60-110)	0.481	92.36±8.168 (75-107)	92.19±9.94 (71-105)	0.474

Table 4 Comparison of ECG parameters before and after treatment with levetiracetam between seizure types

Seizure Type	Pretreatment Mean±SD (Min–Max)			Posttreatment 6.months Mean±SD (Min–Max)		
	Focal	Generalized	P value (Pre)	Focal	Generalized	P value (Post)
PR interval (sec.)	0.140±0.018 (0.12-0.16)	0.132±0.020 (0.11-0.18)	0.189	0.126±0.012 (0.12-0.16)	0.134±0.016 (0.12-0.16)	0.081
QTc (sec.)	0.409±0.023 (0.4-0.5)	0.412±0.024 (0.4-0.5)	0.623	0.396±0.017 (0.38-0.42)	0.406±0.024 (0.35-0.45)	0.966
Heart rate (beat/min.)	90.23±12.6 (60-107)	98.41±10.7 (78-115)	0.066	92.85±6.90 (85-107)	91.82±10.52 (71-105)	0.764

CONCLUSION

Although one study in the literature reported no change in heart rate compared to the pre-treatment values in the third month of levetiracetam therapy in adults, there has been no research comparing pre- and post-treatment ECG findings related to the use of levetiracetam in children.

The present study examined ECG parameters before and after levetiracetam therapy. No significant difference was observed in this study between pre-treatment ECG parameters and those on the sixth month of treatment (PR interval, QTc, and peak heart rate). This was also independent of the type of epilepsy and of gender. Further studies on the subject are now required.

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