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Adolescent-Onset Epilepsy: Clinical Features and Predictive Factors for First-Year Seizure Freedom

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Abstract

Background Teenagers with epilepsy require special attention to ensure a successful treatment journey. Our objective was to delineate the clinical characteristics of adolescent-onset epilepsy (AOE) and investigate the predictive factors influencing first-year seizure freedom.

Methods We retrospectively analyzed the medical records of patients whose first seizure occurred between the ages of 10 and 19 years and who received antiseizure medication (ASM) treatment for at least 12 months.

Results A total of 67 patients were included, with an average age of 13.5 ± 2.3 years at the onset of their first seizure. The average follow-up period was 45.2 ± 16.9 months, and comorbid conditions were present in 23 patients (34.3%). The majority of the patient population (83.6%) was affected by generalized epilepsy. The most common epilepsy syndrome was epilepsy with generalized tonic-clonic seizures alone at 70.1% (juvenile myoclonic epilepsy 11.9%, juvenile absence epilepsy 1.5%). Regarding ASM treatment, 31 patients (46.3%) received monotherapy, and 28 (41.8%) received dual therapy. Five patients (7.5%) encountered issues related to medication adherence. First-year seizure freedom was observed in 42 patients (62.7%). In multivariate analysis, a negative family history of epilepsy (odds ratio 12.1, 95% confidence interval 1.27–115.44, $p = 0.030$) was identified as a strong predictive factor of first-year seizure freedom, along with ASM monotherapy (odds ratio 3.99, 95% confidence interval 1.05–15.21, $p = 0.043$).

Conclusion These findings suggest that AOE typically exhibits effective control of seizures. A negative family history of epilepsy and ASM monotherapy emerges as robust predictor of achieving favorable outcomes within the early stage of treatment.

Keywords
- adolescent
- seizures
- epilepsy

Introduction

Epilepsy in adolescence represents a considerable neurological burden, with a prevalence ranging from approximately 1.5 to 2%.[1] The World Health Organization defines adolescence as the period of life between 10 and 19 years of age.[2] Adolescence is a period of substantial change involving growth into adulthood across physiological, psychological, and behavioral aspects.[3–5] During this period, the population faces challenges associated with their pursuit of independence, perception of

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invulnerability, tendency toward risk-taking behavior, and emphasis on peer relationships.[3–7] Special attention is particularly crucial for teenagers with epilepsy, as epilepsy and its long-term treatment can pose additional difficulties.[6,7] Furthermore, these individuals gradually become more actively involved in treatment of their epilepsy, no longer relying solely on parents or caregivers. Therefore, having accurate information and a proper understanding of epilepsy becomes crucial for maintaining a successful treatment journey.

Adolescent epilepsy encompasses not only epilepsy that emerges during adolescence but also various epilepsy syndromes that manifest in infancy or childhood and persist through adolescence such as photosensitive occipital lobe epilepsy, Lennox–Gastaut syndrome, generalized epilepsy with febrile seizure plus, childhood absence epilepsy, and epilepsy with myoclonic astatic seizures.[1,8,9] Although it is challenging to precisely categorize epilepsy with onset during adolescence, several epilepsy syndromes have been recognized including juvenile myoclonic epilepsy (JME), juvenile absence epilepsy (JAE), and epilepsy with generalized tonic-clonic seizures alone (GTCA), which are commonly grouped under the term idiopathic generalized epilepsy (IGE). Additionally, later-onset self-limited epilepsy with centrotemporal spikes (SeLECTS), mesial temporal lobe epilepsy, and focal epilepsy syndromes have been defined.[1,8–10] Adolescent-onset epilepsy (AOE), which warrants particular attention, is recognized for its positive clinical trajectory, being quite responsive to medication, and often resolving on its own.[4] This disease is highly associated with a nonlesional etiology and infrequent neurological and psychiatric comorbidities.[11]

