

Long-term outcome in children with infantile epileptic spasms syndrome: a multicenter retrospective study in Korea

Sun Ah Choi, MD, PhD¹, Minhye Kim, MD², Hye Jin Kim, MD³, Woo Joong Kim, MD⁴, Byung Chan Lim, MD, PhD⁴, Ji Yeon Han, MD⁵, Hunmin Kim, MD, PhD⁶, Min-Jee Kim, MD, PhD⁷, Mi-Sun Yum, MD, PhD⁷, Jiwon Lee, MD, PhD⁸, Jeehun Lee, MD, PhD⁸, Hyewon Woo, MD⁹, Jon Soo Kim, MD, PhD⁹

¹Department of Pediatrics, Ewha Womans University Mokdong Hospital, Ewha Womans University College of Medicine, Seoul, Korea; ²Department of Pediatrics, Inje University Haeundae Paik Hospital, Busan, Korea; ³Department of Pediatrics, Seoul National University Boramae Hospital, Seoul National University College of Medicine, Seoul, Korea; ⁴Department of Pediatrics, Seoul National University Children's Hospital, Seoul National University College of Medicine, Seoul, Korea; ⁵Department of Pediatrics, Inha University Hospital, Inha University College of Medicine, Incheon, Korea; ⁶Department of Pediatrics, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea; ⁷Department of Pediatrics, Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Korea; ⁸Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; ⁹Department of Pediatrics, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Korea

Background: Infantile epileptic spasms syndrome (IESS) is a severe form of infantile epilepsy with a high lifetime morbidity burden.

Purpose: We aimed to assess the long-term epilepsy and neurodevelopmental outcomes based on how children with IESS have been managed over the past few decades.

Methods: This retrospective multicenter study included children diagnosed with IESS between 1994 and 2021 with a minimum follow-up period of 2 years. Data on demographics, clinical features, medical history, diagnostic evaluations, and treatments used to control spasms were collected. Epilepsy and neurodevelopmental outcomes were assessed at final follow-up.

Results: A total of 378 infants with IESS were included. The mean age at onset of spasms was 7.3 (range, 1–24) months and mean follow-up duration was 7.9 (range, 2–28) years. Etiologies were identified in 65.1% of cases, with acquired structural etiologies being the most prevalent (29.9%). Among the genetic and genetic-structural etiologies, tuberous sclerosis complex (n=35), Down syndrome (n=8), Miller-Dieker syndrome (n=3), and 15q duplication syndrome (n=3) were the most common. Vigabatrin was prescribed to 93.9% of the patients, suggesting that it was the mainstay of treatment. At the last follow-up, 77.8% of the children remained on antiseizure medications and 29.1% had drug-resistant epilepsy. Approximately 90% had intellectual disabilities, and half of the eligible individuals had received special education.

Conclusion: The IESS imposes a substantial burden on affected children and their families and often leads to chronic epilepsy and impaired cognitive function. Consensus diagnostic and treatment guidelines tailored to the Korean clinical practice are necessary to ensure early diagnosis and timely treatment.

Key words: Infantile spasms, Epilepsy, Treatment outcome, Growth and development, Practice guideline

Key message

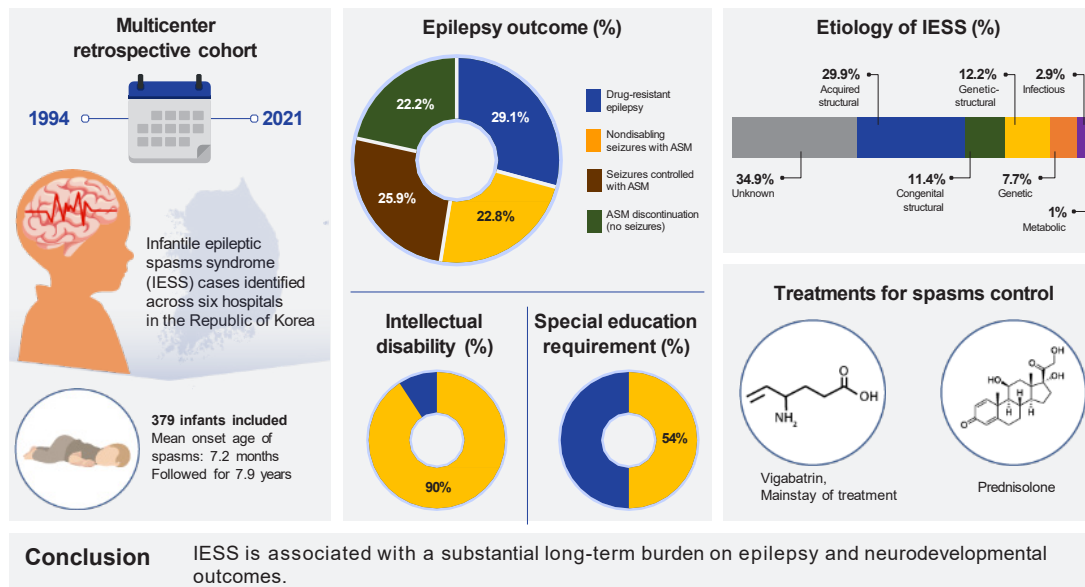
Question: How have epilepsy and cognitive outcomes of children with infantile epileptic spasms syndrome (IESS) evolved over the past 20 years?

