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ORIGINAL RESEARCH

# The Side Effects of Levetiracetam Monotherapy in Pediatric Epilepsy Patients

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**ABSTRACT**

Levetiracetam is a broad-spectrum second-generation anti-seizure drug. Several side effects can be observed during treatment. In this study, we retrospectively evaluated the side effects of levetiracetam monotherapy in the pediatric epilepsy population and investigated potential indicators that could predict these side effects in the pediatric epilepsy population. The study included pediatric epilepsy patients aged 1-17 who were treated with levetiracetam monotherapy. Data collected included age, gender, body weight, blood pressure, duration of levetiracetam use, dosage, seizure semiology, epilepsy type, EEG and MRI findings, hematological and biochemical laboratory results, and observed side effects. Eighty-five patients were included in the study, with 25 (29%) experiencing side effects. Treatment was discontinued in 11 patients due to these effects. The most common side effects were agitation (9%), headache (6%), and fatigue (5%). No significant relationship was found between side effects and gender, body weight, seizure type, levetiracetam dose, treatment duration, EEG results, or MRI findings. However, vitamin B12 levels were lower in patients with side effects compared to those without. Additionally, side effects were more frequently observed in older age groups. Levetiracetam treatment has been linked to both physical and behavioral side effects, which were more commonly observed in older age groups. The most frequently reported side effects were agitation, headache, and fatigue. Additionally, lower B12 levels may contribute to the onset of certain side effects.

**Keywords: Levetiracetam. Anti-seizure medication. Vitamin B12. Side effects. Agitation.**

**Pediatrik Epilepsi Hastalarında Levetirasetam Monoterapisinin Yan Etkileri**

**ÖZET**

Levetiracetam geniş spektrumlu ikinci nesil anti-nöbet ilacıdır. Tedavi sırasında çeşitli yan etkiler görülebilir. Bu çalışmada, pediatrik epilepsi popülasyonunda levetiracetam monoterapisinin yan etkilerini retrospektif olarak değerlendirdik. Çalışmaya levetiracetam monoterapisi ile tedavi edilen 1-17 yaş arası epilepsili hastalar dahil edildi. Yaş, cinsiyet, vücut ağırlığı, kan basıncı, levetiracetam kullanım süresi, doz, semiyoloji, epilepsi tipi, EEG ve MRI bulguları, hemogram ve biyokimyasal laboratuvar bulguları ve gözlenen yan etkiler kaydedildi. Çalışmaya 85 hasta dahil edildi. Yirmi beş (%29) hastada yan etki görüldü. Yan etkiler nedeniyle 11 hastada tedavi kesildi. En sık görülen üç yan etki ajitasyon (8 hasta, %9), baş ağrısı (5 hasta, %5) ve yorgunluktu (3 hasta, %4). Yan etkiler ile cinsiyet, vücut ağırlığı, nöbet tipi, levetirasetam dozu, süresi, EEG ve MRI bulguları arasında ilişki bulunmamıştır. Yan etki görülen grupta B12 vitamini düzeyleri daha düşük bulunmuştur. Yan etkiler daha yaşlı yaş gruplarında daha sık görülmüştür. Levetirasetam tedavisinde fiziksel-davranışsal yan etkiler gözlenmiştir. Yan etki görülen yaş grubu daha yüksekti. En sık görülen üç yan etki ajitasyon, baş ağrısı ve yorgunluk olmuştur. Düşük B12 düzeyleri bazı yan etkilerin başlamasında rol oynayabilir.

**Anahtar Kelimeler: Levetirasetam. Nöbet önleyici ilaç. B12 vitamini. Yan etkiler. Ajitasyon.**

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Levetiracetam (Lev) is a second-generation anti-seizure medication with broad-spectrum efficacy[1,2]. To a great extent, it doesn't interact pharmacodynamically with other drugs and it doesn't induce p450 cytochrome enzymes thus having fewer side effects compared to the other anti-seizure medication (ASM). Lev has a unique mechanism of action compared to other antiepileptic drugs, as it specifically binds to synaptic vesicle protein 2A (SV2A). This protein, located in presynaptic terminals, is thought to mediate its antiepileptic effects