A limited number of studies have described the profile of AOE and identified potential risk factors for unfavorable outcomes such as seizure recurrence.[11–15] Regrettably, many of these analyses focused on specific epilepsy syndromes in adolescence or investigated all types of epilepsy during this period, not just AOE. Furthermore, cultural differences, societal perceptions such as social stigma, and treatment environments within the society to which the adolescents belong must also be considered. Consequently, it has been challenging to provide a comprehensive understanding of the characteristics unique to AOE. The initial treatment response, which can provide insight into the final prognosis, is crucial not only for patients and their families facing AOE but also for clinicians. The objective of this study was to outline the clinical attributes of AOE and explore predictive factors influencing first-year seizure freedom.

Methods

Patients

This retrospective study included patients with AOE, who were prescribed antiseizure medication (ASM) treatment at the pediatric epilepsy center of the Chungbuk National University Hospital (CBNUH) in South Korea, spanning from March 2018 to February 2023. We classified epilepsy syndromes according to the recently published International League Against Epilepsy classification of epilepsy syndromes.[8,16] All patients who met the following inclusion criteria and did not meet any of the exclusion criteria were enrolled in the study. The inclusion criteria encompassed (a) first unprovoked seizure (UPS) occurring between the ages of 10 and 19 years, (b) a presumptive diagnosis of epilepsy (comprising at least two UPSs) or a specific epilepsy syndrome, (c) prompt treatment following the first UPS, and (d) a minimum follow-up duration of 12 months after ASM treatment initiation. Patients with a history of prior epilepsy treatment, insufficient data due to reasons like transfer to another hospital, or those who had not received ASM treatment were excluded.

Treatment Approach

Our standard protocol for pediatric epilepsy treatment follows these steps: For patients presenting with their first UPS, a comprehensive approach is taken. This includes detailed medical history collection, neurological examination, blood tests, interictal electroencephalogram (EEG), and brain magnetic resonance imaging (MRI). The decision to initiate ASM treatment is made through discussions with the patient and their caregivers. The factors under consideration encompass the diagnosis of epilepsy and the assessment of the risk associated with future seizures. In other words, depending on the seizure burden, ASM treatment may be initiated even if it was a single episode of UPS. In patients with two or more epileptic seizures, a more proactive treatment approach is recommended. The choice of ASM is based on the unique characteristics of the patient's epilepsy syndrome and their treatment adherence. If persistent seizures occur after initiating the first ASM, the clinical decision may involve switching to another ASM or adding a second ASM. In cases where adverse events occurred, we either switched ASM or adjusted the dosage, sometimes adding another medication based on tolerability. Follow-up EEGs are scheduled initially between 6 and 12 months after treatment initiation and subsequently on an annual basis. Patient compliance is assessed by direct questioning during visits, along with periodic measurement of blood drug levels when feasible. Generally, we advise gradually discontinuing ASMs if the patient remains seizure-free for at least 2 years and maintains a normal EEG. However, considering patient and caregiver preferences, treatment periods can be extended. This assessment involves considering potential risks and the potential impact of seizure recurrence on a child's school life and overall well-being.

Data Collection

The retrospective collection of data was conducted by reviewing electronic medical charts. The gathered information included sex, family history of epilepsy, prior history of epilepsy treatment, comorbid conditions such as developmental delay (DD), intellectual disability (ID), and autism spectrum disorder (ASD), seizure type at presentation (predominant seizure semiology by eyewitness), type of epilepsy syndrome, age at the occurrence of the first epileptic seizure and the commencement of ASM, results from EEG and brain MRI, frequency of seizures, time interval between the first

UPS and ASM initiation, details about the number, types, and adverse events associated with ASM use, duration of ASM treatment, and any issues related to compliance. We evaluated the effectiveness of treatment by assessing seizure frequency at the 6-, 12-, and 24-month marks following ASM initiation. Additionally, we evaluated clinical predictive factors associated with first-year seizure freedom.

