

Cognitive and ADHD disorders in benign epilepsy with centrotemporal spikes: An Egyptian study.

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Abstract

Background: Benign epilepsy with centrotemporal spikes is the most common type of focal epilepsy in children as it accounts for 15% to 25% of epilepsy in children. It is associated with neuropsychological problems which are suspected to be related to spike-wave index, the site of epileptic form discharge, age at onset, and seizures frequency. Therefore, we aimed to study the incidence of the problems associated with BECTS as ADHD, and cognitive disorders and to detect their relation to seizure criteria.

Methods: At Assiut University Children Hospital from August 2018 to December 2020, 80 children, ages 3-14 years, were identified to have BECTS. Full history was taken. A complete examination, prolonged sleep EEG, ADHD-SC4 test, IQ assessment was done for all patients.

Results: Mentally retarded was detected in 28.6% of BECTS patients. Cognitive disorders are more common in BECTS patients with more frequent seizures, mixed diurnal, and nocturnal seizures, and higher SWI (P-value<0.001). We did not find a relationship between cognitive disorder and the age at onset of seizures, sex, or laterality of epileptic focus in EEG. ADHD was detected in 72.5% of BECTS patients. The inattentive type was present in 16.25% of patients, the hyperactivity impulsive type in 11.25%, combined ADHD in 45%.

Conclusions: Mentally retarded was detected in 28.6% of BECTS patients, ADHD was detected in 72.5% of BECTS patients. The inattentive type was present in 16.25% of patients, the hyperactivity impulsive type in 11.25%, combined ADHD in 45%.

Keywords: Benign epilepsy with centrotemporal spikes, ADHD, Cognitive disorder, Spike-wave index.

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Introduction

Benign Epilepsy with Centro Temporal Spikes (BECTS) is the most common type of focal epilepsy in children as it accounts for 15% to 25% of epilepsy in children. The age of onset ranges from one to 14 years [1]. BECTS in general is characterized by infrequent focal seizures in the face during sleep, which may secondarily generalize, resulting from excitability from Rolandic regions without any organic brain lesion. The prognosis is usually considered to be excellent but neuropsychological deficits, such as cognitive and behavioral impairments were noted to be common problems in BECTS children [2,3]. These problems are suspected to be related to the sleep-wake cycle and Spike-Wave Index (SWI), the site of epileptiform discharge, age at onset, frequency of seizures, and duration of disease [4]. Also, the SWI is closely related to the atypical evolution of BECTS as Landau-Kleffner Syndrome (LKS), and epileptic encephalopathy with Continuous Spike-And-Wave during Sleep (CSWS), which are thought to be a single spectrum of disorders [5]. The evolution of BECTS to CSWS occurs when SWI exceeds 25% to 85% with a controversy between different studies [6].

Cognitive disorders, ADHD, and learning disorders are more common in epileptic children, and about 50% of them need specific education programs [7]. Several factors contribute to neuropsychiatric impairments in these children including interactions between seizures, anti-seizure drugs, underlying

causes of epilepsy, and the innate properties of epilepsy [8]. Cognitive affection in children newly diagnosed to have epilepsy before the first seizure suggests the presence of common biological mechanisms. Also, the relationship between ADHD and epilepsy is thought to be bidirectional [9].

The prevalence of cognitive deficits in children with BECTS is reported as 21.8% [10] compared to the prevalence of intellectual disability in the general population is 1% to 3% [11]. In a systematic review, Aricò et al. found the prevalence of ADHD in patients with BECTS was about 60% [12]. Cognitive and behavioral problems are important issues in children with BECTS because they are at a critical phase of neurodevelopment, education, and acquiring skills [13]. Therefore, we aimed to study the incidence of the problems associated with BECTS as ADHD, learning, and cognitive disorders, and to detect their relation to seizure criteria.

Materials and Methods

At Assiut university children hospital from August 2018 to December 2020, 80 children, ages 3-14 years, were identified to have BECTS from history and EEG findings. Children with genetic disorders, metabolic or neurodegenerative disease, and motor deficit were excluded. Full history including name, age, sex, age of seizure onset, the type of convulsions and their relation to sleep, developmental history, behavioral problems, and school performance was taken. The EEG was done during

sleep, and we looked at the full sleep recording and visually picked the epoch with the highest spike density. The counting started with a page of high spikes and continued for 10 consecutive minutes. The site and laterality of epileptic spikes were detected and the SWI was calculated for every patient. ADHD assessment with ADHD-SC4 test and IQ assessment with Stanford-Binet scales, version IV was done. Written consent was obtained from every parent whose children were included in the study. Obtaining approval from the ethical committee of the faculty of medicine at Assiut University.