by influencing presynaptic processes that control synaptic vesicle release. However, its precise mechanism of action is not completely understood[2,3]. Lev is rapidly and almost completely absorbed following oral administration, with a bioavailability of nearly 100%, unaffected by food intake. Peak plasma concentrations are reached within 1 hour, and steady-state levels are achieved within 2 days when taken twice daily. Its pharmacokinetics are linear, dose-proportional, and time-independent. The drug undergoes limited metabolism, with 27% excreted as inactive metabolites within 24 hours. Lev is primarily eliminated via the renal route, with 66% excreted unchanged[3]. Dose adjustments are advised only for patients with moderate to severe renal or severe hepatic impairment accompanied by renal insufficiency. In children, the body clearance of Lev is 30–40% higher than in adults[3,4]. One of its noteworthy is that it is an effective drug with a good safety profile and is prescribed as a first-line drug or combination therapy[1]. However, as with all medicines, Lev can cause side effects in some patients[5,6]. Side effects may vary from mild symptoms like drowsiness and dizziness to more serious ones, such as mood changes, irritability, suicidal thoughts, and, in rare cases, allergic reactions. Understanding these potential side effects is vital for both patients and healthcare providers, enabling early recognition and prompt intervention to ensure safe and effective treatment outcomes. Few studies have assessed the tolerability and safety of Lev monotherapy in pediatric epilepsy patients[1,7]. In this study, we retrospectively evaluated the side effects of Lev monotherapy and investigated potential indicators that could predict these side effects in the pediatric epilepsy population.

## Material and Method

The medical records of patients aged 1 to 17 years approached Diyarbakır Children's Hospital from December 2021 to March 2023 were retrospectively reviewed to detect the following ICD-10 codes: G40.0 Epilepsy · G40.1 epilepsy G41.2 Complex partial epilepsy · G41.8 Other epilepsy · G41.9 Epilepsy unspecified. The patients with the above ICD codes who adhered to Lev as ASM with reliable seizure records were included in the study. Demographic and clinical variables comprised of age, gender, weight, blood pressure, duration of ASM use, type of seizure, etiology, diet(normal/vegetarian), MRI (normal/with lesion), EEG (normal/epileptic), and hemogram biochemical test results were recorded, either at the end of one year / at the day of cessation Lev due to intolerable side effects. The patients were divided into two groups, a group with no side effects (group 1) and a group with side effects (group 2). The exclusion criteria were changes in the ASM schedule before one year, using other drugs in addition to ASM, history of other systemic or psychiatric diseases. Clinical and demographic data were collected through a questionnaire during follow-up visits and from medical record files. The dose of lev was evaluated as an initial dose (20 mg/kg/day), medium dose (30-50 mg/kg/day), and high dose (> 60mg/kg/day). Epilepsy type and etiology were considered according to the International League Against Epilepsy (ILAE) classification. Our study was approved by the ethics committee of Health Sciences University Gazi Yaşargil Training and Research Hospital, on 17-05-2023 with the approval number 417.

*Statistical Analysis*

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and min-max where appropriate. To compare categorical variables between the groups, the Pearson Chi-Square Test or Fisher's Exact Test was used depending on whether the expected value problem arises or not. The normality of distribution for continuous variables was confirmed with the Shapiro-Wilk test. For comparison of continuous variables between the side effect groups, the Student's t-test or Mann-Whitney U test was used depending on whether the statistical hypotheses were fulfilled or not. Logistic regression analysis was performed to determine significant predictors of Side effects. In univariate analysis, variables significant at the $P < 0.25$ level were entered in logistic regression analysis. All analyses were performed using the IBM SPSS Statistics Version 20.0 statistical software package. The statistical level of significance for all tests was considered to be 0.05.

## Results

Among the 85 patients included in this study, 42% were male, and 29% of patients experienced side effects. The mean age was 7.5 ± 4.6 years in group 1 (no side effects) and 9.9 ± 5.2 years in group 2 (with side effects) ($p = 0.046$). The duration of levetiracetam use was 18.1 ± 5.5 months in group 1 and 12.7 ± 9.4 months in group 2 (whether the drug was stopped or not). No significant difference was observed in the blood profile between the two groups. Treatment was discontinued in 11 patients due to serious side effects. The three most common side effects were agitation (9%), headache (6%), and fatigue (5%). The average age of patients with side effects was older than those without. There was no correlation between side effects and gender, body weight, seizure type, levetiracetam dose, duration of use, EEG results, or MRI findings. Birth history, family history, and diet type did not

influence the results. Vitamin B12 levels were lower in group 2 (with side effects), although B12 levels were within the normal range for both groups.

