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Original Article

Learning Disabilities in Children with Self-limited Epilepsy with Centrotemporal Spikes - A Cohort Study

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Abstract

Introduction: Contrary to the benign evolution, the normal intellectual efficiency in children with self-limited epilepsy with centrotemporal spikes (SeLECTS) has been challenged by recent observations of academic backwardness. We aimed to determine the frequency of Specific Learning Disabilities (SLD) in children with SeLECTS.

Methods: This prospective cohort study was conducted in a tertiary care hospital in South India over 12 months. Forty-one children with clinical and electrographic features consistent with SeLECTS (cases) and 41 age-matched healthy controls were recruited. The IQ (Intelligence quotient) of children in both groups was tested by the Malin's Intelligence Scale for Indian Children and those with normal IQ were subjected to a validated NIMHANS SLD testing battery. Children with a performance below two standards of their expected grade were considered to have a SLD.

Results: The mean age of seizure onset ± standard deviation (± SD) was 7.6 (1.6) years. The mean duration of epilepsy with ± SD was 12 (4.7) months. The EEG spikes distribution was centrotemporal in 63.4% of cases, with a median spike index of 30% (IQR 20 - 39). The mean IQ with ± SD was 81.2 (2.1) % and 81.5 (2.6)% in cases and controls respectively. Specific learning disability was reported in 17 cases (41.5%) and five (12.2%) controls (P = 0.003). Younger children with SeLECTS (5 - 7 years) had a significant occurrence of difficulty in visual memory (P = 0.01). Older children with SeLECTS (8 - 12 years) had difficulties in reading (P = 0.01), spelling (P = 0.03), and reading comprehension (P = 0.02), which were statistically significant.

Conclusion: Children with SeLECTS showed a significant occurrence of SLD as compared to healthy controls.

Introduction

Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS), formerly called benign childhood epilepsy with centrotemporal spikes or benign Rolandic epilepsy, is a common localization-dependent electroclinical syndrome in children of school-going age. The distinctive clinical features include unilateral, self-limiting, facial sensorimotor seizures, that are largely nocturnal in onset, with or without oropharyngolaryngeal symptoms, speech arrest, or hypersalivation.[1] An interictal electrographic recording of sleep-activated, high amplitude, sharp slow complexes localized to the centrotemporal region with a normal background confirms the diagnosis of SeLECTS.[1] The prognosis is excellent with fewer than ten seizures during the natural course of the epileptic syndrome and complete remission by late adolescence.

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Contrary to the benign evolution, the normal intellectual efficiency in children with SeLECTS has been challenged over the last decade by observations of academic underperformance.[2] This growing concern of subtle neuropsychological dysfunction is not restricted to the diverse spheres of learning disability but also includes visuomotor coordination, memory, and executive functioning.[3,4] A meta-analysis of literacy and language skills in children with SeLECTS from 22 studies highlights the reading and phonological processing deficits in these children.[5]

Indian studies on this area are few, and the cognition assessment tools vary amongst countries. An unexpected failure to acquire or use new information may pose a significant disadvantage in the educational and occupational domains of these children. Identification of at-risk children and focused remedial intervention at the earliest shall potentially reverse this academic underperformance, not attributable to intellectual impairment. Therefore, we aimed to assess the frequency of specific learning disabilities (SLD) in children with SeLECTS when compared to controls with normal neurological status.