Statistical analysis

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS) release 22.0 program (SPSS for Windows; SPSS Inc, Chicago, IL). Numerical data were expressed as mean ± standard deviation and compared using independent student's t-test. Categorical data were reported in frequencies and percentages and compared with the chi-square test when appropriate. Statistical significance was accepted at P-value less than 0.05

Results

The study included 80 children (47 males, 33 females) with benign epilepsy with centrotemporal spikes attended to Assiut university children hospital during the period from August 2018 through December 2020. The median age at the time of diagnosis was 7.9 years with a range of 3-14 years old (Figures 1 to 7).

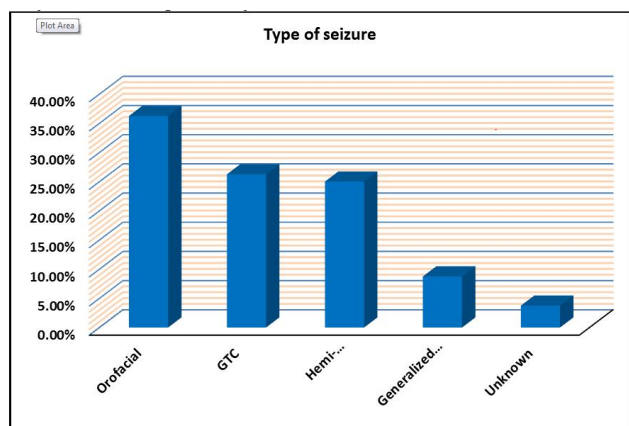


Figure 1. Type of seizure among the studied cohort.

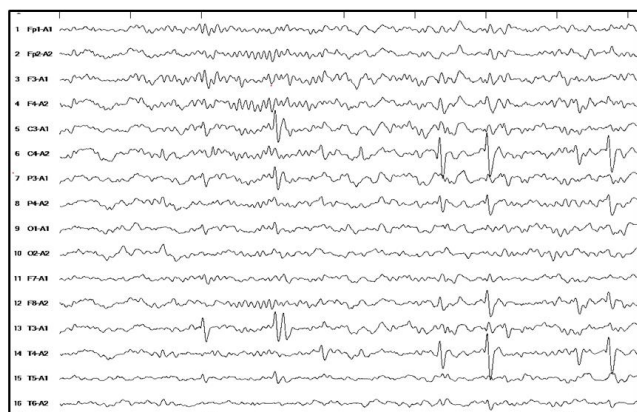


Figure 2. Centrotemporal spikes occurring bilaterally and independently on the left and right sides.

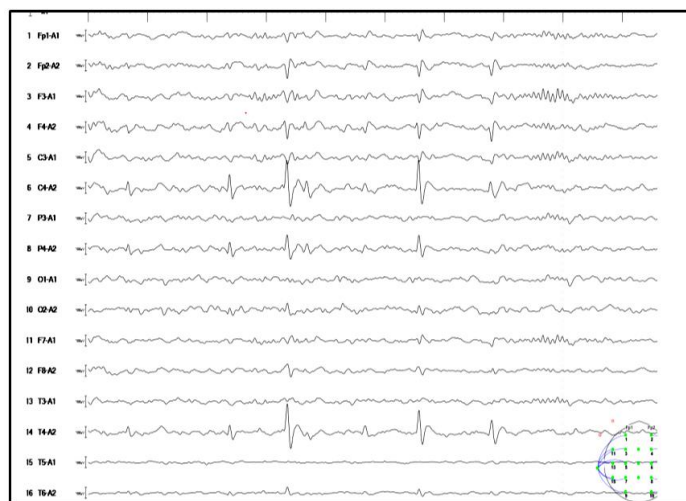


Figure 3. Centrotemporal spikes occurring at the right side.

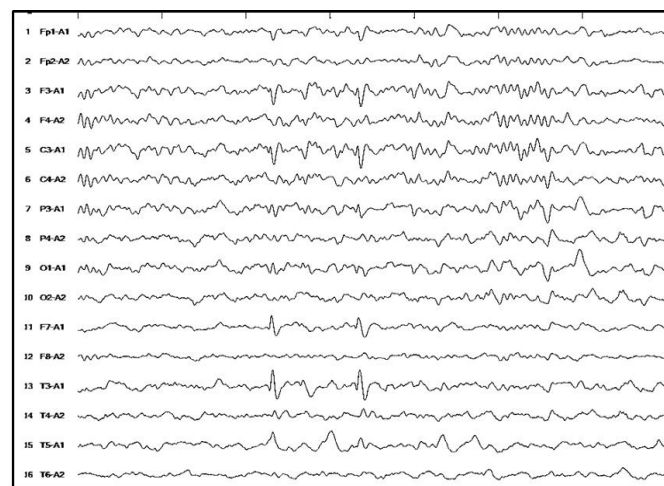


Figure 4. Centrotemporal spikes occurring at left side.



