ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

Effectiveness of Antiseizure Medications and the Clinical Utility of the Spike-Wave Index in Children Diagnosed with SeLECTS With and/or Without ADHD

DEHB Eşlik Eden ve Etmeyen SeLECTS Tanılı Çocuklarda Antiepileptik İlaçların Etkinliği ve Spike-Wave İndeksinin Klinik Faydası

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Abstract

Introduction: This study aims to investigate the clinical and electroencephalographic characteristics of children diagnosed with SeLECTS (Self-limited epilepsy with centrotemporal spikes), comparing the effectiveness of antiseizure medications (ASMs) based on the presence or absence of Attention Deficit Hyperactivity Disorder (ADHD), and evaluating the prognostic value of the spike-wave index (SWI).

Materials and Methods: A retrospective review was conducted on 914 children diagnosed with SeLECTS between 2005–2023. A total of 542 patients who met the inclusion criteria were followed for a minimum of three years with at least three EEG recordings. SWI values were analyzed according to the type of ASM valproic acid (VPA), carbamazepine (CBZ), and levetiracetam (LEV), ADHD status, and age. The predictive power of SWI for EEG improvement and seizure control was assessed using ROC curve analysis.

Results: The mean age was 8.18±3.35 years; the male-to-female ratio was 1.47:1. Onset before age five was associated with more frequent seizures (p=0.003). VPA was more effective for EEG improvement, while LEV provided better seizure control. SWI was significantly higher in children with ADHD. SWI values decreased over time. ADHD prevalence was 19.9%.

Conclusion: SWI is a valuable tool for assessing treatment response. Epilepsy burden is higher in patients with ADHD. VPA is superior in EEG normalization, whereas LEV offers more effective seizure control.

Keywords
SeLECTS, attention deficit hyperactivity disorder, antiseizure medications, spike-wave ındex, EEG, childhood epilepsy

Öz

Giriş: Bu çalışma, SeLECTS (Self-limited epilepsy with centrotemporal spikes) tanısı almış çocukların klinik ve EEG özelliklerini incelemeyi, dikkat eksikliği hiperaktivite bozukluğu (DEHB) eşlik edip etmediğine göre antiepileptik ilaçların (AEİ) etkinliğini karşılaştırmayı ve spike-wave indeksinin (SWI) prognostik değerini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: 2005-2023 yılları arasında SeLECTS tanısı almış 914 çocuk retrospektif olarak değerlendirildi. Dahil edilme kriterlerini karşılayan 542 çocuk çalışmaya alındı. Hastalar en az üç yıl boyunca, üç EEG kaydı ile takip edildi. SWI değerleri, AEİ türü valproik asit (VPA), karbamezapin (CBZ, levetirasetam (LEV), DEHB varlığı ve yaşa göre analiz edildi. SWI'nin EEG iyileşmesi ve nöbet kontrolü üzerindeki öngörü gücü ROC eğrisi ile değerlendirildi.

Anahtar kelimeler
SeLECTS, dikkat eksikliği ve hiperaktivite bozukluğu, antinöbet ilaçları, diken-dalga indeksi, EEG, çocukluk çağı epilepsisi

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Bulgular: Ortalama yaş 8.18±3.35 yıl; erkek/kız oranı 1.47:1 idi. Beş yaş altı başlangıç, daha sık nöbet ile ilişkiliydi (p=0.003). VPA EEG iyileşmesinde; LEV ise nöbet kontrolünde daha etkiliydi. DEHB'li çocuklarda SWI daha yüksekti. Zamanla SWI değerlerinde azalma izlendi. DEHB sıklığı %19.9'du.
Sonuç: SWI, tedavi yanıtını değerlendirmede faydalı bir araçtır. DEHB eşlik eden hastalarda epilepsi yükü daha fazladır. VPA EEG normalleşmesinde, LEV nöbet kontrolünde daha başarılıdır.