Finding: Approximately 78% of children developed chronic epilepsy, and one-third progressed to drug-resistant epilepsy, while 90% of them exhibited intellectual disabilities.

Meaning: Given the poor outcomes associated with IESS, consensus guidelines tailored to Korean clinical practice are required to ensure timely treatment and improve outcomes.

Introduction

Infantile epileptic spasms syndrome (IESS) is a severe form of epilepsy syndrome, characterized by clusters of brief spasmodic seizures and a distinct electrographic pat-



Graphic abstract

tern, often accompanied by developmental regression.¹⁾ IESS is associated with poor long-term outcomes, such as a high risk of persistent epilepsy and neurodevelopmental impairment. About 70% of patients develop other types of epilepsy, and 18%–23% progress to Lennox-Gastaut Syndrome (LGS).²⁾ In addition, 80% of patients have combined intellectual disability, and often accompanied by autism spectrum disorder.³⁾ Several factors such as persistent spasms or tonic seizure after 90 days, developmental delay before onset of spasms, and abnormal brain imaging have been reported as poor prognostic factors.⁴⁾

Hormonal therapy and vigabatrin are known as the standard treatment for IESS. Numerous randomized controlled trials have been published exploring various treatments, dosages, and combinations to achieve both electroclinical remission and neurodevelopmental outcomes. For short-term outcome controlling spasms, hormonal therapy is generally more effective than vigabatrin, although vigabatrin shows greater efficacy in tuberous sclerosis complex (TSC)-associated spasms.⁵⁾ In hormonal therapy, outcome of adrenocorticotrophic hormone (ACTH) was better than that of prednisolone. The difference in long-term neurodevelopmental outcomes according to treatment regimens have not yet been clarified. However, it is certain that early initiation of the first-line treatment regimen and a timely electroencephalography (EEG) assess for resolution of spasms improve neurodevelopmental outcomes.⁶⁾

Management of IESS exhibits considerable variation across the countries, reflecting differences in treatment prioritization, diagnostic protocols, and regional resource availability. Several countries made consensus guidelines for diagnosis and treatment of IESS.^{7–9)} In Korea, the next-generation sequencing (NGS) panel testing and chromosomal

microarray (CMA) are actively utilized in clinical practice.¹⁰⁾ However, there is no consensus guidelines for etiologic investigation and treatment of IESS. This study aimed to evaluate long-term outcomes of children with IESS and review the evaluation and treatment in a real-world Korean multicenter clinical practice over the past decades.

Methods

1. Study design

This is a retrospective cohort study conducted across 6 pediatric epilepsy centers. For this retrospective study, each center used the International Classification of Diseases 10th Revision diagnostic code G40.4 (representing West syndrome and infantile spasms) to identify children with IESS from their clinical data warehouses. Investigators reviewed cases from electronic medical records (EMRs) and identified cases of IESS based on the 2021 International League Against Epilepsy (ILAE) diagnostic guidelines. Based on the 2021 ILAE guideline, children with a history consistent with epileptic spasms, with an onset between 1 and 24 months of age, and EEG features of hypsarrhythmia, modified hypsarrhythmia, or diffuse slowing with multifocal spikes were included.¹⁾ For a long-term outcome, we included cases of IESS who were followed for at least 2 years. We excluded cases lacking complete information on treatment regimes, as treatment approach could not be assessed.