Methods

This prospective, cohort study was conducted at a tertiary hospital in South India over 12 months from July 2019 to June 2020. Two groups (cases and controls) of children were recruited for the study. Children in the age group of five to 12 years attending the OPD with clinical suspicion of one or more primarily nocturnal seizures were eligible for the study. Of the eligible cohort, a child with electrographic evidence of high voltage diphasic spikes with a predominant centrotemporal distribution in a normal background without any evidence of focal slowing was recruited as a case for the study. Thus, all those children who fulfilled both electrographic and clinical criteria by ILAE for the diagnosis of typical SeLECTS were included in the study group.[1] Children with chronic neurological disorders such as intellectual disability, cerebral palsy, pervasive developmental disorder, or other electroclinical epileptic syndromes were excluded from the study. Electrographic evidence of variants of SeLECTS including Landau Kleffner syndrome, Continuous Spike Wave during sleep (CSWS) characterized by spike-wave index > 85%, and persistent focal slowing were secondarily excluded. For the control group, age-matched children of five to 12 years, without a history of epilepsy or neurological or developmental disorders, attending the Paediatric OPD of the same hospital for trivial illnesses (not needing hospitalization) were recruited. The study was approved by the Institutional Human Ethics Committee (RES/MGMCRI/04/2019/XX/IHEC/09). The sample size, calculated using the Epitools software (https://epitools.ausvet.com.au/samplesize) with a power of 80% and an alpha level of 0.05, was 41 in each group with a total of 82, considering a prevalence of SLD in healthy Indian children as 16.5%.[6] Clinical details and demographic profiles of the cases and controls were obtained on a data recording form that was then transcribed into Epi Info 2003 database software (Center for Disease Control and Prevention, Atlanta, GA, USA). The age of onset of seizures, seizure semiology, seizure burden, and the scholastic grades were recorded. Thirty-minute sleep electroencephalography (EEG) was obtained for the eligible children fulfilling clinical criteria and the spike foci distribution and spike-wave index were analyzed by a paediatric neurologist. The cases and controls were recruited as consecutive samples after obtaining written informed consent from parents or caregivers. After recruitment, both the cases and age-matched controls were subjected to psychometric testing by a child psychologist using Malin's Intelligence Scale for Indian Children (MISIC), which is an Indian adaptation of Wechsler's Intelligence Scale for Children (WISC). MISIC is a validated tool and is commonly used to assess IQ in Indian children.[7] The performance intelligence quotient (IQ), verbal subscale IQ, and full-scale IQ were measured. Children with full-scale IQ < 70 were deemed ineligible for further testing and excluded from the study. Post IQ assessment, children underwent formal testing for SLD using the NIMHANS Index. NIMHANS SLD battery is a well-formulated indigenous assessment tool for processing deficits and testing proficiency in reading, writing, spelling, and mathematics.[8] The validity and reliability of this standard tool have been well established and is the ideal choice for academic assessment in Indian children.[8] The NIMHANS SLD battery is a curriculum-based assessment tool and is practical for Indian children. This SLD testing was also performed by the same child psychologist, in English, over a minimum period of 45 minutes. Two levels of testing based on the age group were included. Level I was for children in the age group of 5 - 7 years and Level II was for 8 - 12 years. Attention, visual and auditory discrimination, visual and auditory memory, speech and language, visuomotor and writing skills were assessed for children in the age group of 5 to 7 years. Testing in the 8 - 12 years group included attention, reading, writing, comprehension, spelling, perceptual-motor, visuomotor integration, memory, and arithmetic skills. Children with a performance two standards below their expected grade were considered to have a specific learning disability in that area. The frequency of each of the specific learning disabilities was compared in both groups. The analyses were conducted by using SPSS software (version 17.0; SPSS Inc). The difference in characteristics of participants between the groups was compared using the Chi-square test for qualitative variables and the independent student t-test for continuous variables. A P-value of less than 0.05 was considered statistically significant.

Results

Forty-one children with SeLECTS were recruited including 28 boys and 13 girls. The disease had a male preponderance (68.2%). The lowest age of onset of seizure was five years. The baseline characteristics of the cases and controls were

comparable as depicted in Table 1. Almost all the patients had nocturnal seizures (95%) and the majority showed centrotemporal spikes in EEG (63.4%) with a median spike index of 30% (20-39). Plain magnetic resonance imaging (MRI) of the brain was normal in all the cases. There was no statistically significant difference between the mean IQ score in cases and controls, including verbal IQ (P = 0.22), performance IQ (P = 0.22), and the full IQ score (P = 0.22). the domains tested in NIMHANS SLD battery, in children aged 5 - 7 years, visual memory (P = 0.01) was significantly affected in cases as compared to controls. Whereas, in children aged 8 - 12 years, reading (P = 0.01), spelling (P = 0.03), and reading comprehension (P = 0.02) were significantly affected in cases as compared to controls.

Table 1: Clinical and cognitive profile of cases and controls in the study

Characteristics	SeLECTS group (N = 41)	Control group (N = 41)	P-value
Age of onset of seizure in years [mean (SD)]	7.6 (1.6)	NA	
Age at presentation in years [mean (SD)]	7.8 (1.6)	7.6 (1.7)	0.28*
Male gender (N (%))	28 (68.2)	30 (73)	0.62#
Duration of epilepsy in months [mean (SD)]	12 (4.7)	NA	
Seizure characteristics [N (%)]			
Nocturnal	39 (95)	NA	
Focal seizures	37 (90.2)	NA	
Generalized seizures	4 (9.8)	NA	
Anti-epileptic medication [N (%)]			
Monotherapy	31 (75.6)	NA	
Polytherapy	3 (7.3)	NA	
Untreated	7 (17.1)	NA	
Electroencephalography features [N (%)]			
Centrotemporal	26 (63.4)	NA	
Midtemporal	3 (7.3)	NA	
Centroparietal	8 (19.5)	NA	
Frontotemporal	3 (7.3)	NA	
Centrooccipital	1 (2.4)	NA	
History of febrile seizures [N (%)]	5 (12.2)	4 (9.7)	0.72#
Family history of epilepsy [N (%)]	2 (4.9)	2 (4.9)	1.00#
Intelligence quotient [mean (SD)]			
Verbal Intelligence score	81.1 (2.4)	81.5 (2.1)	0.22*
Performance intelligence score	81.2 (2.4)	81.5 (2.6)	0.22*
Full Intelligence score	81.2 (2.1)	81.5 (2.6)	0.22*
Specific learning disability [N (%)]	17 (41.5)	5 (12.2)	0.003#