Introduction

Attention deficit and hyperactivity disorder (ADHD) is reported as the most common disorder accompanying epilepsy in preschool and school-age children (1-6). It has been reported that the risk of developing ADHD in children with epilepsy is 2.5-5.5 times higher than in healthy children (7). Literature also indicates that epilepsy symptoms are more serious and seizures start at an earlier age in patients with epilepsy who develop ADHD (4,5). The prevalence of ADHD in Self-limited epilepsy with centrotemporal spikes (SeLECTS) is higher than in other epilepsies. Of note, the prevalence of ADHD in such patients was reported as 64.9% in one study and 24.6% in another study, while it was much higher than 3.7%-5.6% in an epidemiological survey (5,6).

In recent years, the clinical significance of SWI in children diagnosed with SeLECTS has been increasingly studied (8). Yılmaz et al. (9) demonstrated its prognostic value based on a ten years follow-up, while our study showed that SWI was significantly higher in patients with comorbid ADHD. The relationship between epilepsy and ADHD comorbidity and neuroimaging findings was examined by Rubinstein et al. (10) who proposed standard neurophysiological mechanisms. Furthermore, the ADHD prevalence of 19.9% identified in our cohort is consistent with the findings of Yuen et al. who systematically reviewed ADHD prevalence in children with epilepsy (11).

Regarding the choice of antiseizure medications, Wirrell et al. (12) emphasized in their systematic review that LEV is particularly effective for seizure control, whereas VPA is more advantageous for EEG normalization. These findings are consistent with the results of our study.

In this study, we aimed to assess the effectiveness of ASM based on EEG parameters (SWI% and SW resolution velocity) and the outcome predictors in a large cohort and prevalence of monotherapy using drug follow-ADHD in SeLECTS

Materials and Methods

Study Settings and Design

We collected clinical and electrographical data regarding the children diagnosed with SeLETCS having at least three EEG recordings during at least three-years follow-up from pediatric neurology center from 2005 to January 2023 in our region.

Total 914 patients demographic and clinical characteristics including age, gender, fever history, seizure type and frequency, family history, and diagnosis and treatment were retrieved from the clinical records of the patients. The patients and their parents completed the general information forms and informed consent forms under the guidance of clinicians.

Inclusion criteria were as follows patients who had their first seizure at the age of 3-15 years, had normal findings on neurological examination and magnetic resonance imaging (MRI), had both initial and follow-up EEGs, and had been followed up for at least three years. Exclusion criteria included seizure Electrical Status Epilepticus during Sleep (ESES) initial EEG (n:74) or presence of Landau-Kleffner syndrome (LKS, n:12), abnormal MRI findings (n:58), abnormal neurodevelopmental status (n:35), and pre-emptive unfollowed EEG examination (n:35) and polytherapy SeLETCS (n:158). Based on these exclusion criteria, 542 patients were recruited into the study.

Diagnosis of SeLECTS and ADHD

We used the following criteria when diagnosing SeLECTS. The clinical and accurate history was to establish the diagnosis: (1) characteristic symptoms (2) presence of motor seizures, (3) normal neurological examination and brain MRI, (4) normal laboratory examination and metabolic screening, and (5) an age of onset between 3-15 years. The EEG criteria used to support the diagnosis of SeLECTS were patients diagnosed according to the International League Aganist Epilepsy (1989) SeLETCS epilepsy diagnostic criteria; It was taken as the dipole indicating a positivity in the general centropemporal region of the waves and within the boundaries of the borders and in the crest or frontal region.

Edition (DSM-IV) criteria based on the clinical interview and diagnostic tests at the Child Adolescent Mental Health and Diseases outpatient clinic, he was diagnosed with ADHD according to DSM-IV-TR criteria. The patients' file records were examined retrospectively. Age, gender, age of first and last seizure, age at diagnosis of ADHD, time of antiseizure

medications (ASMs) initiation, seizure characteristics, AED and other treatments used, electroencephalography (EEG) and brain magnetic resonance imaging (MRI) findings, the relationship between ADHD treatment and seizures, and the time between the onset of ADHD and epilepsy were recorded. In addition, in patients with epileptic activity at the first EEG findings and who underwent periodic EEG monitoring at intervals of 1-6 months, EEG recovery times were determined based on the time when the first normal EEG examination was detected.