Statistical Analysis

The statistical analysis was performed using R software, version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Numerical values are presented as number (percentage) or median (interquartile range). The comparison of variables was conducted using Student's *t*-test, Wilcoxon's signed-rank test, chi-square test, and Fisher's exact test. To determine the relationship between various independent variables and first-year seizure freedom, we employed logistic regression analysis. Variables demonstrating a statistically significant difference ($p < 0.2$) in univariate analysis were incorporated into the multivariate logistic regression model. The results are presented as adjusted odds ratios (ORs) with their corresponding 95% confidence intervals (95% CIs). For all statistical tests, $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

Out of 76 patients diagnosed with AOE, 9 patients were excluded from the study due to ASM treatment duration of less than 12 months (8 patients) and insufficient data (1 patient). Consequently, 67 patients (44 [65.7%] male) were included in this study, and their summarized details are presented in ►**Table 1**. The median age at the onset of the first UPS and the initiation of ASM was 13.4 (11.2–15.6) years and 13.8 (12.2–16.5) years, respectively, demonstrating an average interval of 2.7 (1.0–9.9) months from onset to treatment initiation. The mean duration of follow-up and ASM treatment was 44.8 (33.4–57.0) and 35.5 (26.0–48.9) months, respectively. Six patients (9.0%) had a first-degree family history of epilepsy (9.0%), and 23 patients (34.3%) had comorbid conditions.

Considering the seizure semiology and EEG findings, 56 patients (83.6%) were categorized as having generalized epilepsy, specifically IGE epilepsy syndrome. Focal epilepsy included late-onset SeLECTS (4 patients), frontal lobe epilepsy (1 patient), occipital lobe epilepsy (1 patient), and other focal epilepsy syndromes (5 patients). The most common type of seizure based on eyewitness accounts was generalized tonic-clonic (GTC) seizures, accounting for 80.6%, followed by myoclonic seizures at 11.9% (with 6 patients experiencing both GTC and myoclonic seizures), focal impaired awareness seizures at 6.0%, and absence seizures at 1.5%. Seven patients (10.4%) exhibited only a single episode of seizure during the follow-up period. Among them, five patients displayed abundant interictal epileptiform discharges on EEG, whereas two patients had both ID and ASD, leading to a higher perceived risk of subsequent seizures, prompting the initiation of ASM treatment. At the initiation of ASM treatment, brain MRI and EEG findings were considered normal in 92.5 and 61.2% of patients, respectively. The abnormal findings on brain MRI included mild cerebral atrophy in two cases, incomplete rotation of the left hippocampus in one case, colpocephaly in one case, and cerebellar atrophy in one case. Two patients (3.0%) exhibited photoparoxysmal responses on EEG, indicating the presence of photosensitivity.

Seizure Outcome

Thirty-one patients (46.3%) received ASM monotherapy, whereas 28 patients (41.8%) underwent dual therapy (►**Table 1**). On average, a total of 1.8 ASMs were used across the entire group. Twelve patients (17.9%) experienced ASM-related adverse events, including sleepiness, dizziness, aggressive behavior, hair loss, tremor, and skin rash. After beginning ASM treatment, 26 patients (38.8%) experienced no further seizures until the last visit. An additional 11 patients (16.4%) achieved seizure freedom within 6 months, and 5 more patients (7.5%) attained a seizure-free status within 12 months. Thus, 42 patients (62.7%) experienced seizure freedom during the first year. Nonetheless, 18 out of 56 patients (32.1%) who were followed up for 24 months continued to experience seizures. Compliance issues with medication adherence were observed in five patients (7.5%).