The primary outcome was the long-term epilepsy outcome and neurodevelopmental status at the last follow-up. Epilepsy outcomes were classified as drug-resistant epilepsy (DRE), nondisabling seizures while taking anti-

seizure medication (ASM), seizure control with ASM, and seizure free after discontinuation of ASM. Neurodevelopmental status was assessed either by clinical assessment by physicians or standardized neuropsychological evaluations. We performed a subgroup analysis by treatment period to assess whether these outcomes improved with recent treatments. The treatment groups were classified as those treated before and after 2012. The secondary outcome was to investigate diagnostic evaluations and treatment approaches such as medication, epilepsy surgery, and dietary therapy. Due to the retrospective nature of the study, the exact date of spasms resolution could not be determined. Therefore, a responder was defined as a child who experienced cessation of spasms within 6 months of onset. Relapse was defined as the reappearance of clinical spasms or hypsarrhythmia on any EEG performed at least one month after initial response.¹¹⁾ Clinical data such as demographics, birth history such as perinatal complications and neonatal seizures, spasms onset, EEG findings, neuroimaging, treatment regimens, and neurodevelopmental status were collected from the EMRs. Results of karyotyping, CMA, targeted single-gene sequencing, NGS epilepsy gene panels, whole exome sequencing (WES) were reviewed. Pathogenic findings, as reported by the laboratory or medical literature, were considered clear abnormalities. Etiologies were categorized based on all available investigations into 8 subgroups: genetic, genetic-structural, congenital structural, acquired structural, metabolic, immune, infectious, and unknown.¹²⁾ TSC was classified as genetic-structure that genetic disorder results in structural brain changes and causes epilepsy. Brain malformation without a documented genetic etiology, such as focal cortical dysplasia, polymicrogyria, simplified gyri were considered as congenital structural etiology. Both perinatal and postnatal etiologies of structural brain changes were considered as acquired structural etiology.

2. Statistical analysis

Baseline characteristics of children with IESS were summarized using frequencies and proportions. Primary and secondary outcomes were calculated as numbers and percentages. Categorical variables including epilepsy outcomes and neurodevelopmental outcomes were compared using the chi-square test or Fisher exact test. For pairwise categorical comparisons, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using Fisher exact test to estimate the strength of association between categorical variables. All analyses were conducted using R ver.4.5.2. (R Foundation for Statistical Computing, Austria). Statistical significance was defined as *P* value less than 0.05.

3. Ethics statement

This study was reviewed and approved by local Institutional Review Board (IRB) of participating individual centers: Ewha Womans University Mokdong Hospital (IRB No. 2022-05-037), Seoul National University Hospital (IRB No. 2207-217-1347), Seoul National University Bundang Hospital (IRB No. B-2301-807-405), Chungbuk National University (IRB No. 2022-07-012-001), Asan Medical Center (IRB No. 2022-0958), and Samsung Medical Center (No. 2022-06-081). Informed consent was waived by the review boards, however, data security and confidentiality were ensured each institution in accordance with its privacy policy.

Results

A total of 378 patients with IESS were included in this study. The mean age at spasm onset was 7.3 (standard deviation [SD] 4.4, range 1-24) months (Table 1). The mean follow-up duration was 7.9 (SD, 5.6; range, 2-28) years.

Table 1. Demographics of children with infantile epileptic spasms syndrome (N=378)

Clinical features	Value
Age of spasms onset (mo)	7.3±4.4 (1-24)
Follow-up duration (yr)	7.9±5.6 (2-28)
Sex, male:female	206:172
Gestational age (wk) (8 missing)	N=370
≤35	52 (14.1)
>35	318 (85.9)
Perinatal complications (11 missing)	137 (37.3)
Neonatal seizure (11 missing)	74 (20.2)
Etiology	
Unknown	132 (34.9)
Acquired structural	113 (29.9)
Congenital structural	43 (11.4)
Genetic-structural	46 (12.2)
Genetic	29 (7.7)
Infectious	11 (2.9)
Metabolic	4 (1.1)
Treatment regime	
Medication only	287 (75.9)
Medication and dietary therapy	84 (22.2)
Epilepsy surgery	15 (4.0)
Corpus callosotomy	6
Lesionectomy	5
Vagus nerve stimulation	3
Hemispherectomy	1
Status epilepticus (2 missing)	15 (4.0)
Special education at kindergarten or elementary school	62 (53.9) (applicable for 115 children)
Special education at high school	28 (59.6) (applicable for 47 children)
Mortality	14 (3.7)

Values are presented as mean±standard deviation (range) or number (%).

The etiology of IESS was identified in 65.1% of the cohort, with acquired structural causes being the most common (29.9%), followed by genetic-structural (12.2%) and congenital structural causes (11.4%) (Fig. 1). Of acquired structural causes, hypoxic-ischemic encephalopathy (42.5%, 48 of 113) and brain injury secondary to prematurity (37.2%, 42 of 113) were common. There were 75 children with genetic and genetic-structural etiologies including 52 single nuclear gene disorders and 23 chromosomal disorders (Supplementary Table 1). Among the single nuclear gene disorders, 35 cases were TSC accounting for 76.1% of genetic-structural etiology. In chromosomal disorders, there were 8 Down syndrome, 3 Miller-Dieker syndrome, and 3 15q duplication syndrome. The responder rate was 36.4%, and relapse occurred in 8.0% (23 of 286 children with available data).