Table I presents the clinical and demographic profile of the patients. Table II displays the blood profile of the patients in both groups. Table III illustrates the observed side effects along with their respective percentages. Table IV presents the effect of various variables on levetiracetam side effects. Table V shows the results of the logistic regression analysis for predicting levetiracetam side effects.

**Table I.** The clinical and demographic profile of the patients.

| | ***Side effect*** | | p |
|---|---|---|---|
| | No-Group 1 | Yes-Group 2 | |
| | n=60 | n=25 | |
| Age(years), *Mean±SD* | 7.5±4.6 | 9.9±5.2 | **0.046** |
| Gender, *n (%)*<br>Male<br>Female | <br>31 (52%)<br>29 (48%) | <br>11 (44%)<br>14 (56%) | 0.519 |
| Weight (kg), *Mean±SD* | 33.1±15.3 | 38.5±13.6 | 0.131 |
| Lev use duration, *Mean±SD*<br>*Median (min-max)*<br>*Month* | 18.1±5.5<br>16.5 (12-36) | 12.7±9.4<br>14 (1-34) | **0.031** |
| Dose, *n (%)*<br>Moderate<br>Low(initial)<br>High | <br>42 (70%)<br>14 (23%)<br>4 (7%) | <br>15 (60%)<br>8 (32%)<br>2 (8%) | 0.624 |
| Semiology, *n (%)*<br>Focal<br>Generalized<br>Unknown | <br>18 (30%)<br>36 (60%)<br>6 (10%) | <br>6 (24%)<br>16 (64%)<br>3 (12%) | 0.845 |
| EEG, *n (%)*<br>Normal<br>Epileptic | <br>17 (28%)<br>43 (72%) | <br>4 (16%)<br>21 (84%) | 0.230 |
| MRI, *n (%)*<br>Normal<br>Lesion | <br>49 (82%)<br>11 (18%) | <br>22 (88%)<br>3 (12%) | 0.749 |
| Type of Epilepsy, *n (%)*<br>Symptomatic-Cryptogenic<br>Idiopathic<br>Structural | <br>28 (47%)<br>24 (40%)<br>8 (13%) | <br>16 (64%)<br>6 (24%)<br>3 (12%) | 0.312 |

EEG: Electroencephalogram, MRI: Magnetic Resonance Image

Age was determined as an effective measure in terms of the occurrence of side effects. Accordingly, the average age of children with side effects was higher than those with no side effects.