Epilepsy Features

►**Table 2** compares the clinical features of patients with AOE based on their epilepsy type. The two groups were not significantly different in terms of age at first seizure, age at ASM initiation, and the interval from onset to initiation. Abnormalities in MRI (3.6 vs. 27.3%, $p = 0.028$) and EEG (32.1 vs. 72.7%, $p = 0.018$) were more frequently observed in the focal epilepsy group. The average number of ASMs was similar in both groups. Although monotherapy was more common in the focal epilepsy group (63.6 vs. 42.9%) and dual therapy was more frequent in the generalized epilepsy group (46.4 vs. 18.2%), this difference was not statistically significant. The proportion of patients with only a single episode of seizure was slightly higher in the focal epilepsy group at 18.2%, compared with 8.9% in the generalized epilepsy group; however, this difference did not reach statistical significance. The percentage of patients who became seizure-free within the first 12 months of treatment was not significantly different between the generalized epilepsy (60.7%) and focal epilepsy (72.7%) groups. Similarly, after 24 months, the percentage of patients who continued to experience persistent seizures was similar in both groups, with rates of 32.7% (16/49) and 28.6% (2/7), respectively. Although the number of cases is limited, compliance issues such as simple forgetfulness and feelings of stigma related to taking ASMs were also comparable, with rates of 7.1 and 9.1%, respectively.

►**Table 3** describes the clinical characteristics and treatment outcomes of 65 adolescents with IGE. Among these, the majority (47 patients, 83.9%) had GTCA, 8 patients (14.3%) had JME, and 1 patient (1.8%) had JAE. Approximately one-third of patients with GTCA were female (29.8%), whereas in JME, this

Table 1 Summarized details of the study population ($n = 67$)

Variable	Value
Sex	
Male	44 (65.7)
Female	23 (34.3)
Age at first UPS, years	13.4 (11.2–15.6)
Age at ASM initiation, years	13.8 (12.2–16.5)
Time interval between first UPS and ASM initiation, months	2.7 (1.0–9.9)
Follow-up duration, months	44.8 (33.4–57.0)
Duration of ASM treatment, years	35.5 (26.0–48.9)
Family history of epilepsy	6 (9.0)
Comorbid conditions (DD, ID, ASD)	23 (34.3)
Epilepsy type	
Generalized	56 (83.6)
Focal	11 (16.4)
Seizure type[a]	
Generalized tonic/tonic-clonic	54 (80.6)
Absence	1 (1.5)
Myoclonic[b]	8 (11.9)
Focal impaired awareness	4 (6.0)
Single episode of seizure	7 (10.4)
Brain MRI	
Normal	62 (92.5)
Abnormal	5 (7.5)
EEG	
Normal	41 (61.2)
Abnormal	26 (38.8)
Photosensitivity[c]	2 (3.0)
ASM treatment	
Monotherapy	31 (46.3)
Dual therapy	28 (41.8)
Polytherapy ($\geq$3 ASMs)	8 (11.9)
Mean number of ASMs, mean $\pm$ SD	1.8 ± 0.8
ASM-related adverse events	12 (17.9)
Seizure occurrence after ASM initiation	
None	26 (38.8)
Seizure-free within 6 months	11 (16.4)
Seizure-free within 12 months	5 (7.5)
Seizure-free within 24 months[d]	8 (14.3)
Persistent seizures at 24 months[d]	18 (32.1)
Documented compliance issue	5 (7.5)

ASD, autism spectrum disorder; ASM, antiseizure medication; DD, developmental delay; EEG, electroencephalogram; ID, intellectual disability; MRI, magnetic resonance imaging; SD, standard deviation; UPS, unprovoked seizure.
Data are *n* (%) or median (interquartile range).
[a]Predominant seizure semiology based on eyewitness reports.
[b]Including coexisting generalized tonic-clonic seizure.
[c]Abnormal EEG response to visual stimuli known as a photoparoxysmal response.
[d]Data available from 56 patients.

