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Original Research

Short-Term and Long-Term Effects of Levetiracetam Monotherapy On Hematological Parameters in Children with Idiopathic Epilepsy

Habibe Koc Ucar,[1] Esra Sarigecili,[1] Sevcan Bilen,[2] Sinem Sari[2]

[1]Department of Pediatric Neurology, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye
[2]Department of Pediatric Emergency Türkiye, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye

Abstract

Objectives: Levetiracetam (LEV) is a broad-spectrum anti-seizure drug (ASD) that has been widely used in recent years. It is thought to have an effect on the release of neurotransmitters that occur as a result of vesicle fusion and exocytosis by binding to synaptic vesicle glycoprotein 2A.

Methods: The study enrolled patients diagnosed in the Pediatric Neurology Outpatient Clinic who were being followed with the diagnosis of childhood idiopathic epilepsy and were receiving LEV as ASD monotherapy. Sixty-four patients with complete blood count data from the pretreatment (Pre-T) period, the short-term period of 3 to 6 months after treatment (Post-TS), and the long-term period after 12 months (Post-TL) were included in the study. The demographic data of the patients included in the study were retrospectively analyzed for seizure frequency, seizure type, initial and subsequent EEG results, starting date of the treatment, and complete blood count data.

Results: Of 64 patients, 36 were male and 28 were female. The mean age of patients was 8.7±3.8 (2.5–16) years. In the whole population, post-TL lymphocyte counts were found to be decreased compared to pre-TL lymphocyte counts. This decrease was statistically significant for patients over 6 years of age (n=46) ($p<0.075$). In the post-TL period, hematocrit, hemoglobin, mean corpuscular volume, and mean platelet (PLT) volume increased, while white blood cell, PLT, neutrophil, and monocyte counts decreased ($p<0.05$). Seizure-free status was achieved in 92.2% of cases. Frequent seizures were observed only in five patients who were older than 6 years. Pre-treatment EEG findings were normal for 15 (23.4%) patients, generalized for 8 (12.5%) patients, and focal for 41 (64.1%) patients. According to the pretreatment EEG findings, all of the patients with improvement in EEG were those whose findings were focal ($p<0.001$).

Conclusion: In children with idiopathic epilepsy, long-term LEV monotherapy may cause significant changes in hematological parameters. LEV seems to have effects on the counts and perhaps functions of PLTs, lymphocytes, monocytes, and neutrophils, particularly in the long-term.

Keywords: Children, Idiopathic childhood epilepsy, Hematological parameters, Levetiracetam, Monotherapy

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Address for correspondence: Habibe Koc Ucar, MD. Department of Pediatric Neurology, University of Health Sciences, Adana City Training and Research Hospital, Adana, Türkiye
Phone: +90 322 455 90 00 **E-mail:** hkocselanik@gmail.com

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Levetiracetam (LEV) is a broad-spectrum anti-seizure drug (ASD) that has been widely used in recent years and is effective against both focal and generalized epilepsy.[1] Although its mechanism of action is not exactly understood, it is known to differ from other ASDs. LEV is thought to affect presynaptic activity by binding to synaptic vesicle glycoprotein 2A (SV2A).[2] The function of this protein is to control vesicle fusion and exocytosis, as well as to reduce the release of neurotransmitters.[3,4] The major route of LEV elimination is renal excretion.[5] The administered dose of LEV in children is usually 20–40 mg/kg/day.[6,7] LEV has well-tolerated, relatively mild-to-moderate side effects that occur most frequently during the initial titration phase.[8,9] In the literature, the common side effects seen due to LEV use has been reported to occur in the first 5 months of treatment in 17.2–51.3% of patients.[10–12]

Most ASDs can lead to various degrees of hematological disorders, which may range from moderate cytopenia (thrombocytopenia, neutropenia, and anemia) to bone marrow failure. Various hematological side effects of LEV leading to cytopenia have been reported in the literature.[13,14] Due to the need for their long-term use, ASDs should be closely monitored for hematological toxicity. Therefore, this study reviewed the hematological effects of LEV monotherapy in children with idiopathic epilepsy in three separate visits in the period from the initial phase of treatment to the end of the 1st year. Initially, pre-treatment effects on blood counts, short-term effects in the first 3–6 months, and long-term effects after 12 months were reviewed. In addition, the effectiveness of LEV monotherapy in the management of different types of seizures in patients with idiopathic epilepsy was evaluated.