542 patients who were followed up with the diagnosis of SeLECTS with/without ADHD, receiving monotheraphy; those who used single medication due to ADHD (n: 108) and those who were followed without medication (n: 434) patients were divided into three groups according to their ages: (i) <5 years, (ii) 5-10 years, and (iii) >10 years. The study group were also categorized seizure burden with seizure frequency (I) >2 seizures and (II) >5 seizures. Seizure outcome was evaluated based on the reduction in seizure frequency over 6-month periods: (1) 50% reduction and (2) seizure-free (complete response).

ASM Drug Initiation Protocol

The following ASMs were reported as initial monotherapy in the patient evaluation chart: CBZ 10-30 mg/kg/day, VPA 10-30 mg/kg/day, and LEV 20-60 mg/kg/day. An ASMs (monotherapy) was administered if the frequency of seizures persisted despite the administration of the full dose of the initial drug.

EEG Recordings

Departmental EEG recording protocols were evaluated each center. Then the following international basic recording parameters were reported. An international 10-20 electrode placement system was used (Nihon Kohden, Tokyo, Japan). Electroencephalograms were recorded by placing scalp electrodes with silver-silver chloride discs according to the international 10-20 system, and recordings were made while awake, drowsy, and asleep (at least 40 minutes with eyes closed, intermittent photic stimulation, and hyperventilation). Response to ASM was evaluated based on the differences among the initial (baseline), second (first year), and third (second year) EEG recordings. EEG records were evaluated by experts with at least ten years experience. The recordings of the spikes occurring during sleep were evaluated as follows: a. Spike-wave-index (SWI) quantified the frequency of spikes in NREM sleep EEG monitoring. SWI was calculated as follows: the number of seconds in which one or more surges were present in the first 30 minutes of non-rapid movements of the first sleep cycle divided by 3600 and then multiplied by 100. Results were expressed as a percentage; b. In the storage of serial EEG according to age; c. Duration and threshold value of response in EEG,; d. EEG recordings in antiepileptic response.

Statistical Analysis

Data analysis was performed using SPSS 23.0 for Windows (Armonk, NY: IBM Corp.). Continuous variables were expressed as mean, standard deviation (SD), comprehensive content, minimum, and maximum and categorical variables were expressed as frequencies (n) and percentages (%). Normal distribution of data was analyzed using one-sample Kolmogorov-Smirnov test, which found that the data was nonnormally distributed. Independent groups were compared using Mann Whitney U test and Kruskal Wallis test with Bonferroni correction. They are dependently estimated data. The metric measurements were tested with the metric values. Preferred assistance program of their first age with the height of Spi in their karaaWs in their observations in their taranaW Spi, and analysis of seizures in the target in seizure prediction with the Receiver Operating Characteristics (ROC) curve and the target. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the cutoff values were calculated. A p value of <0.05 was considered significant.

This study was approved by the Clinical Research Ethics Committee of Karadeniz Technichal Universty under the decision numbered 2023/512, and was conducted as a single-center, retrospective study.

Results

Demographcis

Table 1 presents demographic and clinical characteristics of children (N=542) with childhood epilepsy, centrotemporal spikes (SeLECTS). Mean age was 8.18±3.35 (range, 3-15) years and the male-to-female ratio was 1.47:1. No significant difference was found between the genders with regard to seizure onset age (male 7.80±3.35 years, female 8.08±3.07 years; p=0.502). Family history was positive in 17.1% of the patients.