At the last follow-up, 77.8% of cohort were considered as having chronic epilepsy taking ASMs while 22.2% had discontinued ASMs (Fig. 2). Among those who take ASMs,

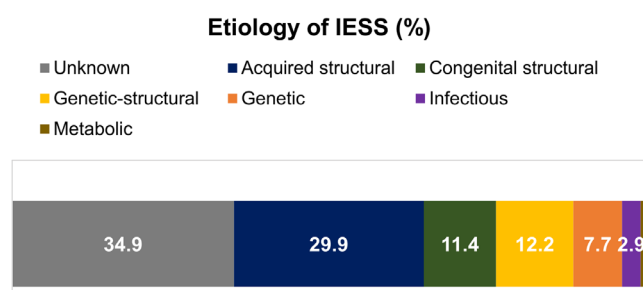


Fig. 1. Etiology of infantile epileptic spasms syndrome (IESS).

Epilepsy outcome (%)

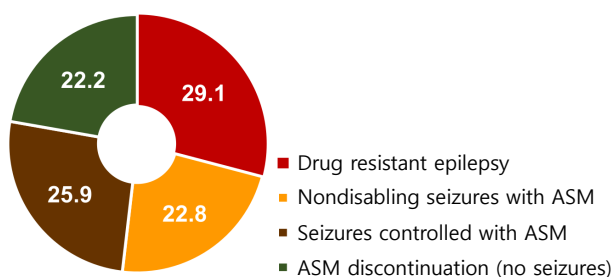


Fig. 2. Long-term epilepsy outcomes at the last follow-up. ASM, antiseizure medication.

29.1% were considered as having DRE, 25.9% achieved seizure control while on ASMs, and 22.8% continued to have nondisabling seizures while on ASMs. Children with an unknown etiology showed better seizure outcomes than those with structural (acquired or congenital), infectious, or genetic-structural etiologies (Table 2, Supplementary Table 2). Records of neurodevelopmental assessments were available for 350 children at the last follow-up. Of these, 225 were assessed by physicians and 154 underwent standardized neuropsychological evaluations such as the Bayley Scales or Wechsler intelligence tests. Overall, 89.7% (314 of 350) were identified as having some degree of intellectual disability (164 of 225 assessed by physicians and 150 of 154 assessed by standardized neuropsychological evaluations). Among the children who met age criteria for school attendance and had available data, 53.9% (62 of 115 eligible children) received special education in kindergarten and/or elementary school. In addition, 59.6% (28 of 47 eligible children) had special educational support in their junior high school. In a subgroup analysis by treatment period, seizure outcomes after 2012 were significantly improved compared with those treated before 2012 (chi-square=23.69, $P<0.001$). The proportion of DRE cases was significantly reduced in children treated after 2012, whereas neurodevelopmental outcomes remained unchanged (Table 3). As natural or synthetic ACTH were not available in Korea, the main treatments used for spasms control were vigabatrin and steroid therapy. In overall cohort, 240 children had vigabatrin monotherapy, 115 had combination of vigabatrin and steroid therapy, 7 children had steroid monotherapy, and 15 had other ASMs (Fig. 3). Two forms of steroids, oral prednisolone (73%, 89 of 122) and intravenous methylprednisolone therapy (37%, 33 of 122) were used. Most children who received intravenous methylprednisolone transitioned to oral prednisolone. In 35 children with TSC, 31 had vigabatrin monotherapy, 3 with combination therapy, and 1 with oral prednisolone. In addition to medical treatment, 22.2% (84 of 378) of the cohort received dietary therapy and 4.0% (15 of 378) had epilepsy surgery. In comparison of outcomes between combination therapy and vigabatrin monotherapy, the proportion of seizure-free children was higher in com-

Table 2. Epilepsy outcomes by etiology

Outcome	Etiology						
	Unknown (N=132)	Structural-acquired (N=113)	Structural-congenital (N=43)	Genetic-structural (N=46)	Genetic (N=29)	Infectious (N=11)	Metabolic (N=4)
Seizure free (ASM discontinuation)	50 (37.9)	13 (11.5)	6 (14.0)	3 (6.5)	11 (37.9)	0 (0)	1 (25)
Seizure controlled with ASM	25 (18.9)	40 (35.4)	11 (25.6)	16 (34.8)	3 (10.3)	3 (27.3)	0 (0)
Nondisabling seizures with ASM	16 (12.1)	30 (26.5)	14 (32.6)	11 (23.9)	8 (27.6)	4 (36.4)	3 (75)
Drug-resistant epilepsy	41 (31.1)	30 (26.5)	12 (27.9)	16 (34.8)	7 (24.1)	4 (36.4)	0 (0)

Values are presented as number (%).
ASM, antiseizure medication.