Methods

Participants and Protocol

For this study, approval was obtained from the Scientific Ethics Committee of the Adana City Training and Research Hospital. Our study was conducted in accordance with the Declaration of Helsinki. The study enrolled patients diagnosed in the Pediatric Neurology Outpatient Clinic between June 2019 and December 2020 who were being followed with the diagnosis of childhood idiopathic epilepsy and who were receiving LEV as ASD monotherapy. Patients who were not followed regularly were excluded, as were those whose hematological data for any period in the 3–6 months before the determined treatment or in the 1st year of the treatment could not be obtained. Patients whose EEG data for the pretreatment period or for the 1st year of treatment could not be obtained were also excluded from the study. The demographic data of the patients included in the study were retrospectively analyzed for seizure frequency, seizure type, EEG data for the pretreatment period and the 1st year of treatment, start date of the treatment, and complete blood count data. The initial dose of LEV administered for all patients was 10–20 mg/kg/day. This dose was increased by 10 mg/kg/day up to 40 mg/kg/day depending on the results of seizure monitoring. Patients who had four or more seizures in a year were identified as patients having frequent seizures.

Sixty-four patients with complete blood count data from the pre-treatment (Pre-T) period, the short-term period of 3–6 months after the treatment (Post-TS), and the long-term period after 12 months (Post-TL) were included in the study. Twenty patients who were not followed regularly, those who did not take their medication regularly, and those with any missing complete blood count data were excluded from the study. Patients with systemic diseases accompanying epilepsy and other drug use were also excluded from the study. The ages of patients in the initial stage of treatment were taken into account. Erythrocytes, hemoglobin (HB), hematocrit (HCT), mean corpuscular volume (MCV), white blood cell (WBC) count, leukocyte subtype (lymphocyte, neutrophil, monocyte, and eosinophil) ratios, platelet (PLT) count, and mean PLT volume (MPV) were recorded. In addition, the neutrophil/lymphocyte ratio (NLR) was calculated.

All hematological parameters were analyzed using a Sysmex XE-2100 automated hematology analyzer (Roche Diagnostics), according to the manufacturer's instructions.

Statistical Analysis

Statistical analysis of the data was conducted using IBM SPSS Statistics 25.0 (SPSS Inc., Chicago, IL, USA). Categorical measurements were summarized as numbers and percentages, while continuous measurements were summarized as mean and standard deviation (or median and minimum-maximum where appropriate). Categorical expressions were compared by Chi-square and Fisher exact tests. Whether parameters showed normal distribution was determined using the Shapiro–Wilk test. The independent Student's t-test was used for the normally distributed parameters, while the Mann–Whitney U-test was used for non-normally distributed parameters. The Wilks lambda method was used for the repeated measurements test intended to analyze repeated measurements of hematological parameters. Wilcoxon rank and paired sample t-tests were used to review the differences between the pre-treatment, short-term, and long-term values of hematological parameters. The level of statistical significance was accepted to be 0.05 in all tests.

Results

This study enrolled a total of 64 patients including 36 (56.3%) male and 28 (43.8%) female patients. Of the patients over 6 years of age, 25 (54.3%) were male and 21 (45.7%) were female. The mean age of patients was 8.7±3.8 (median: 8.3, range: 2.5–16) years. The demographic and clinical characteristics of patients were similar in each age group. While 15.7% (n=10) of patients had focal seizures (eight of the patients who had focal seizures were >6 years old), 84.4% (n=54) had generalized seizures (38 of the patients who had generalized seizures were >6 years old). The pretreatment EEG findings was found to be normal for 15 (23.4%) patients, generalized for 8 (12.5%) patients, and focal for 41 (64.1%) patients. Seizure-free status was achieved in 62% of cases. Frequent seizures were observed only in five patients aged >6 years (Table 1).