Table 1. The comparison of demographic and EEG characteristics (N=513) with using monotherapy in SeLECTS's patients with /without ADHD

Monotherapy	**ADHD -**	**ADHD +**	**P**
Demographic and EEG	**434 (78.5%)**	**108 (%19.9)**	
Age (years)	9.3±2.3	8.8±5.3	**0.003**
Female/Male	167/238	39/69	
Age at onset of seizures (months)	10.2±3.8	8.1±4.3	**0.004**
Family history of epilepsy	65 **(14.4%)**	17 **(15.7%)**	0.320
Age at onset of seizures (years) <5 5-10 >10	 34 (6.0 %) 316 (75.5%) 85 (18.5%)	 4 (3.8 %) 75 (69.4%) 29 (26.8%)	 **0.007** 0.060 **0.014**
Seizure semiology Sleep / wakeful	269 (66.4%)/136 (33.6%)	85 (66.6%)/23 (33.4)	**0.0040**
İnitiation time of ASM types (months, mean ± SD)	70.6±0.9	45.1±12.9	0.005
EEG discharges on initial record Unilateral Bilateral	 135 (33.3%) 270 (66.7%)	 32 (29.7%) 76 (70.3%)	 **0.023** **0.005**
EEG improvement with SWI % ≥50% <50%	 37.2 72.8	 69.3 20.7	 **0.008** 0.060

SWI: Spike-wave index

ASM selection

Most commonly preferred initial ASM was CBZ (n=266; 49.1%), followed by VPA (n=119; 21.9%) and LEV (n=157; 29.0%). In hospitalized patients receiving CBZ, VPA, and LEV as the initial drug, respectively.

Monotherapy

Monotherapy was administered in 64.6% of children aged below 5 years, in 75.9% of children aged 5-10 years, and in 85.6% of children aged over 10 years. Seizure control was achieved with monotherapy in 80.2% of patients aged 5-10 years. Table 1 presents the clinical and electroencephalographic characteristics of the groups receiving monotherapy.

Seizure Semiology and Seizure Burden

Most of the patients (n=473; 78.3%) had their first seizure during sleep. Additionally, 19.3% of the patients who had seizures more than twice a year during their follow-up, who were initiated on drug therapy, those who received monotherapy (p=0.000). Patients that had their first seizure before 5 years of age had more repetitive number of seizures in sleep than the other patients (p=0.000). An analysis of the drugs used and the frequency of seizures indicated that 75.7% of those who had seizures 2-5 times a year were in the LEV group, while the frequency of seizures was higher in the CBZ group compared to other groups (p<0.001). Table 2 presents the comparison of monotherapy groups with respect to ASM response and EEG.

EEG Improvement

In the LEV group, 86.9% of the patients achieved seizure control with ASMs. Additionally, LEV was superior to CBZ about its effectiveness in controlling seizures and reducing the burden of interictal discharges, while VPA achieved the highest EEG response (60.8%). On the other hand, the presence of bilateral EEG findings was the most important risk factor for VPA therapy and patients that received VPA therapy had frequent bilateral discharges and their SWI values were ≥50%. Mean SWI value before the initiation of monotherapy was 31.7±29.7, 33.9±28.8, and 23.5±19.6 in the VPA, CBZ, and LEV groups, respectively, and the mean SWI value at the end of the second year in subsequent EEG recordings showed a significant decrease in the LEV group (17.9±14.0) compared

to the others (p=0.000). SWI increased with decreasing age (p=0.000). The effect of baseline SWI value on seizure recurrence varied with age, whereby baseline SWI value was higher in patients with a lower age at onset (Table 3). On the other hand, baseline SWI value decreased in subsequent EEG recordings and was lower in higher ages, children receiving monotherapy are shown in Figure 1.

The Predictive Value of SWI for ADHD

In our study, ADHD was observed in 19.9% (n=108) of the patients followed up with the diagnosis of SeLECTs. Of note, ADHD was present in 16.8% of girls vs 21.9% of boys (p=0.120). There was no relationship between the coexistence of AHDH and family history, epilepsy history, and number of siblings. On the other hand, ADHD was detected in 19.2% of the patients diagnosed before the age of five years, in 72.5% of patients diagnosed between 5-10 years of age, and in 8.3% of children diagnosed after the age of 10 years. On the other hand, ADHD was detected in 37.0% (n=40) of patients using VPA, in 41.6 % (n=45) of patients using CBZ, and in 21.2 % (n=23) of patients using LEV (p=0.410, p=0.001, and p=0.041, respectively). Additionally, patients with ADHD had a higher