Table 3. Epilepsy and neurodevelopmental outcomes by treatment period

Outcome	Treatment before 2012 (N=184)	Treatment after 2012 (N=194)	Odds ratio (95% CI)	P value
Seizure free (ASM discontinuation)	40 (21.7)	44 (22.7)	1.06 (0.63-1.77)	0.902
Seizure controlled with ASM	41 (22.3)	57 (29.4)	1.45 (0.89-2.38)	0.127
Nondisabling seizures with ASM	29 (15.8)	57 (29.4)	2.17 (1.28-3.73)	0.003
Drug-resistant epilepsy	74 (40.2)	36 (18.6)	0.35 (0.21-0.56)	<0.001
Intellectual disability	151 (82.1)	161 (83.0)	1.06 (0.50-2.26)	0.862

Values are presented as number (%) unless otherwise indicated.

ASM, antiseizure medication; CI, confidence interval.

Boldface indicates a statistically significant difference with $P < 0.05$.

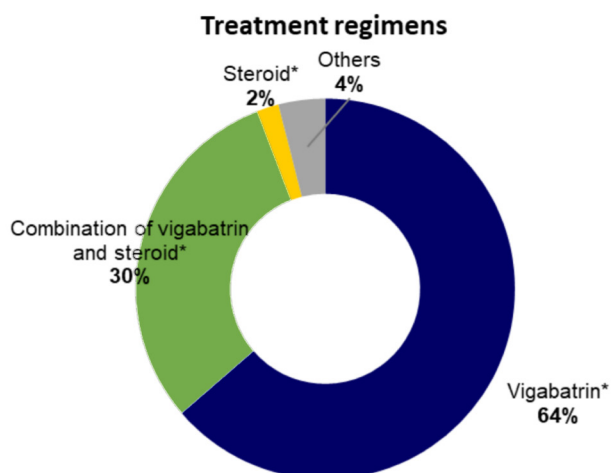


Fig. 3. Treatments used to control epileptic spasms. *Combination with other antiseizure medications of diet therapy are included.

Combination therapy while a higher proportion of children achieving seizure control with ASM in vigabatrin monotherapy (Supplementary Table 3). However, there were no significant differences in other seizure outcomes such as DRE or in neurodevelopmental outcomes.

Discussion

This study demonstrates the long-term epilepsy and developmental outcomes based on how children with IESS were treated from the late 1990s to the early 2020s. Overall, three-quarters of the children eventually developed chronic epilepsy, with one-third of the children being considered as DRE. This is in keeping with the literature which describes that, in long-term, two-thirds of the children had seizures and 18-23% evolved into LGS.^{2,3,13} In a subgroup analysis, we found out that the proportion of DRE cases was significantly reduced in children treated after 2012. This improvement may be attributed to the broad range of therapeutic options available for DRE and the more aggressive treatment strategies for IESS. Children with an unknown etiology showed better seizure outcomes than those with structural, infectious, or genetic-structural etiologies. This is consistent with the well-established observation that idiopathic etiologies generally have a

more favorable prognosis than symptomatic etiologies.⁴ In this study, we measured neurodevelopmental outcomes by clinical assessment and found out that 90% of children with IESS experienced some degree of neurodevelopmental delay and half of them had special education. These findings are comparable to the long-term Finnish study which reported 83% (122 of 147 survivors) had mild to severe intellectual disabilities and required educational support.² Various prognostic factors of neurodevelopmental outcome have been reported, such as cryptogenic etiology, short latency time to treatment, and normal development before the onset of spasms. It is clear that early recognition and prompt treatment of spasm remains the most crucial factor for better neurodevelopmental outcome.^{14,15} Children with IESS are generally at high risk of having poor neurodevelopmental outcomes, therefore they should be referred for early evaluation and intervention if there are any developmental concerns.

Similar to the results from United Kingdom Infantile Spasms Study (UKISS) and National Infantile Spasms Consortium (NISC), 65.1% of children with IESS had a proven etiology.^{12,16} Specifically, acquired structural etiologies made up the largest proportion in our cohort (29.6%) which also comprised 22.4% in the NISC.^{12,17} Hypoxic-ischemic encephalopathy and brain insults associated with prematurity were major findings in acquired structural etiology. Brain magnetic resonance imaging demonstrated causal abnormalities in 53.4% of children, and thus necessary as a first-line investigation. If there is structural lesion related to a genetic disorder, relevant specific genetic testing would be recommended. If imaging is uninformative, combination of genetic testing such as CMA or NGS epilepsy gene panels would be considered. When considering genetic and genetic-structural etiology, nuclear gene disorders were more common than chromosomal disorders. The recent Indian study of genetic IESS demonstrated wide heterogeneity of monogenic disorders and reported that monogenic disorders are the common genetic cause of genetic IESS.¹⁸ On contrary, when we focused on 29 children with pure genetic IESS, we found a higher frequency of chromosomal disorders (62%, 18 of 29) than in nuclear gene disorders (38%, 11 of 29). This could be