Compared to pretreatment counts, long-term lymphocyte counts were found to be decreased in all patients. When evaluated according to age groups, the decrease in lymphocyte counts was found to be insignificant in patients younger than 6 years (n=18), while it was statistically significant in patients older than 6 years (n=46) (p<0.075). When the decreases in long-term and short-term lymphocyte counts were compared, the decrease in long-term lymphocyte counts was not significant in patients older than 6 years, while it was significant in the population under 6 years of age and in the general population (p<0.022 and p<0.044, respectively) (Table 2).

In the general population, HCT, HB, MCV, and MPV values increased in the long-term, that is, after 12 months (Post-TL). WBC, PLT, neutrophil, and monocyte values were found to be decreased (p<0.05) (Table 2 and Fig. 1). When classified as values for patients younger and older than 6 years, HCT values were high in patients of <6 years of age, while neutrophil and NLR values were found to be decreased (p<0.05). In patients over 6 years of age, HCT, HB, MCV, MPV, and monocyte values were found to be high, while WBC, PLT, and neutrophil values were low (p<0.05) (Table 2). Thirty-one patients (62%) had improved EEG results. There were improved EEG results for 66.7% and 60.5% of patients under 6 years of age and over 6 years of age, respectively, but this was not statistically significant (Table 3) (p>0.05). The gender distributions in the groups with and without EEG improvement were similar. The rate of generalized seizures in both groups was high but not statistically significant. According to the pre-treatment EEG findings, all of the patients with significant EEG improvement were patients whose findings were focal (Table 3) (p<0.001).

The relationship between EEG improvement and changes in hematological parameters in the post-TL period was also evaluated separately. WBC, neutrophil, and PLT counts were found to be significantly reduced in patients with improved EEG results. In patients without EEG improvement, WBC and lymphocyte values were found to be significantly reduced, while there was no change in PLT values. HCT and MPV values were found to be increased in both groups (Table 4).

Table 1. Demographic characteristics and clinical features of the patients according to each age group

	≤6 years	>6 years	Total	p
	n (%)	n (%)	n (%)	
Gender, n (%)				
Male	11 (61.1)	25 (54.3)	36 (56.3)	0.624[c]
Female	7 (38.9)	21 (45.7)	28 (43.8)	
Seizure type, n (%)				
Focal seizure	2 (11.2)	8 (17.4)	10 (15.7)	0.791[c]
Generalized seizure	16 (88.9)	38 (82.6)	54 (84.4)	
Seizure frequency, n (%)				
No	18 (100)	41 (89.1)	59 (92.2)	0.145[c]
Yes	–	5 (10.9)	5 (7.8)	
Pretreatment EEG findings, n (%)				
Focal	12 (66.7)	29 (63.0)	41 (64.1)	0.122[c]
Generalized	–	8 (17.4)	8 (12.5)	
Normal	6 (33.3)	9 (19.6)	15 (23.4)	
EEG improvement				
No	4 (33.3)	15 (39.5)	19 (38.0)	0.702[c]
Yes	8 (66.7)	23 (60.5)	31 (62.0)	

[c]Chi-square and Fisher exact tests; EEG: Electroencephalography.

Table 2. Comparison of mean values of hematological parameters before and after (short-term and long-term) levetiracetam administration