Table 2. The comparison of selected drugs with respect to seizure outcome and EEG parameters in SeLECTS patient with/without ADHD

	VPA (n=111)		**CBZ (n=269)**		**LEV (n=133)**		**P**
			ADHD (-/+)				
Seizure frequency (N)							
<5 per year	60/35		136/65		91/39		
>5 per year	10/6		43/25		2/1		
Seizure outcome							
Seizure-free achivement time (months)	32.7±19.0	36.9±28.0	26.9±14.8	29.8±21.0	22.4±15.2	16.9±8.0	p^1:0.208, p^2:**0.023**, p^3:**0.013**
Overall seizure outcome	86 (88.6%)		208 (86.6%)		108 (**95.5%**)		
EEG Improvement							
EEG remission time (months)	23.9±11.9	26.9±9.2	18.9±17.6	16.7±10.5	17.4±15.3	18.9±12.9	p1:0.025, p^2:0.126, p^3:0.212
Spike-free EEG response (at 2years of ASM)	19 (**19.5%**)		25 (10.4%)		18 (15.9%)		p^1:<**0.001**, p^2:0.07 p^3:<**0.001**
Overall EEG remission rate	59 (**60.8%**)		143(34.2%)		63 (55.7%)		

(*) Spike-wave clearence in the two-year follow-up EEG, VPA: Valproic acid, CBZ: Carbamazepine, LEV: Levetiracetam

Table 3. Spike wave index (SWI) evolution in serial EEG; SeLECTS patient with/without ADHD

Monotherapy	**ADHD - (n=434)**				**ADHD + (n=108)**				
Age groups (n)	**Baseline SWI**	**First-year SWI**	**Second-year SWI**	**p**	**Age groups (n)**	**Baseline SWI**	**First-year SWI**	**Second-year SWI**	**p**
<5 years (n=108)	31.3±13.8	31.8±15.8	26.0±16.5	0.000	**<5 years (n=27)**	34.16±10.5	41.7±33.0	35.5±15.0	0.005
5-10 years (n=254)	29.0± 17.3	27.5± 16.5	20.0± 15.8	0.000	**5-10 years (n=63)**	37.6±18.6	38.1±34.6	34.2±12.2	0.002
>10 years (n=72)	28.4±14.4	26.4±10.0	26.6±14.6	0.000	**>10 years (n=18)**	20.9±19.4	30.2±20.4	35.0±16.3	NS
P	0.042	0.024	0.032		**P**	0.012	0.019	0.550	

SWI: Spike-wave index, NS: non-significant. (Ÿ) p<0.05

seizure frequency (p = 0.06) and a more extended seizure-free period (p=0.005), but when compared in terms of seizure reduction and EEG regression time, especially <5 years old patients, the VPA-using group showed faster seizure freedom and long-term EEG improvement (p=0.005). In subsequent EEG recordings of patients with ADHD, SWI was higher in the first-year (34.8±15.2) and third-year (21.25±12.25) recordings compared to patients without ADHD (p=0.0035). In children aged below five years, SWI was higher in patients with ADHD than in patients without (p=0.0038). Figure 1 illustrates the importance of the diagnostic value of SWI in subsequent EEG recordings in patients with ADHD. SWIs of patients with ADHD decreased significantly regardless of age, and the absence of ADHD findings in patients with decreased SWI values on subsequent EEG recordings was diagnostic (Figure 1).

Discussion

SeLECTS is a benign inherited epileptic syndrome characterized by age-dependent seizure semiology and EEG characteristics (1). This study evaluated the clinical features of patients with SeLECTS as well as their frequency of seizures, semiology, treatment decisions, EEG characteristics, and ASM selection trend in a large patient group. The results indicated that patients who had their first seizure before 5 years of age had more number of seizures than the other age groups. Among the ASMs, VPA group had the shortest time to the achievement of 50% reduction in seizures with monotherapy. Additionally we also investigated the predictive value of interictal paroxysmal discharges (spike-wave index -SWI) for seizure outcome, and differentiating antiseizure medications. SWIs of patients with ADHD decreased significantly regardless of age, and the absence of ADHD findings in patients with decreased SWI values on subsequent EEG recordings was diagnostic.

