

Benign epilepsy with centro-temporal spikes (BECTS): relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on EEG and the effectiveness of anti-epileptic medication

Pavlou E¹, Gkampeta A¹, Evangeliou A², Athanasiadou- Piperopoulou F¹

¹ 2nd Department of Pediatrics, Aristotle University of Thessaloniki, "AHEPA" Hospital

² 4th Department of Pediatrics, Aristotle University of Thessaloniki, "Papageorgiou" Hospital

Abstract

Background and Aim: Benign epilepsy with centro-temporal spikes (BECTS) is one of the most frequent epileptic syndromes in children. It is placed among the idiopathic localization-related epilepsies. However, the relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on electroencephalogram (EEG) and the effectiveness of anti-epileptic drugs has not been studied yet.

Patients and Methods: We studied 55 neurodevelopmentally normal children who had been diagnosed with BECTS. Children were subdivided into two groups, based on EEG findings: Group A comprised 30 children with unilateral findings on EEG and Group B 25 children with bilateral findings on EEG. All patients in the present study were started on an anti-epileptic medication after the third seizure (Sodium Valproate, Carbamazepine, Oxcarbazepine) and we studied the response to medications.

Results: Children with bilateral findings on EEG had the same response to treatment with either Sodium Valproate or Carbamazepine or Oxcarbazepine. Other side, children with unilateral findings on EEG corresponded best to Carbamazepine or Oxcarbazepine.

Conclusions: Children diagnosed with BECTS and bilateral discharges on EEG have good response to treatment with either Sodium Valproate or Carbamazepine or Oxcarbazepine. Hippokratia 2012; 16 (3): 221-224

Key words: Benign epilepsy with centro-temporal spikes (BECTS), electroencephalogram (EEG), unilateral, bilateral, medication response, children

Corresponding author: Evangelos Pavlou, St. Kyriakidi 1, Thessaloniki, 54636. Tel: +302310 994815, Fax: +302310 993514, e-mail: eepav@yahoo.gr

Epilepsy is a common condition in childhood. It is characterized by chronic seizures as a result of excessive, synchronous discharge of cerebral neurons. The onset of seizures in more than 50% of cases occurs in childhood, with prevalence from 0.7% to 1%¹. In Greece, the number of people with epilepsy is approximately 60,000-70,000². There are many epileptic syndromes which have been subdivided into groups based on clinical presentation, neuropsychomotor development, neurological examination, electroencephalogram (EEG) and Magnetic Resonance Imaging (MRI) findings³. The exact diagnosis of an epileptic syndrome is important for the choice of medication.

Benign epilepsy with centro-temporal spikes (BECTS) is considered to be the most common childhood epilepsy syndrome, accounting for 8-20% of pediatric patients with epilepsy^{4,5}. It is placed among the idiopathic localization-related epilepsies. It has a characteristic age of onset, seizure pattern, neurodevelopmental profile, imaging and electroencephalographic pattern. The age of onset ranges from 1 to 14 years, with 75% starting between 7 and 10 years. No gene has been identified, but

an autosomal dominant inheritance has been postulated⁶. Classically, BECTS occurs in neurodevelopmentally normal children. Ictal manifestations occur more frequently (75%) during NREM (Non-Rapid Eye Movement) sleep, mainly at sleep onset or just before awakening. The seizures are usually brief lasting for 1-3 minutes. Seizures are somatosensory and motor focal, mainly affecting the face and oropharynx, with speech arrest and hypersalivation and in some cases involving the upper limb⁷. The characteristic EEG shows high-voltage spikes or spike and waves in the centrottemporal region that may shift from side to side with a normal background. Neuro-imaging is normal. The term "benign" refers to the excellent prognosis of the disorder, regarding seizure control and the long term seizure and developmental outcome⁸⁻¹⁰. Children become seizure free by the age of 14, with normalization of the EEG and without neurological deficits. Carbamazepine or Oxcarbazepine is considered to be the first line drug of choice, although some children with BECTS do not need antiepileptic therapy (infrequent seizures, mild or nocturnal, onset close to the natural age of remission)^{2,11}.

Table 1: Clinical and EEG characteristics, medications and outcome (n=55).

	Group A	Group B
Number of subjects	30	25
Male	11	15
Female	19	10
Mean age (years)	7.5	8
EEG findings		
Unilateral	30	
Bilateral		25
Seizure type		
Simple partial	12	7
Complex partial	4	2
Generalized	14	16
Medication		
Carbamazepine/Oxcarbazepine	12	12
Sodium Valproate	18	13
Medication's efficiency		
Good response to Carbamazepine/Oxcarbazepine	10	7
Good response to Sodium Valproate	13	7
Change of treatment with Carbamazepine/Oxcarbazepine	2	5
Change of treatment with Sodium Valproate	5	6
Outcome		
Seizure free at 1 or 2 years	23	14
Change of medication	7	11

The prospective study objective was to find the relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on electroencephalogram (EEG) and the effectiveness of anti-epileptic medication. There are no similar reports neither in international nor in greek literature.