	Pre-T	Post-TS	Post-TL	p1	p2	p3	p4
	Mean±SD	Mean±SD	Mean±SD				
All patients (n=64)							
HCT	36.2±3.5	37.4±2.8	38.1±3.2	<0.001**	<0.001**	<0.001**	0.011*
HB	12.5±1.2	12.8±0.9	13.0±1.1	<0.001**	0.015*	<0.001**	0.027*
MCV	79.1±4.6	79.2±5.8	80.6±4.7	0.012*	0.958	0.002**	0.017*
WBC	9.3±3.1	8.6±3.4	7.4±1.9	<0.001**	0.068	<0.001**	0.019*
MPV	8.1±.2	8.3±1.2	8.5±1.0	0.001**	0.125	<0.001**	0.014*
PLT	315.4±108.9	309.4±89.4	275.5±65.8	<0.001**	0.549	0.001**	<0.001**
NE#	5.1±0.3	4.3±0.4	3.6±0.2	<0.001**	0.007**	<0.001**	0.132
MON#	0.73±0.3	0.62±.3	0.65±0.3	0.023*	0.008**	0.108	0.320
LY#	3.1±1.2	3.2±1.4	2.8±0.9	0.122	0.659	0.118	0.044*
NLR	1.97±1.5	1.63±1.8	1.45±0.8	0.108	0.167	0.029*	0.506
<6 years (n=18)							
HCT	34.4±2.7	36.2±2.4	36.3±1.9	0.038*	0.003**	0.031*	NA
HB	11.9±0.9	12.4±0.8	12.4±0.7	0.214	0.218	0.157	0.433
MCV	77.8±3.8	78.3±4.9	79.6±3.5	0.073	0.327	0.015*	0.014*
WBC	10.5±3.3	9.8±3.4	8.7±2.4	0.195	0.632	0.061	0.687
MPV	7.9±1.2	8.2±1.2	8.2±1.1	0.052	0.060	0.009**	0.962
PLT	319.8±121.4	310.5±77.9	282.9±78.2	0.279	0.879	0.199	0.139
NE#	5.9±3.0	3.7±2.1	4.2±1.5	0.015*	0.004**	0.127	0.157
MON#	0.82±0.4	0.77±0.2	0.82±0.3	0.705	0.730	0.835	0.528
LY#	3.38±1.5	4.41±1.8	3.27±1.2	0.078	0.098	0.897	0.022*
NLR	2.26±1.8	1.06±0.9	1.51±0.9	0.003**	0.002**	0.327	0.078
>6 years (n=46)							
HCT	36.9±3.6	37.8±2.9	38.9±3.3	<0.001**	0.016*	<0.001**	0.001**
HB	12.7±1.3	12.9±0.9	13.2±1.1	0.007**	0.097	0.003**	0.019*
MCV	79.7±4.8	79.5±6.1	80.9±5.0	0.045*	0.926	0.007**	0.010*
WBC	8.8±2.9	8.1±3.3	6.9±1.6	0.003**	0.044*	0.001**	0.035*
MPV	8.1±1.2	8.3±1.2	8.5±1.0	0.003**	0.330	0.006**	0.002**
PLT	313.6±105.0	308.9±94.4	272.6±60.9	0.001**	0.509	0.002**	<0.001**
NE#	4.8±2.5	4.5±3.1	3.4±1.2	0.007**	0.057	<0.001**	0.023*
MON#	0.69±0.3	0.56±0.2	0.58±0.2	0.002**	0.001**	0.017*	0.490
LY#	2.99±0.9	2.71±0.8	2.62±0.8	0.147	0.195	0.075	0.409
NLR	1.85±1.4	1.86±2.0	1.43±0.8	0.224	0.924	0.114	0.077

*P<0.05; **: P<0.001; p1: repeated measures test; p2: pre-treatment vs. short-term; p3: pre-treatment vs. long-term; p4: short-term vs. long-term, paired sample t-test, Wilcoxon test. HCT: Hematocrit; HB: Hemoglobin; MCV: Mean corpuscular volume; WBC: White blood cell count; MPV: Mean platelet volume; PLT: Platelet count; NE#: Neutrophil count; MON#: Monocyte count; LY#: Lymphocyte count; NLR: Neutrophil/lymphocyte ratio.

Discussion

The effectiveness of LEV monotherapy in patients with idiopathic childhood epilepsy, its effect on hematological parameters, and the relationship between them were evaluated in this study. In a prospective study conducted by Dinopoulos et al.,[13] lymphocyte counts of 22 patients who had started receiving LEV therapy were evaluated 2 and 6 months after the treatment began, and a statistically significant decrease was found in the values for the first 2 months while there was a significant decrease in lymphocyte counts in the 6th month.[12] In our study, there was no significant decrease in lymphocyte counts within the period of 3–6 months after the treatment (Post-TS period). However, in the post-TS period, an increase was observed in the lymphocyte counts of patients under 6 years of age. On the other hand, post-TS evaluations were not homogeneous, and most of the evaluations were made in the first 3–4 months after the treatment. The statistically insignificant decrease in our short-term lymphocyte counts may be related to the fact that these evaluations were performed after <6 months.