attributed to our inclusion criteria of which include few children who underwent NGS gene panel. Wirrell et al.¹²⁾ mentioned the combination of array comparative genomic hybridization and epilepsy gene panel provide a high yield of definitive diagnosis in more than 40% of children without obvious cause, suggesting CMA and gene panel as compatible for the first-tier assessment. Single nuclear gene disorders were the dominant cause of genetic IESS and these involved genes are widely heterogeneous, WES can be considered as a second-tier assessment.¹⁹⁾ Our study suggest that metabolic disorders are a rare cause of IESS, 1.1% of our cohort (Supplementary Table 4).

ACTH, prednisolone, or vigabatrin are commonly used as first-line treatment for IESS. There were various clinical trials comparing natural or synthetic ACTH, high or low doses of ACTH, high or low doses of vigabatrin, and combinations of hormonal therapy with vigabatrin.⁶⁾ Vigabatrin either as monotherapy or combination therapy with steroid has been the mainstay treatment for spasms in Korea over the past 20 years. Oral prednisolone or intravenous methylprednisolone was used as hormonal therapy, but these steroid monotherapies were less common than we expected. Hormonal therapy is known as superior to the vigabatrin that responder rate of hormonal therapies ranges from 70%–87%, while that of vigabatrin ranges 35%–54%.^{20–22)} A recent systematic review which compared the efficacy of vigabatrin and hormonal therapy recommended hormonal monotherapy for non-TSC-associated spasms while vigabatrin as the first-line treatment for TSC-associated IESS.²³⁾ They concluded that there is limited evidence for combination therapy of vigabatrin and steroid. Yet, there is no specific treatment which has advantage on the neurodevelopmental outcome. The UKISS study reported better developmental outcomes in children with cryptogenic etiology who were treated with steroids, but there were no significant differences in epilepsy or developmental outcomes at age 4 between those treated with hormonal therapy and those treated with vigabatrin.^{14,24)} The ICISS trial also demonstrated that combination therapy (hormonal and vigabatrin) was more effective at controlling spasms but did not show any advantage in developmental outcomes.^{25,26)} Furthermore, no advantage in developmental outcomes was observed between ACTH and oral prednisolone.²⁷⁾ The proportion of DRE and intellectual disability did not differ significantly between the combination therapy and vigabatrin monotherapy groups. Although there were differences in specific epilepsy outcomes between the 2 treatment groups, we were unable to determine the underlying reasons for these differences due to the retrospective nature of the study. Confounding factors such as etiology or lead time to treatment may have influenced the epilepsy outcomes

rather than a direct effect of the treatment. Given that ACTH is not available in Korea and high dose steroid are as effective as ACTH, high dose prednisolone of 40 to 60 mg/day would be strongly recommended for controlling spasms.^{5,28)} Vigabatrin could be considered a first-line treatment for children with TSC and those contraindicated to steroid therapy. Combination of high dose prednisolone and vigabatrin could also be another option, however, there are limited data on long-term outcomes and concerns of adverse effects. We found that there was a considerable variation in the dosage and duration of vigabatrin prescription. Thus, consensus guidelines are needed for each treatment approach in detail. In addition, while one-third of cohort were considered as DRE, most of them relied on the medical treatment. Only 4% had epilepsy surgery which can be another beneficial option for DRE. This might be attributed to underutilization of surgical interventions and neuromodulations in Korea which highlighting the importance of considering surgical interventions.

Our study has several limitations. As a retrospective study, there was variability in individual follow-up durations which might have influenced the overall outcomes. In addition, data on the time from diagnosis to treatment initiation and definite date of spasms cessation were not available. We were unable to determine how the treatment latency and early treatment response affected the overall outcomes. We assessed neurodevelopmental status by clinical assessment rather than comprehensive neuropsychiatric evaluations. This may lead to variations in neurodevelopment outcome according to the criteria applied for neurodevelopmental assessment. For the long-term outcomes, we included children who followed up at least 2 years. This could act as a selection bias by excluding children who were recently diagnosed and underwent gene panels or WES. Despite these limitations, our study provides real-world evidence how children with IESS have been managed. Also, this study highlights the needs of diagnostic and treatment consensus guidelines based on the Korean healthcare setting. The nationwide consensus guidelines including diagnostic approach for etiological investigation and a timely stepwise treatment selection would be necessary to improve the overall outcomes.