Materials and methods

Patients' data were collected from the 2nd Department of Pediatrics, Aristotle University of Thessaloniki, "AHEPA" Hospital, from January 2008 to January 2010. A total of 55 patients (children) diagnosed with BECTS, participated in the present study [26 male (47.2%), 29 female (52.7%), mean age 7.5 with range 2.5-13 years, mean age at onset 5.5 years]. All of them had a classical seizure history for BECTS, at least two EEGs consistent with spikes in one or both centrottemporal region, normal neurodevelopment and normal neuro-imaging.

Children were subdivided into two groups, based on EEG findings: Group A comprised children with persistently unilateral findings on two EEGs and Group B those with persistently bilateral findings on two EEGs.

All patients in the present study were started on an anti-epileptic medication (Sodium Valproate, Carbamazepine, Oxcarbazepine) after a third seizure in a short period of time (two months) and had clinical, biochemical and EEG examination every 3 months. Table 1 shows clinical and EEG characteristics, medications and outcome of all 55 patients.

Sixteen-channel EEG recording was performed for all patients both during sleep states and during wakefulness. Electrodes were placed using the 10-20 International System with bipolar and referential montages. Hyperventilation and intermittent photic stimulation from 1-30 Hz was performed during each EEG recording that lasted at least 30 minutes.

In the present study, EEGs during wakefulness only were undertaken.

Results

Of all patients (55 children), 30 children (54.5%) had generalized tonic-clonic seizures, 6 children (10.9%) had complex partial seizures and 19 children (34.5%) had simple partial seizures.

All patients had stereotyped focal spikes in the centrotemporal region on electroencephalogram (EEG). Of these, 30 children (54.5%) exhibited unilateral findings, either on the right or left hemisphere and 25 children (45.4%) had bilateral findings.

Of all 55 patients, 17 children (30.9%) responded well to treatment with Carbamazepine or Oxcarbazepine and 20 children (36.3%) responded well to Sodium Valproate. 7 children (12.7%) started treatment with Carbamazepine or Oxcarbazepine but due to incomplete control of seizures they had to change medication. Eleven children (20%) started treatment with Sodium Valproate but due to uncontrollable seizures they had to change medication.

According to medication's efficiency, 26 children (47.3%) became seizure-free by two years after seizure onset, 11 children (20%) became seizure-free by one year after seizure onset, 11 children (20%) had to change medication due to uncontrollable seizures and 7 children (12.7%) were on more than one anti-epileptic drug, due to incomplete seizure control. All 37 children (23 from Group A and 14 from Group B) who became seizure-free by one or two years after seizure onset were under the age of 16 years (we clarify that because it's well known that remission usually occurs after 2-4 years of onset and before the age of 16 years).

With regard to EEG findings and medications' efficiency, 10 (83.3%) from 12 children in Group A (unilateral findings on EEG) started Carbamazepine or Oxcarbazepine had a favorable respond, 13 (72%) from 18 children started Sodium Valproate responded well to medication. Two children (16.6%) started with Carbamazepine or Oxcarbazepine had to change medication. Five children (27.7%) started Sodium Valproate and had to change their anti-epileptic therapy due to incomplete control of seizures.

From 25 children in Group B (bilateral findings on EEG), 12 started Carbamazepine or Oxcarbazepine and from those 7 children (58.3%) responded well to treatment. Five children (41.6%) had to change their anti-epileptic therapy due to incomplete control of seizures. Thirteen children started Sodium Valproate and from those, 7 children (53.8%) responded well to treatment, while 6 children (46.1%) had to change their anti-epileptic therapy due to incomplete control of seizures.

Discussion

Benign epilepsy with centro-temporal spikes (BECTS) is one of the most frequent epileptic syndromes in children. It is placed among the idiopathic localization-related epilepsies^{4,5}. However, the relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on electroencephalogram (EEG) and the effectiveness of anti-epileptic drugs has not been studied yet. There are no similar reports neither in international, nor in greek literature. At the present prospective study, children diagnosed with BECTS and bilateral discharges on EEG have good response to treatment with either Sodium Valproate or Carbamazepine or Oxcarbazepine, while

children with unilateral discharges on EEG respond better to treatment with Carbamazepine or Oxcarbazepine.

Previous literature demonstrated that the major effect of drowsiness and sleep is to increase spike frequency rather than affect spike location or the number of foci¹⁰, although it has been repeatedly reported that patients with benign epilepsy with centrotemporal spikes frequently have bilateral independent or bilateral synchronous discharges. The spikes can be ipsi- or contralateral to the symptomatogenic side and they are frequently multifocal¹²⁻¹⁴.