Figure 5. Centrotemporal spikes evolution to ESES with SWI>56.5% of the whole record.

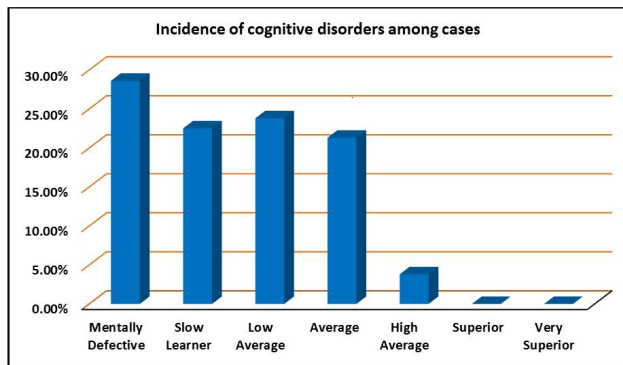


Figure 6. Incidence of cognitive disorders among cases.

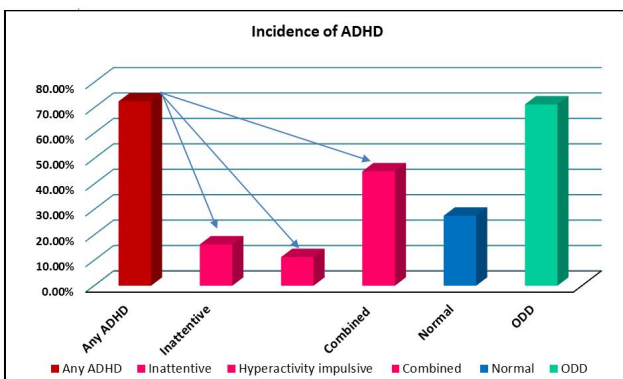


Figure 7. Incidence of ADHD among cases.

Discussion

The study included 80 children (47 males, 33 females) with benign epilepsy with centrottemporal spikes attended to Assiut university children hospital during the period from August 2018 through December 2020. The median age at the time of diagnosis was 7.9 years with a range of 3-14 years old. Seizures were nocturnal in 86.3% of cases, nocturnal and diurnal in 13.7% of cases. The mean number of seizures was 1.71 ranging from one to 7 attacks. The type of seizures was or facial in 36.25% of patients, generalized tonic-colonic in 26.25%, hemi convulsions in 25%, generalized tonic in 8.75%, and unknown in 3.75%. The occurrence of generalized convulsions is overestimated because most of them occur at night and the onset is seen [14]. This may explain the high percentage of generalized tonic-colonic convulsions and hemi convulsions in our study.

Interictal Epileptic Discharges (IEDs) were unilateral in 50% (left in 28.7% and right in 21.3%) and bilateral in 50%. The spike site is unilateral in 60% and sometimes changes from one side to the other over time or maybe in both sides in 40% in BECTS [15]. Berroya et al. [16] studied the laterality of IEDs of BECTS in wakefulness, drowsiness, and sleep. They reported unilateral IEDs in 74.5% (45.4% right and 29.1% left) and bilateral IEDs in 25.5% in wakefulness. During drowsiness unilateral IEDs were in 62.2% (35.5% right and 26.7% left) and bilateral IEDs in 37.8%. During sleep unilateral IEDs were in 51.5% (30% right and 21.5% left) and bilateral IEDs in

48.5%. During the transition from wakefulness to sleep, the IEDs become more abundant and more bilateral.

In the present study, SWI was calculated for every patient from a prolonged sleep EEG. The SWI was <25% in 55% of patients, >25% to 50% in 25% of patients, >50% to 85% in 17.5% of patients, and >85% in 2.5% of patients. CSWS was first described by Patry et al. [17] as a subclinical “electrical status epilepticus” induced by sleep in children. The term “continuous spikes and waves during slow sleep” is synonymous with electrical status Epilepticus in Slow-Wave Sleep (ESES) [18]. In our study, 20% of patients with BECTS had ESES (SWI>50%). Tovia et al. [10] reported 4.6% of patients with BECTS to have ESES and Ross et al. [4] reported 6.6% meet the criteria for either LKS or CSWS. On the other hand, Berroya et al. [16] reported 51.5% of patients with BECTS to have ESES (SWI>50%). Kessi et al. [19] surprisingly reported a higher prevalence of ESES among patients with BECTS. They detect 10.3% of 185 patients having SWI>85% and 49.7% of 185 patients having SWI>50%.