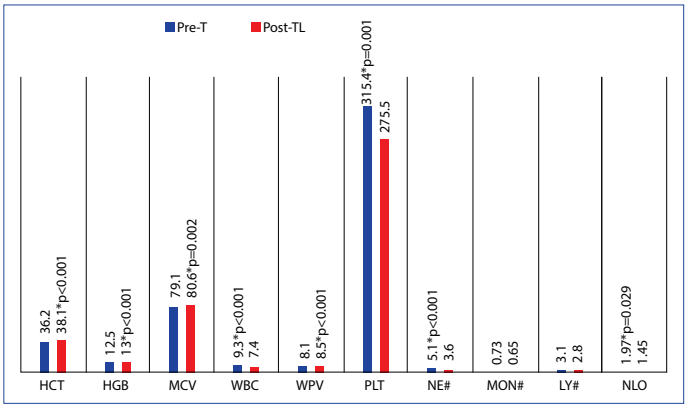

Figure 1. Comparison of the pre-treatment (Pre-T) period and the long-term period after 12 months (Post-TL) in all patients.

The study conducted by Attilakos et al.[14] with 20 children to identify the long-term hematological side effects of LEV showed that lymphocyte and PLT counts were significantly reduced at 12 months regardless of the LEV dosage.[13] In our study, post-TL lymphocyte counts decreased in the whole population compared to counts in the pre-treatment period, but the decrease was statistically significant only among patients aged >6 years. However, post-TL lymphocyte counts decreased in all groups compared to short-term counts and the decrease in patients over 6 years of age was not statistically significant while the decreases in lymphocyte counts in patients younger than 6 years and in the general population were significant. The decrease in lymphocyte counts may be associated with an increased incidence of unexplained pharyngitis and rhinitis with LEV treatment. Piña-Garza et al.[15] reported the increased incidence of the upper respiratory tract infections in LEV-treated patients between 1 month and <4 years of age to be 27.6%, while Schiemann-Delgado et al.[16] reported an increased incidence of the upper respiratory tract infection in patients between 4 and 16 years of age of 21.4%. Similar findings have also been reported in adult patients in various clinical studies (up to 13.4%, compared to 7.5% in the placebo group).[15–17]

In another study that evaluated adult patients, there were no significant changes in the values of complete blood counts with 3 months of LEV therapy, but a decreased ratio of CD4+ and CD25+ lymphocytes was reported.[17] The mechanism through which LEV can affect lymphocyte counts has not yet been investigated. A study on interictal changes of blood leukocytes in patients with active epilepsy found a tendency toward increased CD8+ T lymphocyte counts.[18] An *in vitro* study that included 15 healthy adult volunteers showed that SV2A, which is LEV's binding site in the brain, is found in human CD8+ T lymphocytes. Those authors showed that LEV had a moderately depressive effect on the degranulation of CD8+ T lymphocytes. This suggests that LEV could disrupt the antiviral function of the immune system, perhaps through SV2A inhibition. This was perhaps the cause of the lymphopenia observed in their patients. Reduced CD8 lymphocyte counts can also cause an increased frequency of viral infections in these patients. These viral infections are thought to be likely to cause the cytopenia observed in these patients. However, it may be difficult to confirm this because viral infections are quite common in childhood, the diagnostic tests for them are difficult to perform, and information provided by families is often inadequate. Further prospective studies evaluating the subpopulations and functions of lymphocytes in patients treated with LEV monotherapy will help to clarify this issue.[19]

Table 3. Demographic characteristics and clinical features of the patients according to EEG improvement