**Table II.** The blood profiles of the patients in both groups

| | Side Effect | | P |
|---|---|---|---|
| | NO -Group 1 | Yes-Group 2 | |
| | n=60 | n=25 | |
| Wbc (×$10^3$/uL), *Mean±SD* | 8.5±3.2 | 8.1±2.5 | 0.574 |
| Neutrophile (%), *Mean±SD* | 47.9±13.9 | 52.8±16.4 | 0.164 |
| Lymphocyte (%), *Mean±SD* | 39.6±12.7 | 35.7±16.2 | 0.239 |
| Monocyte (%), *Mean±SD* | 7.5±2.9 | 7.8±2.2 | 0.671 |
| Eosinophils (%), *Mean±SD*<br>*Median (min-max)* | 3.4±3.3<br>2.3 (0.1-14.6) | 3.6±3.1<br>2.9 (0.6-11.9) | 0.783 |
| Basophyle (%), *Mean±SD* | 0.43±0.28 | 0.5±0.35 | 0.393 |
| ANC (×$10^3$/uL), *Mean±SD* | 4.2±2.5 | 4.2±1.9 | 0.987 |
| ALC (×$10^3$/uL), *Mean±SD* | 3.3±1.6 | 2.9±1.6 | 0.209 |
| RBC (× $10^6$/µL), *Mean±SD* | 4.7±0.5 | 4.6±1 | 0.531 |
| RDW-CV (%), *Mean±SD* | 13.9±2.1 | 14.2±2.3 | 0.560 |
| PLT (×$10^3$/uL), *Mean±SD* | 325.8±120.6 | 304.8±121.6 | 0.466 |
| MPV (fL), *Mean±SD* | 9.7±1.7 | 9.7±1.1 | 0.890 |
| Hg (g/dl), *Mean±SD* | 12.4±1.6 | 12.6±1.6 | 0.754 |
| HCT (%), *Mean±SD* | 39.2±7.1 | 38.9±4 | 0.873 |
| B12 (pmol/l), *Mean±SD* | 365.7±147.7 | 411±126 | 0.192 |
| Ferritin (ng/ml), *Mean±SD* | 42.6±14.0 | 42±12.9 | 0.851 |
| Systolic Blood Pressure (mmHg), *Mean±SD* | 100.1±14.4 | 107.2±20.1 | 0.082 |
| Diastolic Blood Pressure (mmHg), *Mean±SD* | 64.1±11.6 | 61.5±12.3 | 0.381 |
| Vitamin D (nmol/L), *Mean±SD* | 26.5±8.3 | 25.1±7.3 | 0.469 |
| CK (IU/L), *Mean±SDMedian (min-max)* | 168.4±87.8<br>165 (54-453) | 145.2±80.7<br>145 (45-324) | 0.260 |
| Glucose (mg/dL), *Mean±SD* | 80.1±10.9 | 77±10.1<br>77 (64-92) | 0.233 |
| ALT (IU/L), *Mean±SD*<br>*Median (min-max)* | 18.7±7.6<br>17 (9-44) | 20.2±8.6<br>23 (12-45) | 0.399 |
| AST (IU/L), *Mean±SD*<br>*Median (min-max)* | 31.4±27.3<br>27.5 (14-228) | 31±8.2<br>33 (13-45) | 0.248 |
| Albumin (g/L), *Mean±SD* | 40.6±1.5 | 40.1±4 | 0.491 |
| Creatine (mg/dL), *Mean±SD* | 0.55±0.12 | 0.54±0.09 | 0.814 |

Wbc: White blood cells, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, Rbc: Red blood cell, RDW-CV: Red cell distribution width - coefficient of variation, PLT: platelet, MPV: Mean platelet volüme, Hg: Hemoglobin, Hct: Hematocrit, CK: Creatine kinase, ALT: Alanine transaminase, AST: Aspartate transferase

**Table III.** The observed side effects are according to their percentages.

| Measurements | Number of patients (%) |
|---|---|
| Side effect | |
| No | 60 (71%) |
| Yes | 25 (29%) |
| Agitation | |
| No | 77 (91%) |
| Yes | 8 (9%) |
| Headache | |
| No | 80 (94%) |
| Yes | 5 (6%) |
| Fatigue | |
| No | 81(95%) |
| Yes | 4(5%) |
| Stomach ache | |
| No | 84(99%) |
| Yes | 1(1%) |
| Allergy | |
| No | 83 (98%) |
| Yes(Maculopapüler/angiodema) | 2 (2%) |
| Weight loss | |
| No | 84 (99%) |
| Yes | 1 (1%) |
| Increased frequency of illness | |
| No | 84 (99%) |
| Yes | 1 (1%) |
| Rhinitis | |
| No | 84 (99%) |
| Yes | 1 (1%) |
| Sleep habit | |
| Normal | 72 (85%) |
| Disturbed (which happened secondary due to other side effects) | 13 (15%) |
| Others* | |
| No | 80 (94%) |
| Yes | 5(6%) |
| Drug discontinuation | 14(56%) |
| No | 11(44%) |
| Yes | |

*Somnolence:1 patient, Tremor:1, enuresis:1, insomnia:1, suicide attempt:1
*Some patients experienced more than one side effect

**Table IV.** The effect of some variables on the side effects of Lev.

| | Side effect | | P |
|---|---|---|---|
| | **No-** Group 1 | **Yes-** Group 2 | |
| | n=60 | n=25 | |
| Birth history, *n (%)* | | | |
| Normal | 57 (95%) | 23 (92%) | 0.628 |
| Eventful | 3 (5%) | 2 (8%) | |
| Family history, *n (%)* | | | |
| No | 36 (60%) | 20 (80%) | 0.076 |
| Yes | 24 (40%) | 5 (20%) | |
| Diet type, *n (%)* | | | |
| Normal | 59 (98%) | 25 (100%) | 0.999 |
| Vegetarian | 1 (2%) | 0 (0%) | |