Mentally retarded was detected in 28.6%, slow learner in 22.5%, low average in 23.8%, average in 21.3%, high average in 3.8%, and no detected superior or very superior IQ. Our findings also support previously published articles that claimed that BECTS is not benign in terms of cognitive deficits [3,10]. Up to 28.6% of the patients in our cohort were diagnosed as having mental retardation. Tovia et al. [10] reported 21.8% of BECTS patients to have cognitive deficits and similar to the findings of Yung et al. [20]. The prevalence of intellectual disability in the general population is about 1% to 3% in western countries and it is 1.5 times more common among males than females with the highest prevalence occurring between the ages of 6 and 16 years [11].

The percentage of our BECTS patients with ADHD in our study was 72.5%. This is similar to the study of Kim et al. [21] which detected 64.9% of the 74 children with BECTS had ADHD, and Danhofer et al. [22] detected 65.6% compared to the rate of 31% reported by Tovia et al. [10], and 11% reported by Datta et al. [23]. In a systematic review, Aricò et al. [12] found the reported prevalence of ADHD in patients with BECTS was around 60%.

The inattentive type was present in 16.25% of patients, the hyperactivity impulsive type in 11.25%, and combined ADHD in 4.75%. ADHD increased by 42% from 2003 to 2011 in the USA. In 2003, 7.8% of children were diagnosed with ADHD, in 2007, they were 9.5%, and in 2011, they were 11% [24]. The prevalence of ADHD in Fayoum City, Egypt, was 20.5% [25]. The annually increasing prevalence of ADHD, the more common in males, the difference according to age groups, and using different diagnostic tools may partially explain the higher prevalence of ADHD in our study. Also, it can be explained by the higher Spike-Wave Index in our study (SWI>50% in 20% of patients).

These neuropsychological deficits are suspected to be related to the sleep-wake cycle and SWI, the localization of epileptiform discharge, age at onset, frequency of seizures, and

duration of disease though these relationships are not always detected [4,26,27]. In our study cognitive disorders are more common in BECTS patients with more frequent seizures (P-value=0.017), mixed diurnal and nocturnal seizures than only nocturnal seizures (P-value=0.005), and higher SWI (P-value<0.001). We did not find a relationship between cognitive disorder and the age at onset of seizures, sex, or laterality of epileptic focus in EEG. This finding provides support for a common mechanism underlying both the neuropsychiatric deficits and epilepsy in this disorder. The lack of effect of the laterality of the electrical focus on cognitive ability in our patients is in agreement with the study of Goldberg-Stern et al. Also, several studies have not found seizure focus lateralization effect on cognitive processes [28]. This may be because both hemispheres contribute to language and cognitive function early in life with an increase in left lateralization of language with advancing age [29]. Also, epileptic focus can travel from one hemisphere to the other in BECTS patients [15]. Some studies show more cognitive impairment in BECTS patients with left-sided focus [30], right-sided focus [31], and other studies in bilateral BECTS [32].

We found a relationship between inattentive ADHD and certain seizure criteria. Inattentive ADHD is more common in BECTS patients with more frequent seizures (P-value=0.024), male patients (P-value=0.042), and SWI (P-value=0.021). We did not find a relationship between inattentive ADHD and the age at onset of seizures, time of seizures, or laterality of epileptic focus in EEG. Also, hyperactive-impulsive ADHD is more common in BECTS patients with more frequent seizures (P-value=0.041), and SWI (P-value=0.033). We did not find a relationship between hyperactive-impulsive ADHD and the age at onset of seizures, sex, time of seizures, or laterality of epileptic focus in EEG. Different studies found a relation between ADHD and age at seizure onset [33], the SWI [21], or the site of epileptic focus [32]. The pathophysiology of ADHD in children with BECTS is unknown but it may be due to common genetic or biochemical factors [34,35]. Also, it may be due to poor maturation of the brain as a result of suppression of the same cortical region by frequent spikes [21].

Conclusion

BECTS is commonly associated with neuropsychological deficits. Mentally retarded was detected in 28.6% of BECTS patients, ADHD was detected in 72.5% of BECTS patients. The inattentive type was present in 16.25% of patients, the hyperactivity impulsive type in 11.25%, combined ADHD in 45%.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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