	No change (n=19)	EEG improvement (n=31)	p
Gender, n (%)			
Male	11 (57.9)	18 (58.1)	0.991[c]
Female	8 (42.1)	13 (41.9)	
Seizure type, n (%)			
Focal seizure	5 (26.4)	5 (16.2)	0.282[c]
Generalized seizure	14 (73.6)	26 (83.9)	
Seizure frequency, n (%)			
No	16 (84.2)	29 (93.5)	0.285[c]
Yes	3 (15.8)	2 (6.5)	
Pretreatment EEG findings, n (%)			
Focal	10 (52.6)	31 (100.0)	<0.001[**c]
Generalized	8 (42.1)	–	
Normal	1 (5.3)	–	

[**]P<0.001; [c]Chi-square and Fisher exact tests. EEG: Electroencephalography.

Table 4. Changes in hematological parameters according to EEG improvement in children with idiopathic epilepsy during levetiracetam monotherapy

	Pre-T	Post-TS	Post-TL	p1	p2	p3	p4
	Mean±SD	Mean±SD	Mean±SD				
No change (n=19)							
HCT	35.8±4.3	36.8±2.8	38.4±2.5	<0.001*	0.142	<0.001**	0.002**
HB	12.4±1.5	12.8±0.9	13.0±0.8	0.092	0.153	0.031*	0.083
MCV	80.9±3.8	81.4±5.7	81.9±5.1	0.496	0.314	0.091	0.344
WBC	8.7±2.0	8.1±2.8	7.3±1.6	0.072	0.116	0.022*	0.356
MPV	7.7±0.9	7.9±0.8	8.1±0.7	0.190	0.521	0.028*	0.255
PLT	322.4±116.2	307.6±83.6	290.2±54.5	0.317	0.372	0.171	0.199
NE#	4.3±1.2	3.5±1.1	3.6±1.1	0.029*	0.006**	0.212	0.408
MON#	0.6±0.2	0.58±0.2	0.63±0.2	0.613	0.721	0.634	0.362
LY#	3.4±1.2	3.2±1.3	2.6±0.9	0.102	0.507	0.019*	0.072
NLR	1.4±0.5	1.2±0.6	1.5±0.8	0.479	0.267	0.872	0.231
EEG improvement (n=31)							
HCT	36.8±3.5	37.7±3.2	38.2±3.8	0.016	0.034*	0.005**	0.253
HB	12.7±1.2	12.8±1.1	13.0±1.3	0.130	0.323	0.052	0.088
MCV	77.8±4.5	77.3±.0	79.8±4.7	0.002**	0.806	0.002**	<0.001**
WBC	8.8±3.0	8.3±2.7	7.2±2.0	0.046*	0.272	0.011*	0.121
MPV	8.2±1.2	8.4±1.1	8.6±.1	0.023*	0.205	0.022*	0.019*
PLT	325.4±108.1	312.9±89.3	271.3±72.6	<0.001**	0.550	0.001**	<0.001**
NE#	4.7±2.6	4.3±2.1	3.5±1.4	0.089	0.289	0.018*	0.096
MON#	0.72±0.3	0.60±0.2	0.61±0.3	0.167	0.052	0.055	0.942
LY#	3.1±1.2	2.9±1.3	2.7±0.8	0.096	0.603	0.194	0.241
NLR	1.7±1.3	1.6±0.9	1.4±0.6	0.088	0.875	0.327	0.203

*P<0.05; **P<0.001; p1: Repeated measures test; p2: Pre-treatment versus short-term; p3: Pre-treatment versus long-term; p4: Short-term versus long-term; paired sample t-test, Wilcoxon test. After excluding those with normal EEG results, Pre-T was n=50. HCT: Hematocrit; HB: Hemoglobin; MCV: Mean corpuscular volume; WBC: White blood cell count; MPV: Mean platelet volume; PLT: Platelet count; NE#: Neutrophil count; MON#: Monocyte count; LY#: Lymphocyte count; NLR: Neutrophil/lymphocyte ratio.