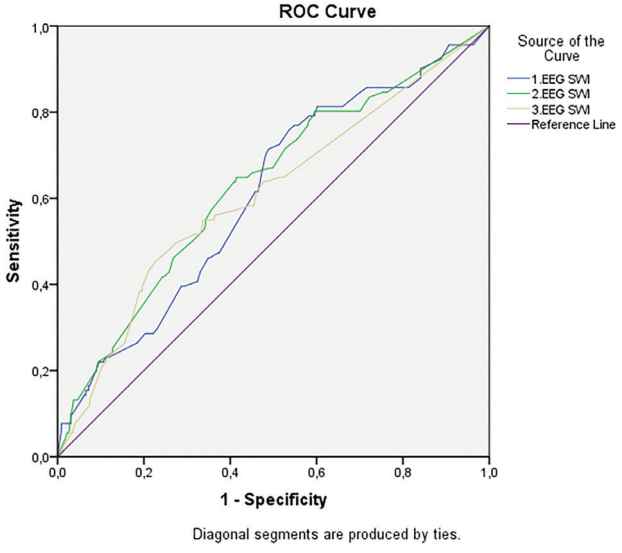

Figure 1. SWI evolution in serial EEG recording of children receiving monotherapy therapy in ADHD patients.
(1.EEG SWI: AUC: 0.607 [CI: 0.552-0.672], Cutoff value:33.5 Sensitivity: 59.8 Specificity: 59.2 PPD: 26.7 NPD: 85.6; 2.EEG SWI: AUC: 0.630 [CI: 0.564-0.696], Cutoff value:10.0 Sensitivity: 61.5 Specificity: 54.1 PPD: 26.9 NPD: 83.6; 3.EEG SWI: AUC: 0.607 [CI: 0.538-0.675], Cutoff value: 3.5 Sensitivity: 69.2 Specificity: 40.2 PPD: 22.4 NPD: 83.9)

To our knowledge, there are only a handful of studies demonstrating the onset and recurrence of seizures and the follow-up and course of rolandic discharges in SeLECTS with respect to seizure outcome and cognitive outcome (9-13). The age at the onset of seizures is significant for the development of brain plasticity, with the ages of 5-6 years constituting the most critical period (14-16). Arhan et al. (13) found that high-amplitude paroxysmal EEG discharges were most commonly seen in the age group of 6-8 years and there was a significant relationship between these discharges and seizure recurrence. In our study, patients that had their first seizure before 5 years had more seizures than the other patients (22.1%). Moreover, it was also noted that SWI decreased with increasing age. Taken together, the findings of our study indicated that seizure recurrence and the high frequency of paroxysmal discharges are dependent on patient age in children with SeLECTS. On the other hand, the presence of bilateral EEG findings was the most important risk factor for ADHD in monotherapy, and patients that received therapy had frequent bilateral discharges, use who have seizure but maximum drug doses and their SWI values were ≥50%. EEG regression time, especially <5 years old patients, the VPA-using group showed faster seizure freedom and long-term EEG improvement (p=0.005). In subsequent EEG recordings of patients with ADHD, SWI was higher in the first-year (34.8±15.2) and third-year (21.25±12.25) recordings compared to patients without ADHD (p=0.0035). In children aged below five years, SWI was higher in patients with ADHD than in patients without (p=0.0038).