Table 2 Comparison of clinical features between epilepsy types

	Generalized ($n = 56$)	Focal ($n = 11$)	*p*-Value
Age at first UPS, years	13.6 (11.3–15.7)	12.5 (10.7–13.5)	0.095
Age at ASM initiation, years	14.1 (12.3–16.6)	12.9 (10.8–14.0)	0.055
Abnormal MRI	2 (3.6)	3 (27.3)	0.028
Abnormal EEG	18 (32.1)	8 (72.7)	0.018
Interval between first UPS and ASM initiation, months	2.9 (1.1–13.6)	1.5 (0.3–6.6)	0.064
ASM treatment			
Monotherapy	24 (42.9)	7 (63.6)	0.322
Dual therapy	26 (46.4)	2 (18.2)	0.104
Polytherapy (≥3 ASMs)	6 (10.7)	2 (18.2)	0.609
Mean number of ASMs, mean ± SD	1.8 ± 0.8	1.6 ± 0.8	0.935
Single episode of seizure	5 (8.9)	2 (18.2)	0.323
Seizure occurrence after ASM initiation			
Seizure-free within 12 months	34 (60.7)	8 (72.7)	0.518
Persistent seizures at 24 months	16 (32.7)[a]	2 (28.6)[b]	>0.999

Data are *n* (%) or median (interquartile range).
ASM, antiseizure medication; EEG, electroencephalogram; MRI, magnetic resonance imaging; SD, standard deviation; UPS, unprovoked seizure.
[a]Data available from 49 patients.
[b]Data available from seven patients.

Table 3 Profiles of idiopathic generalized epilepsies ($n = 56$)

	GTCA	JAE	JME
Patients	47 (83.9)	1 (1.8)	8 (14.3)
Female sex	14 (29.8)	1 (100.0)	4 (50.0)
Age at first UPS, years	13.5 (11.2-15.6)	11.2	15.3 (12.5-17.2)
Age at ASM initiation, years	14.1 (12.2-16.5)	13.1	15.4 (13.5-18.0)
Interval[a], months	2.7 (1.1-14.3)	22.9	4.7 (0.8-10.6)
Family history of epilepsy	4 (8.5)	0 (0.0)	1 (12.5)
Normal MRI	45 (95.7)	1 (100.0)	8 (100.0)
Normal EEG	32 (68.1)	1 (100.0)	6 (75.0)
First choice of ASM			
Levetiracetam	27 (57.4)	0 (0.0)	6 (75.0)
Lamotrigine	13 (27.7)	0 (0.0)	0 (0.0)
Valproate	7 (14.9)	0 (0.0)	2 (25.0)
Ethosuximide	0 (0.0)	1 (100.0)	0 (0.0)
ASM monotherapy	18 (38.3)	0 (0.0)	6 (75.0)
Seizure-free within 12 months	27 (57.4)	1 (100.0)	6 (75.0)

Data are *n* (%) or median (interquartile range).
ASM, antiseizure medication; EEG, electroencephalogram; GTCA, epilepsy with generalized tonic-clonic seizures alone; JAE, juvenile absence epilepsy; JME, juvenile myoclonic epilepsy; MRI, magnetic resonance imaging; UPS, unprovoked seizure.
[a]Inteval between first unprovoked seizure and antiseizure medication initiation.

applied to half of the patients (50.0%). The median age of the first seizure was higher in JME at 15.3 years, but the time to treatment initiation was longer compared with GTCA, with a median interval of 4.7 months. Two-thirds of patients with GTCA (68.1%) and JME (75.0%) showed a normal EEG. For patients with GTCA, levetiracetam was the first-choice ASM for about half (57.4%), followed by lamotrigine (27.7%) and valproate (14.9%). Among patients with JME, levetiracetam was also chosen in 75% of cases, with valproate (25.0%) being used in the remaining cases. Only 38.3% of patients with GTCA received monotherapy, whereas for JME, it was as high as 75.0%. The percentage of patients with a favorable treatment outcome was 57.4% in the GTCA group and 75.0% in the JME group. While only one patient with JAE was included in this study, making comparative analyses difficult, the results were consistent with the characteristic clinical features of JAE. Seizure onset occurred at the age of 11.2 years during early adolescence, with a considerable gap of 22.9 months until treatment initiation. Ethosuximide was the first medication used, and seizure freedom was achieved within 12 months.