In total, three randomized controlled trials (RCTs) and no meta-analyses specifically examined the initial monotherapy of children with BECTS. None of these RCTs met the criteria for a class I or II study. No anti-epileptic medication (AED) reaches the highest levels of evidence (level A or B) for efficacy / effectiveness for children with BECTS, while Carbamazepine and valproic acid are possibly efficacious or effective as initial monotherapy for children with BECTS (level C)¹⁵⁻¹⁷.

Based on the results of the present study, we conclude the following concerning the relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on EEG and the effectiveness of anti-epileptic medication: a)from all children with unilateral findings on EEG (Group A), only 16.6% of those who started treatment with Carbamazepine or Oxcarbazepine had to change medication due to incomplete control of seizures, while 27.7% of those who started on with Sodium Valproate had to change their anti-epileptic drug and b)from all children with bilateral findings on EEG (Group B), more than half of them became seizure-free either with Carbamazepine or Oxcarbazepine or with Sodium Valproate.

The present findings confirm our suspicion that children diagnosed with BECTS and bilateral discharges on EEG have good response to treatment with either Sodium Valproate or Carbamazepine or Oxcarbazepine. Furthermore, children with unilateral discharges on EEG respond better to treatment with Carbamazepine or Oxcarbazepine. Further research in larger number of children is needed to evaluate the relationship between unilateral or bilateral localization of interictal stereotyped focal spikes on EEG and the effectiveness of anti-epileptic medication.

References

1. Cowan LD. The epidemiology of the epilepsies in children. *Ment Retard Dev Disabil Res Rev.* 2002; 8: 171-181.
2. Camfield P, Camfield C. Epileptic syndromes in childhood: clinical features, outcomes, and treatment. *Epilepsia.* 2002; 43: 27-32.
3. Pazzaglia P, D'Alessandro R, Lozito A, Lugaesi E. Classification of partial epilepsies according to the symptomatology of seizures: Practical value and prognostic implications. *Epilepsia.* 1982; 23: 343-350.
4. Holmes GL. Benign focal epilepsies of childhood. *Epilepsia.* 1993; 34: 49-61
5. Wirrell EC. Benign epilepsy of childhood with centrotemporal spikes. *Epilepsia.* 1998; 39: 32-41.

6. Bali B, Kull LL, Strug LJ, Clarke T, Murphy PL, Akman CI, et al. Autosomal dominant inheritance of centrotemporal sharp waves in rolandic epilepsy families. *Epilepsia*. 2007; 48: 2266–2272.
7. Eeg-Olofsson O, Lundberg S, Raininko R. MRI in rolandic epilepsy. *Epilept Disord*. 2000; 2: 51-53.
8. Kellaway P. The electroencephalographic features of benign centrotemporal (rolandic) epilepsy of childhood. *Epilepsia*. 2000; 41: 1053-1056.
9. Datta A, Sinclair DB. Benign epilepsy of childhood with rolandic spikes: typical and atypical variants. *Pediatr Neurol*. 2007; 36: 141–145.
10. Berroya AM, Bleasel AF, Stevermuer TL, Lawson J, Bye AM. Spike morphology, location, and frequency in benign epilepsy with centrotemporal spikes. *J Child Neurol*. 2005; 20: 188-194.
11. Kwan P, Brodie MJ. Neuropsychological effects of epilepsy and antiepileptic drugs. *Lancet*. 2001; 357: 216-222.
12. Petersen J, Nielsen CJ, Gulmann NC. Atypical EEG abnormalities in children with benign partial (Rolandic) epilepsy. *Acta Neurol Scand Suppl*. 1983; 94: 57-62.
13. Lerman P, Kivity S. Focal epileptic EEG discharges in children not suffering from clinical epilepsy. *Epilepsy Res Suppl*. 1992; 6 :99-103.
14. Guerrini R, Belmonte A, Veggiotti P, Mattia D, Bonanni P. Delayed appearance of interictal EEG abnormalities in early onset childhood epilepsy with occipital paroxysms. *Brain Dev*. 1997;19: 343-346.
15. Rating D, Wolf C, Bast T. Sulthiame as monotherapy in children with benign childhood epilepsy with centrotemporal spikes: a 6-month randomized, double-blind, placebo- controlled study: Sulthiame Study Group. *Epilepsia*. 2000; 41: 1284–1288.
16. Mitsudome A, Ohfu M, Yasumoto S, Ogawa A, Hirose S, Ogata H, et al. The effectiveness of clonazepam on the Rolandic discharges. *Brain Dev*. 1997; 19: 274–278.
17. Bourgeois B, Brown LW, Pellock JM, Buroker M, Greiner M, Garofalo EA. Gabapentin (Neurontin) monotherapy in children with benign childhood epilepsy with centrotemporal spikes (BECTS): a 36-week, double-blind, placebo-controlled study. *Epilepsia*. 1998; 39: 163.