See the article “Limited improvement in outcomes of infantile epileptic spasms syndrome despite therapeutic advances” via <https://doi.org/10.3345/cep.2026.00745>

Footnotes

Supplementary materials: Supplementary Tables 1-4 are available at <https://doi.org/10.3345/cep.2025.02089>.

Conflict of Interest: The authors have nothing to disclose.
Funding: This research was supported by Seoul National University Hospital Lee Kun-hee Child Cancer & Rare Disease Project, Republic of Korea (grant numbers: 22C-005-0000, 25C-053-0100).

Acknowledgments: We thank to CIPHEROME for supporting statistical analysis.

Author Contribution: Conceptualization: HJK, BCL, MSY, JL; Formal Analysis: SAC, JSK; Investigation: MK, HJK, JYH, MJK, JL; Methodology: SAC; Project Administration: SAC, WJK, HW, JYH, MJ, JL; Writing – Original Draft: SAC; Writing – Review & Editing: JSK

ORCID:

Sun Ah Choi  <https://orcid.org/0000-0001-6164-8706>
 Minhye Kim  <https://orcid.org/0000-0001-5014-246X>
 Hye Jin Kim  <https://orcid.org/0000-0001-9111-5572>
 Woo Joong Kim  <https://orcid.org/0000-0002-0539-1448>
 Byung Chan Lim  <https://orcid.org/0000-0002-8509-4135>
 Ji Yeon Han  <https://orcid.org/0000-0001-8671-5215>
 Hunmin Kim  <https://orcid.org/0000-0001-6689-3495>
 Min-Jee Kim  <https://orcid.org/0000-0002-8081-6522>
 Mi-Sun Yum  <https://orcid.org/0000-0002-5986-5258>
 Jiwon Lee  <https://orcid.org/0000-0002-8456-684X>
 Jeehun Lee  <https://orcid.org/0000-0002-8499-3307>
 Hyewon Woo  <https://orcid.org/0000-0002-1407-3441>
 Jon Soo Kim  <https://orcid.org/0000-0003-2586-1942>

References

- Zuberi SM, Wirrell E, Yozawitz E, Wilmschurst JM, Specchio N, Riney K, et al. IIAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the IIAE Task Force on Nosology and Definitions. *Epilepsia* 2022;63:1349-97.
- Riikonen R. Long-term outcome of patients with West syndrome. *Brain Dev* 2001;23:683-7.
- Riikonen R. Infantile spasms: outcome in clinical studies. *Pediatr Neurol* 2020;108:54-64.
- Arai Y, Okanishi T, Kanai S, Nakamura Y, Sunada H, Murakami H, et al. Prediction model for long-term seizure and developmental outcomes among children with infantile epileptic spasms syndrome. *Front Neurol* 2023;14:1195252.
- Jain P, Sahu JK, Horn PS, Chau V, Go C, Mahood Q, et al. Treatment of children with infantile spasms: a network meta-analysis. *Dev Med Child Neurol* 2022;64:1330-43.
- Go CY, Mackay MT, Weiss SK, Stephens D, Adams-Webber T, Ashwal S, et al. Evidence-based guideline update: medical treatment of infantile spasms [retired]. Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 2012;78:1974-80.
- Sampaio LP, Henriques-Souza AM, Silveira MR, Seguti L, Santos ML, Montenegro MA, et al. Brazilian experts' consensus on the treatment of infantile epileptic spasm syndrome in infants. *Arq Neuropsiquiatr* 2023;81:844-56.
- Sharma S, Kaushik JS, Srivastava K, Goswami JN, Sahu JK, Vinayan KP, et al. Association of Child Neurology (AOCN) - Indian Epilepsy Society (IES) consensus guidelines for the diagnosis and management of West syndrome. *Indian Pediatr* 2021;58:54-66.
- Ramantani G, Bölsterli BK, Alber M, Klepper J, Korinthenberg R, Kurlmann G, et al. Treatment of infantile spasm syndrome: update from the interdisciplinary guideline committee coordinated by the German-Speaking Society of Neuropediatrics. *Neuropediatrics* 2022;53:389-401.
- Next generation sequencing gene panel [Internet]. Seoul (Korea): Health Insurance Review and Assessment Service; c2017 [cited 2017 Jan 31]. Available from: <https://www.hira.or.kr/bbsDummy.do?brdBltno=6321&brdScnBltno=4&pgmId=HIRAA020002000100>.
- Hussain SA, Schmid E, Peters JM, Goyal M, Bebin EM, Northrup H, et al. High vigabatrin dosage is associated with lower risk of infantile spasms relapse among children with tuberous sclerosis complex. *Epilepsy Res* 2018;148:1-7.
- Wirrell EC, Shellhaas RA, Joshi C, Keator C, Kumar S, Mitchell WG. How should children with West syndrome be efficiently and accurately investigated? Results from the National Infantile Spasms Consortium. *Epilepsia* 2015;56:617-25.
- Messer R, Knupp KG. Infantile spasms: opportunities to improve care. *Semin Neurol* 2020;40:236-45.
- O'Callaghan FJ, Lux AL, Darke K, Edwards SW, Hancock E, Johnson AL, et al. The effect of lead time to treatment and of age of onset on developmental outcome at 4 years in infantile spasms: evidence from the United Kingdom Infantile Spasms Study. *Epilepsia* 2011;52:1359-64.
- Auvin S, Hartman AL, Desnoux B, Moreau AC, Alberti C, Delanoe C, et al. Diagnosis delay in West syndrome: misdiagnosis and consequences. *Eur J Pediatr* 2012;171:1695-701.
- Osborne JP, Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, et al. The underlying etiology of infantile spasms (West syndrome): information from the United Kingdom Infantile Spasms Study (UKISS) on contemporary causes and their classification. *Epilepsia* 2010;51:2168-74.
- Jiang Y, Zou N, Luo Y, Cheng M, Liao S, Hong S, et al. Cohort study of infantile epileptic spasms syndrome: etiological analysis and treatment of corticosteroids. *Seizure* 2022;101:120-6.
- Nagarajan B, Gowda VK, Yoganathan S, Sharawat IK, Srivastava K, Vora N, et al. Landscape of genetic infantile epileptic spasms syndrome-A multicenter cohort of 124 children from India. *Epilepsia Open* 2023;8:1383-404.
- Liu LY, Lu Q, Wang QH, Wang YY, Zhang B, Zou LP. Diagnostic yield of a multi-strategy genetic testing procedure in a nationwide cohort of 728 patients with infantile spasms in China. *Seizure* 2022;103:51-57.
- Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, et al. The United Kingdom infantile

