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Original article

Prognostic significance of failure of the initial antiepileptic drug in children with benign childhood epilepsy with centrotemporal spikes

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Abstract

Background: Benign epilepsy with centrotemporal spikes is the most common partial epilepsy syndrome in children. The long-term prognosis for children with BECTS is believed to be generally excellent with seizures usually responding well to AEDs. The goal of the present study was to determine the risk factors associated with a poor prognosis. *Methods:* Eighty-four children with BECTS were retrospectively analyzed. Fifty-four (64.3%) were boys and 30 (35.7%) were girls with the mean age at seizure onset 7.1 ± 2.01 years (range: 3–12 years). *Results:* Of the 84 patients, 72 (85.7%) were treated successfully with the first AED (Group A), and 12 (14.3%) failed to responded to the initial AED treatment (Group B [poor prognosis]). Univariate analyses suggested that younger age of seizure onset, presence of generalized seizures, and frequent seizures (>3 prior to the initial treatment) were associated with failure to control seizures with the initial AED. Multivariate analysis suggested that younger age of seizure onset was the independent risk factor predicting a poor response to initial AED treatment. *Conclusion:* About 14% of our cohort of children with BECTS continued to have seizures following the initial AED treatment. Further prospective studies are warranted to determine how well prognosis can be predicted by age of seizure onset, type of seizures, and frequency of pre-existing seizures in children with BECTS.

Keywords: Benign epilepsy with centrotemporal spikes; Failure risk factors; First antiepileptic drug; Children

1. Introduction

Rolandic epilepsy or benign epilepsy with centrotemporal spikes (BECTS) is one of the most common childhood epilepsy syndromes, occurring in 15–25% of pediatric epilepsy patients [1]. Characteristically the seizures begin in middle childhood, between 3 and 13 years of age, and resolve by puberty. BECTS is slightly more frequent in boys [1–3].

The seizures have typically a focal onset involving arm and oral facial tonic or clonic contractions associated with guttural sounds and drooling. A focal seizure may progress, on occasion, secondarily generalization. The seizures are usually brief, but status epilepticus has also been reported. The seizures predictably occur during sleep, often in the early morning hours. Seizure frequency is low, typically 2–5 total seizures, but also quite variable, ranging from a single lifetime episode to multiple seizures per day [4].

Most children have only rare seizures and, when treated, the response to antiepileptic drugs is good. However, in a poorly identified subset of children with BECTS, more than one AED is required for an effective

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control of seizures. In literature, only a few studies are reavailable on factors associated with initial poor response to AEDs [5,6]. Therefore, we conducted a retrospectively study designed to identify the risk factors associated with initial poor response to AEDs in children with BECTS.

2. Materıals and methods

This study was conducted a retrospective study of 84 children diagnosed with BECTS and started on an antiepileptic drug in the pediatric neurology department of our hospital.

Children were included in the study if they met both the clinical and electroencephalographic criteria of benign childhood epilepsy with centrotemporal spikes as set out by the International League Against Epilepsy (ILAE) in 1989 [7] and treated with AEDs for the first time. We studied with only BECTS with patients on AED treatment. The AED treatment has started if they have at least two unprovake typical seizures and abnormal findings on EEG. Children with obvious neurological deficit were excluded from the study. They were followed at the clinic until they achieve seizure remission and were taken off treatment. Successful treatment meant that only one AED was used for seizure control during the first year of treatment. Failed treatment meant that more than one AED was used for seizure control during the first year of treatment. The data were retrospectively collected from the clinic files and included age, sex, age of seizure onset, consanguinity, neonatal seizures, family history of epilepsy, history of febrile seizure, type of seizures, time and frequency of seizures, history of status epilepticus and Todd's paresis, history of behavior disorders, duration of starting first treatment, investigation results on electroencephalogram (EEG), and treatment.

Interictal EEG was recorded with 18 electrodes (10–20 system) both during wakefulness and during sleep. Intermittent photic stimulation and hyperventilation were performed routinely. The investigation results on EEG were included focus of spikes, localization and generalization. Focus of spikes were divided centrotemporal region (CT), centroparietal region (CP), and frontocentral region (FC). Localization are divided unilateral hemisphere and bilateral hemisphere.

The SPSS version 19.5 was used for statistical analysis. Statistical significance was accepted at $p < 0.05$. The chi-square tests were used to determine the associations between categorical data. We carried out univariate and multivariable analyses of potential predictors of recurrence risk using by Cox regression analysis. The level of statistical significance was established at p- value of <0.05. Initially, first we performed a univariate analysis, in order to determine which would used in multivariate analysis.

3. Results

Eighty-four children, mean age 7.8 ± 2.1 years (4–13 years), were included in this study. Among the 84 patients, 54 (64.3%) were boys and 30 (35.7%) were girls, and the mean age at the seizure onset was 7.1 ± 2.01 years (3–12 years).

Of the 84 patients, 72 (85.7%) were treated completely seizure free with the first AED (Group A), and 12 (14.3%) were not responsed initial AED treatment (Group B [poor prognosis]).

Ten patients (11.9%) had past history of febrile convulsion, and twenty-six patients (31.0%) had family history of epilepsy. Among the all patients, 59 of them (70.2%) had partial seizures, 20 patients (23.8%) had partial seizures with secondary generalized, and 5 patients (6.0%) had primary generalized seizures. Seizures occurred only during sleep in 62 (73.8%), during both sleep and wakefulness in 19 patients (22.6%), and during wakefulness alone in three patients (3.6%). No patient progressed to status epilepticus.

All children had a full lead EEG at presentation and all of them also had a sleep EEG. The background rhythms were normal of all the children. In 83.3% of patients, the spike foci were unilateral, whereas in 16.7%, there were bilateral spike foci. All of them had typical morphology of high amplitude and diphasic waveforms.

The most widely used first-line antiepileptic drugs were valproic acid, carbamazepine, and oxcarbazepine. Other first-line used medication included levetiracetam. Among the 84 treated patients, 36 patients (42.8%) were treated with sodium valproate, 27 patients (32.1%) were treated with carbamazepine, 17 patients (20.2%) were treated with oxcarbazepine, and 4 patients (4.9%) were treated with levetiracetam. All of the children had been followed up for a period of at least 3 years. The mean duration of follow-up was 4.05 years after the initial seizure.

There was no correlation between response to initial AED and sex, consanguinity, neonatal seizure, history of family epilepsy and febrile seizure, time of seizures, history of status epilepticus, Todd's paresis, history of behavior disorders, duration of starting first treatment, and EEG findings. But, there was statistically significant correlation between response to initial AED and age of seizure onset, type of seizures, and frequency of seizure. In the multivariate analysis, age of seizure onset was only the risk factor influencing response to initial AED.

The general characteristics of children treated with initial AED, overall and for successful vs failed treatment shown in Table 1.

4. Discussion

More than 10 million children worldwide have some form of epilepsy [8]. Where treatment is deemed