*- Independent sample t-test, #- Chi-square test, NA - Not Applicable

Children with SeLECTS showed a significantly higher frequency of SLD as compared to the control group (P = 0.003) as shown in Table 1. Tables 2 and 3 depict the results of the NIMHANS SLD

battery test done in cases and controls, for age groups 5 – 7 years (Level 1), and 8 - 12 years (Level 2) respectively. Amongst

Table 2: Comparison of NIMHANS SLD battery testing for in SeLECTS and control group –Level 1 (5 - 7 years age group)

NIMHANS SLD Battery	SeLECTS group (N = 15) %	Control group (N = 10) %	P- value (Chi-square test)
Specific learning disability [N (%)]	7 (46.6)	1 (10)	0.05
Domains [N (%)]			
Attention	4 (26.7)	1 (10)	0.31
Visual discrimination	6 (40)	1 (10)	0.10
Visual memory	7 (46.6)	0 (0)	0.01
Auditory discrimination	7 (46.6)	1 (10)	0.05
Auditory memory	0 (0)	0 (0)	--
Verbal language expression	4 (26.7)	1 (10)	0.31
Visuomotor skills	4 (26.7)	1 (10)	0.31
Writing skills	4 (26.7)	1 (10)	0.31

Table 3: Comparison of NIMHANS SLD battery testing in SeLECTS and control group –Level 2 (8 - 12 years age group)

NIMHANS SLD Battery	SeLECTS group (N = 26) %	Control group (N = 31) %	P- value (Chi-square test)
Specific learning disability [N (%)]	10 (38.4)	4 (12.9)	0.02
Domains [N (%)]			
Attention	5 (19.2)	3 (9.7)	0.30
Reading	10 (38.4)	3 (9.7)	0.01
Writing	3 (11.5)	1 (3.2)	0.22
Spelling	7 (26.9)	2 (6.4)	0.03
Reading comprehension	10 (38.4)	4 (12.9)	0.02
Perceptual motor	3 (11.5)	2 (6.4)	0.50
Memory	5 (19.2)	3 (9.7)	0.30
Arithmetic	3 (11.5)	1 (3.2)	0.22

Discussion

Learning difficulties are emerging comorbidities in SeLECTS and the disorder may not be benign as the name indicates. Cognitive deficits such as reading difficulty, decreased phonological awareness, impaired auditory processing, and language dysfunction are concerning since they might impede their scholastic performance and behaviour, if unattended.[9-14] The current study showed a significantly higher frequency of SLD (41.5%) in children with SeLECTS when compared to healthy controls. The results are in agreement with the study by Vinayan et al. who identified educational problems in 52% of SeLECTS children.[15]

In our study, visual memory deficit was noted in children less than seven years while difficulties in reading, spelling, and reading comprehension were noted in children above eight years. The reading comprehension difficulties in our study align with a cross-sectional study by Currie et al. who recognized lower reading comprehension scores in 25 children with Rolandic epilepsy.[16] Three other studies that assessed the academic skills in SeLECTS found that these children had reading difficulties.[17-19] The reading comprehension difficulty noted in our study could be possibly due to differences in brain network organization. Children with SeLECTS were found to recruit a wider brain network to perform sentence reading comprehension task, with specific activation in the left dorsal striatum.[19] In contradiction to our study, poor writing was noted in 33% of children with SeLECTS by Papavasiliou et al.[20] Also, few studies have found poor mathematical skills in SeLECTS children.[18,21,22] Writing and arithmetic domains were not affected in our study. This could be due to the small sample size and the heterogeneity of our cohort.

The pathophysiology behind cognitive impairments in children with SeLECTS is not clearly understood. These children show changes in brain volume and structural connectivity which correlates to the presence of subtle neurodevelopmental

changes.[23] Specifically, white matter abnormalities (reduced fractional anisotropy) over the central epileptogenic zone and distant regions such as the splenium of the ipsilateral corpus callosum have been demonstrated.[24-26]

Our study assessed the intelligence and learning profile of children using validated instruments which we consider as strength of the study. However, we did find limitations such as a small sample size and including cases who were and were not on medications. Thus, there is a possibility of bias in ascertaining the cognitive impairment which may be modified by anti-epileptic drugs.

Conclusion

This study points to the importance of screening for learning problems in all children with SeLECTS. Timely diagnosis and remediation of these specific learning disabilities will go a long way in ameliorating the academic underachievement in these children. We recommend follow-up studies to delve into the long-term academic performance of these children.

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Conflict of Interest None

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