Several studies have examined the differences among the drugs used in SeLECTS with regard to their effects on seizures and EEG (17-25). One of these studies evaluated the effects of LEV on EEG in SeLECTS and showed that it reduced epileptiform discharges (21,22). Literature indicates that children with similar bilateral findings on EEG respond well to VPA, CBZ, and OXC, while children with unilateral EEG findings respond better to CBZ or OXC (23). It has also been shown that low-dosage VPA and LEV monotherapies

are equally effective in controlling seizures and that VPA is more effective than LEV in improving electrophysiological abnormalities in children (20). CBZ is the initial drug of choice in children diagnosed with SeLECTS, while VPA is the first choice of monotherapy in pediatric patients with high SWI values (8). In our study, the selection of a patient population with a lower seizure frequency and a lower SWI value might have led to faster remission in the LEV group. In SeLECTS patients diagnosed with ADHD, bilateral SWIs of patients in EEG discharge and being younger than 5 years of age are important in choosing VPA receiving monotherapy.

SWI, a quantitative scoring system of the EEG calculated during NREM sleep. SWI is frequently used in the evaluation of electroencephalogram in CSWS patients (25-29). SWI can be highly useful in the follow-up period, particularly in patients with neuronal network problems, intense discharges, and high percentile rates. Accordingly, the present study aimed to investigate the utability of SWI in showing the intensity and load on EEG in SeLECTS patients (8). Among the studies investigating the suppression of interictal EEG abnormalities with drugs in patients with recurrent seizures, there have been very few studies examining the differences among the drugs with respect to the changes in the localizations of EEG patterns in subsequent EEG recordings (29). A study by Tekgul et al. (8) found no significant difference among the drugs with regard to EEG features (sharp waves and ripples [SWRs], localization, and topography) both before ASM treatment and just before ASM discontinuation. However, the rate of spike was more pronounced in the second year of treatment in children receiving monotherapy and in the third year of treatment in children receiving dual therapy. Kanemura et al. (20) evaluated EEG data based on spike activity in minutes, number of spikes, and localization and reported that the EEG response in patients that received LEV was faster than those who received CBZ/VPA. Our study had a remarkably larger patient population than those of other studies and, to our knowledge, it is the first study in the literature to analyze SeLECTS patients with SWI. Although SWI measured before the initiation of monotherapy was higher in the VPA group, it showed a significant decrease in the LEV group in subsequent EEG recordings compared to other groups. Moreover, LEV had the lowest SWI value (≤5.5) for the prediction of initial drug to be used in patients followed up for RE, which could be a reason as to why the LEV group had better seizure control and EEG response compared to other groups.

The present study also aimed to find clues about the relationship between ADHD and SeLECTS in children coexisting with these diseases. The prevalence of ADHD in SeLECTS is reported with higher rates when compared to other epilepsies. Of note, a previous study reported the prevalence of ADHD in SeLECTS patients as 64.9% (19). In our study, ADHD was present in 19.9% of the patients that were followed up with the diagnosis of SeLECTS. ADHD symptoms are reported to worsen as the age of seizure onset decreases (29). In addition, in epileptic patients, the presence of epileptic discharge or electrographical seizures on EEG in the periods when no or minimal seizures are seen may impair the attention and cognitive functions of the patients (26,29). Our study also examined the seizure status and the abnormalities in subsequent EEG recordings in patients with both ADHD and SeLECTS. In line with the literature both the seizure frequency and SWI were higher in children with ADHD in our patients. A previous study compared patients with temporal lobe epilepsy, a form of focal epilepsy, and patients with idiopathic generalized epilepsy with respect to seizure types and reported that attention control was more impaired in patients with temporal lobe epilepsy (29). In our study, patients with ADHD had more frequent seizures and had a more extended seizure-free time, while there was no significant difference between these two groups with regard to seizure reduction and EEG remission. It has also been shown that the presence of <50% EEG discharges in the NREM phase at the time of diagnosis, male gender, and coexistence of bilateral discharges. The fact that VPA is a frequently used ASM in ADHD with SeLECTS might be associated with the high prevalence of SeLECTS in our patients; however, the age at the first seizure was lower in the VPA group. Even so, no significant difference was found between VPA and other ASMs with regard to seizure control, EEG recovery time, ADHD onset age, and the coexistence of SeLECTS and ADHD. Age at the diagnosis of ADHD differs significantly among patients coexisting with ADHD and SeLECTS (18). In our study, it was observed that epilepsy and the requirement of ASMs were concentrated in two periods: early childhood and school-age. Additionally, keeping in mind the coexistence of these two diseases will contribute to the early diagnosis and treatment of patients. Although it is well known that ADHD can also be seen in preschool children, this disease is difficult to diagnose in this age group since it can be confused with normal age-related behaviors (23). Accordingly, clinicians need to be aware of the coexistence of these two diseases, particularly in younger age groups. Additionally, we suggest that the measurement of SWI on EEG may be important for clinical follow-up for the prediction and follow-up of these two diseases (30). In our study, SWI was higher in children aged below 5 years with ADHD than in those without. In