**Table V.** Logistic regression analysis of predicting Lev side effects.

| | P | Odds Ratio (OR) | 95% CI for OR |
|---|---|---|---|
| B12 level | 0.031 | 1.05 | 1.01 – 1.09 |

OR: odds ratio; CI: confidence interval

## Discussion and Conclusion

Lev is a broad-spectrum ASM that can be used in all age groups. It can be considered a great choice with a safe profile. But still, some side effects can be seen. Tekgül et al. (2016) conducted a study on 351 pediatric patients, reporting that 17% of them experienced adverse effects, irritability 67%, hyperactivity 8%, somnolence 6%, behavioral disorders 5%, restlessness 5%, increased seizure frequency 3%, enuresis 2%, headache 2% and attempted suicide 2% were the most observed side effects. The same study concluded that there was no relation between the dose, age, and side effects, meanwhile, the adverse effects were seen more frequently in patients with partial focal seizures and who have psychiatric disorders and abnormal EEG patterns. In our study, the three most common side effects were agitation 9%, headache 6% and fatigu 5%. Tremor 4%, somnolence 4%, enuresis 4%, insomnia 4%, and suicide attempt 4% were other observed side effects. In our study, the average age of patients with side effects was higher than those with no side effects, which could be because the younger children could have better body clearance of Lev.

ASMs can cause psychiatric symptoms due to their impact on neurotransmitter systems and neural circuits. They alter the balance of key neurotransmitters such as gamma-aminobutyric acid (GABA), glutamate, and serotonin, which regulate mood, cognition, and behavior, potentially leading to anxiety, irritability, or depression. By modifying electrical activity to prevent seizures, ASMs may also affect brain regions involved in mood regulation and cognition, causing emotional instability or cognitive impairment. Individual susceptibility plays a significant role in this process, as genetic factors and pre-existing mental health conditions can increase vulnerability to these side effects. Additionally, higher doses or drug interactions can intensify psychiatric symptoms by disrupting mood-related pathways. Some ASMs also influence immune activity in the brain, which may contribute to mood disturbances. As a result, individuals taking ASMs, particularly during dosage adjustments, may experience psychiatric symptoms, highlighting the need for careful monitoring and management[8,9]. In our study, psychiatric side effects were observed in 9% of the patients who experienced agitation. Mood changes

can be observed in epilepsy patients and in those who use ASM such as Lev, lamotrigine, phenobarbital, and clonazepam and the cause behind this could be either biological or psychosocial. Researchers have found that people with epilepsy are 5 times at risk of suicide. In addition, the risk is still higher even in surgically treated patients. Other studies suggest that suicide attempt is higher in patients with temporal lobe epilepsy which can be due to abnormal function of the limbic system[10]. A suicide attempt was observed in one patient. She was a conventional school-attending 14-year-old girl. MRI was normal, and there were spike-waves in the left temporal region on EEG. The drug was stopped immediately, and the patient was monitored in the intensive care unit for a few days and switched to another ASM.

Dermatological and non-dermatological changes can be experienced in patients who are treated with Lev. The dermatological side effects mostly appeared on the face, and extremities, characterized by dark-colored skin, and morbilliform macular rash. The non-dermatological side effects experienced were fever, headache, abdominal pain, facial edema, pharyngitis, and periorbital eye swelling[11-13]. Despite these side effects being less likely with Lev compared to other ASMs, still such adverse effects can be seen and immediate withdrawal should be done. In our study, maculopapular rash in one patient and angioedema in another one were observed during Lev treatment. The drug was discontinued.

Drug cessation should be approached for serious side effects. Lev treatment had to be discontinued in 11 patients. The discontinuation of Lev was sometimes immediate, while in other cases, it was delayed until it was confirmed that the side effect was caused by Lev. Lev was stopped in three of the five patients with headaches. Lev was also stopped in patients with allergy (2), stomachache (1), enuresis (1), fatigue (1) suicide tendency (1), weight loss (1), and increased frequency of infection (1) The dose of Lev was adjusted in some patients with tolerable side effects.

Lev may reduce the degranulation of CD8 lymphocytes, leading to an increased incidence of upper respiratory tract infections[14,15]. Drug-induced immunoglobulin decreases have been reported in some patients[15,16]. In our patient group, an increase in the frequency of infection was observed in one patient. Lymphocyte count was low, 1270/uL, but lymphocyte subgroup and immunoglobulin levels could not be analyzed. Lev was stopped in this patient.