Bachmann et al.[20] reported that in adult patients treated with LEV for a period of at least 6 months, the decreases in PLT counts were significantly greater than the values observed in the control group. Attilakos et al.[14] also reported a significant decrease in PLT counts in the 12th month in a similarly long-term study involving children. In our study, PLT counts decreased significantly in the post-TL period, and when the findings were reviewed in terms of age groups, the decreases seen in patients over 6 years of age were significant. This may be associated with increased age, but, in general, the effect of LEV therapy on decreased PLT counts cannot be ignored. LEV seems to have an effect on PLT counts and perhaps functions as well. There is no information about the mechanism through which LEV may affect PLT count or function. In our study, MPV values of patients were also observed to be increased in all groups together with a decrease in PLT counts. Particularly in patients with immune thrombocytopenia, the magnitude of the MPV value may be due to the large volume of PLT s newly produced as a consequence of immune-induced PLT destruction.[14,21] Based on the reported cases of LEV-related thrombocytopenia, Sahaya et al.[9] suggested that there may be immune-mediated pathogenesis at work, but there are insufficient data on this in the literature.

In a 1-year study, Misiroglu[22] found no significant changes in the hematological parameters of patients using LEV. French et al.,[23] on the other hand, reported a significant decrease in HB and HCT values of their LEV and placebo groups. In contrast, Attilakos et al.[14] showed a significant increase in neutrophil, HTC, and MCV values in the 12th month after LEV treatment. Similarly, in our study, MCV, HCT, and MPV values were found to be significantly increased in the post-TL period. Contrary to the study cited above, neutrophil, monocyte, and WBC values were significantly decreased in the long-term. There was also a decrease in lymphocyte values, but it was not statistically significant. Whether the decrease in WBC counts in the post-TL period can be explained by age-specific variations or whether it is related to reductions in absolute leukocyte count and absolute neutrophil count should be evaluated

by comprehensive and prospective studies.

Gao and Jiang[24] evaluated the efficacy and tolerability of LEV monotherapy in children with epilepsy. In their study, 25 of 31 patients had at least 50% fewer seizures, while 22 had no seizures at all. In the study conducted by Verrotti et al.,[25] 11 of 12 patients (91.6%) were seizure-free as of their 6-month evaluation. These studies suggested LEV as a potentially effective and well-tolerated medication for children with epilepsy. Similarly, 92.2% of patients (excluding only five patients) were seizure-free in our study. Patients who could not achieve seizure-free status were in the age group of >6 years.

Several studies have studied the effects of LEV on changes in EEG. Specchio et al.[26] reported that LEV seems to be effective in reducing epileptiform EEG abnormalities and in suppressing the photoparoxysmal response. In their study, Arican et al.[27] stated that patients who achieved seizure-free status showed significant EEG improvements compared to those who did not respond to LEV monotherapy. They also suggested that the effect of LEV on EEG abnormalities is associated with its effect on the management of epileptic seizures. In our study, we observed no association between seizure frequency and EEG abnormalities when we looked at the effect of LEV on EEG changes independently of seizure type. This may be related to the number of our patients. However, consistent with the literature, LEV seems to be a very effective option for reducing EEG abnormalities in patients with focal EEG findings.

The main limitation of this study was its retrospective design. This study was also limited by non-standardized LEV dosing. The short-term evaluation period was similarly limited by a non-standardized time frame, ranging from 3 to 6 months but mostly comprising the first 3–4 months. In addition, the relationships between causes of infection parameters at the time were unknown due to the retrospective design of the study. There is a need for further prospective, randomized, controlled studies intended to evaluate the effects and side effect profiles of LEV monotherapy in pediatric patients with idiopathic epilepsy.

Conclusion

Long-term LEV monotherapy may cause significant changes in hematological parameters in children with epilepsy. LEV seems to have effects on the counts and perhaps functions of PLT s, lymphocytes, monocytes, and neutrophils, particularly in the long-term. There is a need for prospective, long-term randomized, controlled, and functional studies that will elucidate the effects of LEV therapy on hematological parameters and the mechanisms of those effects.

Disclosures

Ethics Committee Approval: The institutional review board of the University of Health Sciences Adana Training and Research Hospital approved this retrospective study (13/01/2021-74-1251).

Peer-review: Externally peer-reviewed.

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