addition, SWIs were significantly higher in patients with ADHD compared to those without. On the other hand, SWIs of patients with ADHD decreased significantly regardless of age, and the absence of ADHD findings in patients with decreased SWI values on subsequent EEG recordings was diagnostic. Accordingly, it is necessary to determine the specific features of the treatment and prognosis as well as the clinical and EEG parameters in children coexisting with SeLECTS and ADHD. SWIs of patients with ADHD decreased significantly regardless of age, and the absence of ADHD findings in patients with decreased SWI values on subsequent EEG recordings was diagnostic.

In recent years, the clinical importance of the Spike-Wave Index (SWI) in children diagnosed with SeLECTS has been increasingly investigated. Yilmaz et al. (9), through a ten years follow-up study, demonstrated the prognostic value of SWI, while our study showed that SWI levels were particularly higher in patients with comorbid ADHD (8,30). The association between epilepsy and ADHD in terms of neuroimaging was evaluated by Rubinstein et al. (10), who suggested standard neurophysiological mechanisms. Furthermore, Yuen et al. (11) systematically reviewed the prevalence of ADHD in children with epilepsy, supporting the 19.9% prevalence found in our study. Regarding the choice of antiseizure medications, a systematic review by Wirrell et al. (12) emphasized that LEV is more effective in seizure control, while VPA is superior in EEG normalization. These findings are consistent with the results of our current study.

Study Limitations

Our study has some limitations of the retrospective studies; first: the selection characteristics of ASM in children with SeLECTS was not based on a standardized protocol. There was no clear single protocol for dosage adjustment or standardization of starting dose. Second; A full spectrum of well-defined SeLECTS patients who stayed on ASM therapy only monotherapy were included into the study group. Data on seizure outcome and drug-related side effects were obtained from the retrospective records of the patients. This situation prevented us from obtaining an opinion about the patients whose drug tolerance development may occur during ASM therapy and treatment withdrawal rate due to adverse events. This study also compares certain demographic, seizure semiology, seizure burden, and EEG characteristics (baseline SWIs and follow-up SWIs on ASMs) in children with /without ADHD in a large SeLECTS cohort.

Conclusion

This study provides following conclusions. Among the most commonly used ASMs CBZ, LEV, and VPA are recommended as first-line agents in the treatment of focal seizures in children, as per NICE guidelines (1). SeLECTS is a characteristics ADHD was seen in 19.9% of the patients followed up with a diagnosis of SeLECTS. As the number of antiseizure drugs used in the therapy increased, the scores associated with attention deficit increased. SWI might be used for prediction of ASM selection and certain cognitive co-mobidities like ADHD. Patients with ADHD had more frequent seizures and had a more extended seizure-free time. SWI was higher in children aged below 5 years with ADHD than in those without. In addition, SWIs were significantly higher in patients with ADHD compared to those without. On the other hand, SWIs of patients with ADHD decreased significantly regardless of age, and the absence of ADHD findings in patients with decreased SWI values on subsequent EEG recordings was diagnostic.

Ethics

Ethical Approval: This study was approved by the Clinical Research Ethics Committee of Karadeniz Technichal Universty under the decision numbered 2023/512, date: 15.04.2021 and was conducted as a single-center, retrospective study.

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

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