Predictive Factors for First-Year Seizure Freedom

►**Table 4** demonstrates a comparison of the first-year seizure freedom rates among predictors. In univariate analysis, only comorbid conditions (OR 3.47, 95% CI 0.20–2.33, $p = 0.037$) and ASM monotherapy (OR 4.66, 95% CI 0.48–2.71, $p = 0.010$) were significantly associated with an achievement of first-year seizure freedom. In the multivariate analysis, which encompassed all independent variables with p-values below 0.2, a negative family history of epilepsy (OR 12.1, 95% CI 1.27–115.44, $p = 0.030$) was identified as a strong predictive factor, along with ASM monotherapy (OR 3.99, 95% CI 1.05–15.21, $p = 0.043$).

Discussion

In the present study, 62.7% of all patients with AOE attained seizure freedom within the first year. Among these patients, 88.1% (37/42) achieved being seizure-free within 6 months after initiating ASM treatment. Moreover, 38.8% (26/67) never had additional seizures until their last visit, with a mean follow-up duration of 40.5 months. In the 24-month evaluation, an even higher seizure-free rate of 74.6% was observed.

Previous studies involving adolescents and adults reported 1-year seizure-free rates ranging from 63.7 to

Table 4 Predictive factors for first-year seizure freedom

Factor	First-year seizure freedom (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Sex		0.67 (−1.44–0.65)	0.625	–	–
Female	13/23 (56.5)	–	–	–	–
Male	29/44 (65.9)	–	–	–	–
Age at first UPS		1.95 (−0.41–1.84)	0.358	–	–
< 13 YO	16/22 (72.7)	–	–	–	–
≥13 YO	26/45 (57.8)	–	–	–	–
Family history of epilepsy		3.81 (−0.38–3.37)	0.186	12.1 (1.27–115.44)	0.030
Negative	40/61 (65.6)	–	–	–	–
Positive	2/6 (33.3)	–	–	–	–
Comorbid conditions		3.47 (0.20–2.33)	0.037	2.09 (0.56–7.73)	0.270
No	32/44 (72.7)	–	–	–	–
Yes	10/23 (43.5)	–	–	–	–
Epilepsy syndrome		1.92 (−0.91–2.63)	0.700	–	–
JME	6/8 (75.0)	–	–	–	–
Other than JME	36/59 (61.0)	–	–	–	–
EEG		0.35 (−2.22–0.003)	0.097	0.22 (0.05–1.04)	0.056
Normal	22/41 (53.7)	–	–	–	–
Abnormal	20/26 (76.9)	–	–	–	–
Epilepsy type		0.58 (−2.14–0.81)	0.518		
Generalized	34/56 (60.7)	–	–	–	–
Focal	8/11 (72.7)	–	–	–	–
Time until ASM initiation[a]		1.31 (−0.76–1.35)	0.811	–	–
≥6 months	16/24 (66.7)	–	–	–	–
< 6 months	26/43 (60.5)	–	0.010	–	0.043
ASM treatment		4.66 (0.48–2.71)	–	3.99 (1.05–15.21)	–
Monotherapy	25/31 (80.6)	–	–	–	–
≥2 ASMs	17/36 (47.2)	–	–	–	–
ASM-related adverse events		2.88 (−0.21–2.39)	0.183	3.05 (0.56–16.47)	0.195
No	37/55 (67.7)	–	–	–	–
Yes	5/12 (41.7)	–	–	–	–

ASM, antiseizure medication; CI, confidence interval; EEG, electroencephalogram; JME, juvenile myoclonic epilepsy; OR, odds ratio; UPS, unprovoked seizure; YO, years old.
[a]Time interval between the first UPS and ASM initiation.