Few studies have assessed the hematological effects of Lev in the pediatric population. Dilber et al. conducted a study on 114 children in 2021 and tested the effect of this antiseizure drug on hemogram, liver function, and B12, it was observed after three years of follow-up that there was an increase in hemoglobin and hematocrit, while there was a decrease in absolute neutrophil count (ANC) and absolute lymphocytes count( ALC) while the platelet count was not affected and there was no correlation between gender and hematological changes, and despite the changes there were no clinical complaints by the patients [16,17]. French et al evaluated adult patients who received Lev monotherapy despite the hematological changes at first, all the parameters returned to normal at the end of three years [13]. A decrease in lymphocyte and ALC was observed in studies conducted by Dinopoulos et al and Attilocks et al[17-19]. There are also studies in which antiepileptic treatment decreased vitamin B12 levels[19,20]. In our study, logistic regression analysis showed that lower vitamin B12 levels were associated with more side effects in spite that the B12 levels were with in normal range in both groups. This raises the discussion of whether a cut-off B12 level should be established for patients on Lev monotherapy and monitoring of vitamin B12 levels during treatment with ASM is recommended [21] But further studies are needed.

Urinary and fecal incontinence was reported in patients with Lev monotherapy and the exact mechanism is still unknown[22]. Incecik et al reported an 11-year-old boy patient who experienced fecal and urinary incontinence at a dose of 20 mg/kg[23]. Investigation as MRI, EEG, and infection parameters were normal. The effect was reversible and the patients could gain control after withdrawing the drug. In our study, an 8-year-old boy experienced urinary and fecal incontinence a few days after starting Lev. All the investigations were normal, urine culture and urine analysis showed no infection. The drug stopped immediately and the control was regained.

Fatigue is reported by lots of studies as an adverse effect of Lev monotherapy. Marco Mula et al reported fatigue in 36% of patients with Lev which could be due to an imbalance between excitatory and inhibitory neurotransmission however the exact mechanism of central fatigue is still unclear and this side effect was seen more frequently in females rather than males[3,24]. Recent studies showed that central fatigue could be due to dysfunction in the non-motor area of basal ganglıon and their interaction with the frontal cortex and amygdala but the effect of Lev on these networks is still unknown[24]. In our study fatigue was seen in 5% of the patients while the rest 95% of patients didn't experience such symptoms. Fatigue could be due to multifactorial etiologies.

Lev is associated with higher total sleep duration, and sleep problems are not commonly reported as a side effect[25]. The recent studies' results are very controversial. Some studies showed that Lev increased the N2 stage of sleep [26]. In another study, it was observed that Lev increased wakingness and in a study conducted by yılmaz et al., it was seen that this drug increased daytime napping episodes and total nap

duration while there was a decrease in total activity score at night in monotherapy in adult patients[27]. In our study, sleep disturbances were reported in 15% of patients and occurred secondary to other side effects.

Physical and behavioral side effects were reported during Lev treatment, with affected patients being older on average. The three most common side effects were agitation, headache, and fatigue. No significant associations were found with body weight, gender, epilepsy type, Lev dose, treatment duration, MR, or EEG findings. Larger studies are necessary to identify clinical and laboratory markers that may predict the side effects of Lev monotherapy in pediatric patients.

Our study is retrospective with a small sample size. Sleep disturbances were based on family and patient reports rather than a validated and reliable scale. Additionally, pre-treatment laboratory data was unavailable, preventing a comparative analysis of hematological and biochemical results before, during, and after treatment or its discontinuation.

## Abbreviations

Lev: Levetiracetam
ASM: anti-seizure medication
SV2A: synaptic vesicle protein 2A
EEG: Electroencephalogram,
MRI: Magnetic Resonance Image
Wbc: White blood cells,
ANC: Absolute neutrophil count,
ALC: Absolute lymphocyte count,
Rbc: Red blood cell,
RDW-CV: Red cell distribution width coefficient of variation,
PLT: platelet,
MPV: Mean platelet volüme,
Hg: Hemoglobin,
Hct: Hematocrit,
CK: Creatine kinase,
ALT: Alanine transaminase,
AST: Aspartate transferase
GABA: Gamma-Aminobutyric Acid

**Ethics Committee Approval Information:**
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