spasms study comparing vigabatrin with prednisolone or tetracosactide at 14 days: a multicentre, randomised controlled trial. *Lancet* 2004;364:1773-8.

21. Baram TZ, Mitchell WG, Tournay A, Snead OC, Hanson RA, Horton EJ. High-dose corticotropin (ACTH) versus prednisone for infantile spasms: a prospective, randomized, blinded study. *Pediatrics* 1996;97:375-9.
22. Appleton RE, Peters AC, Mumford JP, Shaw DE. Randomised, placebo-controlled study of vigabatrin as first-line treatment of infantile spasms. *Epilepsia* 1999;40:1627-33.
23. Xu Z, Gong P, Jiao X, Niu Y, Wu Y, Zhang Y, et al. Efficacy of vigabatrin in the treatment of infantile epileptic spasms syndrome: a systematic review and meta-analysis. *Epilepsia Open* 2023;8:268-77.
24. Darke K, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Lux AL, et al. Developmental and epilepsy outcomes at age 4 years in the UKISS trial comparing hormonal treatments to vigabatrin for infantile spasms: a multi-centre randomised trial. *Arch Dis Child* 2010;95:382-6.
25. O'Callaghan FJ, Edwards SW, Alber FD, Hancock E, Johnson AL, Kennedy CR, et al. Safety and effectiveness of hormonal treatment versus hormonal treatment with vigabatrin for infantile spasms (ICISS): a randomised, multicentre, open-label trial. *Lancet Neurol* 2017;16:33-42.
26. O'Callaghan FJ, Edwards SW, Alber FD, Cortina Borja M, Hancock E, Johnson AL, et al. Vigabatrin with hormonal treatment versus hormonal treatment alone (ICISS) for infantile spasms: 18-month outcomes of an open-label, randomised controlled trial. *Lancet Child Adolesc Health* 2018;2:715-25.
27. Sumanasena SP, Wanigasinghe J, Arambepola C, Sri Ranganathan S, Muhandiram E. Effect of intramuscular ACTH versus oral prednisolone on the developmental trajectories of children with West syndrome over 24 months: a randomised control study. *Eur J Paediatr Neurol* 2021;32:98-105.
28. Guang S, Mao L, Zhong L, Liu F, Pan Z, Yin F, et al. Hormonal therapy for infantile spasms: a systematic review and meta-analysis. *Front Neurol* 2022;13:772333.

How to cite this article: Choi SA, Kim M, Kim HJ, Kim WJ, Lim BC, Han JY, et al. Long-term outcome in children with infantile epileptic spasms syndrome: A multicenter retrospective study in Korea. *Clin Exp Pediatr* 2026;69:386-93.