68.0%, which aligns with our findings.[17,18] These findings are also similar to the results recently reported by Kim et al, where seizure freedom at 1 year was 58.4%.[14] This Korean study, which involved a 10-year follow-up observation of 137 AOE patients aged 13 to 19 years, reported that terminal remission was achieved in 67.9% of cases. Additionally, through bivariate logistic regression analysis, they confirmed a strong association between seizure freedom at 1 year and terminal remission. By contrast, in a large-scale Scottish study involving 332 adolescents aged 13 to 19 years who received their first-time ASM, the overall 1-year seizure-free rate was reported to be lower at 38.0% (126/332).[15] Considering that 29% in their study achieved seizure freedom beyond 12 months, the higher rate of poor ASM tolerability at 21% could be a reason for the delayed seizure control.

In the current study, 88.1% of all patients achieved seizure control with the use of either one or two ASMs. However, the percentage of patients who achieved first-year seizure freedom with monotherapy was lower at 59.5% (25 patients), compared with findings in previous studies.[11,15] A Canadian study involving 65 adolescents stated that successful control of seizures with monotherapy was achieved in approximately 85% of cases.[11] In the Scottish study, 83% of patients who achieved seizure freedom managed to do so with monotherapy.[15] This difference can be attributed to a preference for dual therapy in our center. When additional seizures or ASM-related adverse events occurred despite appropriate dosages and treatment durations, our approach involved introducing combination therapy with lower doses rather than switching to another medication and escalating the dosage. Recent research targeting patients with IGE suggested that, when the first-line monotherapy fails, switching to levetiracetam or lamotrigine monotherapy might be less effective than employing combination therapy involving medications such as lamotrigine, levetiracetam, or valproic acid.[19] This second-line combination therapy broadens the treatment spectrum mechanistically and effectively reduces the occurrence of dose-dependent adverse events. A previous Korean study had results similar to ours, with 65.0% utilizing monotherapy regimens. The authors also mentioned that approximately 50% of patients with IGE required polytherapy to achieve seizure freedom.[14]

The present study reported several interesting findings in patients with AOE. The proportion of male patients was rather high at 65.7%, but this is not significant because previous studies found no clear sex differences in patients with AOE.[11–13,15] Comorbid conditions such as DD/ID or ASD were relatively more frequent at 34.3%, but the frequency of structural abnormalities in brain MRI was very low (7.5%). Hence, it is likely that the inclusion of patients exhibiting complex phenotypes is due to our institution being a referral center. Nevertheless, this factor is not considered to have a direct contribution to the underlying causes of epilepsy. In the initial EEG, 38.8% of our patients showed focal or generalized interictal epileptiform discharges. This was similar to the 33.6% observed in the Scottish study.[15] On the other hand, it is worth noting that about two-thirds of patients with AOE had a normal initial EEG. When diagnosing AOE, it is important not to overly rely on EEG testing and to focus on thorough history taking. Additionally, repeat EEG testing is necessary to verify any abnormal findings. In our study, two patients diagnosed with JME were found to have generalized epileptiform discharges in subsequent EEG testing although the initial EEG was normal. Furthermore, the high rate of GTC seizures at 80.6% is noteworthy. This might be attributed to the fact that patients with IGE accounted for 83.6% and that focal to secondary generalized seizures were included without differentiation. Previous studies also showed rates ranging from 65.1 to 76.9% when including focal to secondary GTC seizures.[11,12,15]

As evident from our study results, the majority of epilepsies in newly diagnosed teenagers were categorized as IGE (83.6%). This proportion is quite substantial and comparable to studies encompassing not only AOEs but also childhood-onset epilepsies, where the percentage of patients diagnosed with IGE ranged from 43.9 to 60.0%.[11,13,20] Within this IGE spectrum, GTCA constituted an absolute majority at 83.9%. This may be attributed to the fact that our patient population had a very low rate of focal epilepsy due to scarce symptomatic etiologies, resulting in a relatively higher occurrence of generalized epilepsy. Thus, these results provide a genuine representation of AOE. Moreover, considering that one-third (33.9%) were adolescent girls undergoing pubertal hormonal changes, levetiracetam or lamotrigine were preferentially selected as initial ASMs over valproic acid.[21] In addition, 11 patients (19.6%) exhibited adverse events like increased sleepiness, dizziness, and mood instability with the initial ASM. These adverse events were effectively managed through the aforementioned combination therapy approach.[19]

We also investigated which predictive factors are associated with first-year seizure freedom in patients with AOE. Many studies reported associations between seizure outcomes, including seizure recurrence, and factors such as female sex, age under 13 years at the first UPS, generalized epilepsy, JME, family history of epilepsy, and EEG abnormalities.[11,12,14,15,22] Our univariate analysis showed significant differences between those who achieved first-year seizure freedom and those who did not in terms of comorbid conditions and ASM monotherapy. Multivariate analysis specifically highlighted the significant association with a negative family history of epilepsy and ASM monotherapy. Including our study results, a family history of epilepsy has been observed in 9 to 15% of patients with AOE.[14,15] A study of adolescents and adults has also reported a family history of epilepsy as a predictive factor for poor outcomes.[22] Furthermore, it is well known that the seizures of most adolescent patients are effectively controlled with monotherapy.[11,15] However, one report indicates a poor tolerability rate of up to 21% for the first ASM.[15] Ultimately, it is necessary to have a tailored ASM regimen for each adolescent patient. Since comorbidity also greatly affects compliance, effectively managing compliance is crucial for achieving positive outcomes for AOE. Numerous previous studies focusing on teenagers with epilepsy consistently emphasize the need for special attention and care for this population.[11,13,20] In many cases, the first seizures that

teenagers encounter are of GTC semiology and have a higher likelihood of occurring at school. This experience can be impactful for both the patients and their families. The rates of medication nonadherence among adolescents with epilepsy vary widely, spanning from 35 to 79%.[23] This behavior is strongly influenced by two significant prognostic factors: young age and a lack of awareness regarding the importance of taking prescribed medications.[4] These challenges are exacerbated by self-esteem issues commonly faced by adolescents. Targeting treatment directly toward adolescents, not just their parents, is essential. Providing proper education and information about epilepsy, involving teenagers in treatment plans, and addressing not only the parents but also the adolescents themselves are crucial steps.[23]

This study has several limitations. The patients were recruited from a single center, which resulted in a small sample size, and the study was conducted retrospectively. Nevertheless, standardized treatment was administered as it is the sole referral center in the region. Additionally, because the follow-up period was short, long-term outcomes could not be analyzed, and information about treatment outcomes and seizure recurrence could not be provided. Nonetheless, considering the findings of previous studies indicating that first-year seizure freedom, as assessed in our study, is correlated with the ultimate outcome, it can serve as a crucial indicator for promoting strong adherence among patients at the treatment outset. Finally, apart from issues related to ASMs, the various physical, psychological, and social changes experienced by teenagers were not investigated in relation to epilepsy treatment. This will be addressed in the future through long-term tracking observations and the operation of specialized clinics for adolescents.

Summary

In summary, our findings suggest that epilepsy onset during adolescence generally demonstrates good control of seizures. Additionally, we have identified that a negative family history of epilepsy and ASM monotherapy serve as strong predictors of achieving favorable outcomes within the early stage of treatment. Understanding not only the seizures but also the characteristics of adolescence is crucial for successful epilepsy treatment. We expect that our study findings will offer support not only to health care professionals but also to individuals and caregivers who are navigating their initial experience with epilepsy and the subsequent treatment process.

Ethics Statement

The study was conducted in adherence to the principles outlined in the Declaration of Helsinki and received approval from the Institutional Review Board of Chungbuk National University Hospital (IRB No. 2023-08-003). Given the retrospective design of the study, the requirement for written consent was waived.

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Conflict of Interest

None declared.

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