SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
Thiruvananthapuram - 695 011

PROJECT REPORT

NAME : **Dr. VINAYAN.K.P**

PROGRAMME : **D.M. NEUROLOGY**

MONTH & YEAR OF SUBMISSION : **NOVEMBER 2002**

PROJECT REPORT

BENIGN EPILEPSY OF CHILDHOOD WITH CENTROTEMPORAL SPIKES (BECTS)- A CLINICAL, ELECTROENCEPHALOGRAPHIC AND NEUROPSYCHOLOGICAL STUDY

NAME	:	**Dr. VINAYAN.K.P**
PROGRAMME	:	**D.M. NEUROLOGY**
MONTH & YEAR OF SUBMISSION	:	**NOVEMBER 2002**

CERTIFICATE

I, ***Dr.Vinayan.K.P,*** hereby declare that I have actually carried out the project under report

Signature

Place: Trivandrum
Date: 10/11/2002.

Forwarded,

He has carried out the project under report

Signature

Head of the Department

ACKNOWLEDGEMENT

I express my deep sense of gratitude to ***Dr. Sanjeev.V. Thomas,*** Additional Professor of Neurology for guiding me through each and every stage of this project.

I sincerely thank ***Prof.K.Radhakrishnan,*** Head of Department of Neurology, SCTIMST for his guidance during my study period.

I express my sincere thanks to Ms. Biji, child psychologist, and to Ms Vidya and Ms Anita, speech pathologists, ICCONS, Trivandrum for their invaluable contributions.

I wish to thank Dr. P. Sankara Sharma, Asst. Prof. of biostatistics for his immense help in the statistical analysis of this study.

I thank the staff of the electrophysiology lab, for their co-operation

I thank Ms Usha for the secretarial assistance

Last but not the least, I also take this opportunity to thank all the children and their parents who were part of this study for their co-operation and good will.

Dr. VINAYAN. K. P

INTRODUCTION

Epilepsy in children have wide spectrum of severity. Conditions like Lennox Gastaut Syndrome are associated with multiple seizures, progressive mental decline and considerable disability. On the other hand syndromes like Benign Epilepsy with Centrotemporal Spikes (BECTS) or Benign infantile convulsions tend to undergo permanent remission and leave little if any serious impairment. Precise classification of seizure type and epileptic syndrome is a prerequisite for appropriate management.

Identification and classification of benign partial epilepsies of childhood constitute an important development in pediatric epilepsy. Although the benign partial epilepsy is not fully defined, the diagnostic criteria proposed include no neurological or intellectual deficits; onset of seizures after age 2 years; brief seizures that are stereotyped in clinical manifestation; frequent nocturnal occurrence; spontaneous remission in adolescence and family history of epilepsy, especially benign types (Holmes GL, 1993).

The principal electroencephalographic (EEG) criteria include normal background activity, spikes with a particular morphology and localization,

activation of epileptiform activity during sleep but not during hyperventilation and occasional generalized spike-wave discharges. By definition, the prognosis of these syndromes, when compared to other partial seizures during childhood, is favorable .

The International Classification of the Epilepsies and Epileptic Syndromes recognizes two idiopathic localization-related epileptic syndromes: benign childhood epilepsy with centrotemporal spikes-BECTS (Benign Rolandic epilepsy, BRE) and childhood epilepsy with occipital paroxysms (benign occipital epilepsy, BOE) (ILAE, 1989). However, other benign syndromes have also been described (Holmes GL 2000).

Originally described by Marinus Rulandus in 1597, BECTS is a genetic disorder confined to children and is characterized by nocturnal generalized seizures of probable focal onset, diurnal partial seizures arising from the lower Rolandic area, and an EEG pattern consisting of a midtemporal central spike foci.

BECTS accounts for between 6-16% of all nonfebrile seizures in childhood. Although classically described as a childhood epilepsy with excellent developmental and seizure outcome, many of the recent reports are showing neuropsychological dysfunction and learning problems in patients with this syndrome(Gunduz E et al 1999). There are also reports indicating

atypical evolution of the clinical picture in children initially diagnosed to have BECTS with marked neuropsychological deterioration later in the course (Fejerman N,2000). Similarities between the syndromes of BECTS, Landau Kleffner Syndrome (LKS) and epilepsy with continuous spike and wave activities in slow wave sleep (CSWS) were also highlighted (GalanoPoulou, 2000). Some authorities consider BECTS as part of a broad continuum of brain maturation disorders with a marked phenotypic variability.

There is only scant data available from India on BECTS and on its impact on the cognitive and academic functions in the affected children. Clinical data correlating of the final outcome with the clinical &EEG features are also lacking which may be important in predicting the course of the disease.

Although BECTS is fairly common among children, it is often under diagnosed. It is often misdiagnosed as complex partial seizures, simple partial seizures, temporal lobe epilepsy, and generalized epilpesy. Such misdiagnosis leads to inappropriate therapy and poor prognostication

The present study was conducted to find out the profile of children with BECT and to assess the impact of this seemingly benign epileptic syndrome on the scholastic achievements of the affected children.

AIMS OF THE STUDY

1. To characterize the clinical profile & EEG features in children with BECTS attending to the epilepsy services of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, India

2. To assess in detail the cognitive and scholastic functions of children with BECTS

3. To identify any possible clinical or electrographic features that are associated with relatively poor prognosis in terms of cognitive outcome or learning disability among the children affected with BECTS

REVIEW OF LITERATURE

As emphasized by Aicardi (1994), "if the designation of epileptic syndromes is to be practical value, the syndrome should be limited to clusters of signs or laboratory findings that are unequivocally identifiable". BECTS is one of the childhood seizure disorders that deserves classification as a syndrome.

DEFINITION

In the International Classification (Commission on Classification and Terminology of the International League Against Epilepsy, 1989), benign childhood epilepsy with centro temporal spikes (BECTS) is defined as a syndrome of brief, simple, partial hemifacial motor seizures, frequently having associated somatosensory symptoms, which have a tendency to evolve into generalized tonic clonic seizures. Both seizure types are often related to sleep. The EEG has blunt high voltage centrotemporal spikes, often followed by slow waves that are activated by sleep and tend to spread or shift from side to side. Oropharyngeal symptoms and arrest of speech are also frequent and should be incorporated into the definition, in addition to hemifacial seizures.

CLINICAL FEATURES

This syndrome represents about 16% of all epileptic seizures in

children aged 0-15 years, being four times more frequent than typical absence seizures. Benign focal sharp waves frequently occur without clinical seizures; only 9% of children with such sharp waves have clinical seizures. The ratio of boys to girls is 6:4.The age of onset ranges from 2 to 12 years, but is mostly between 4 and 10 years with a peak at 7-9 years.

There is a high incidence of a positive family history of epilepsy and of sharp waves on EEG (Holmes, 1993), suggesting that genetic factors are important in this order. This is also supported by the study of monozygotic twins. Most authors postulate an autosomal dominant inheritance with age dependent penetrance.

Some 7-10% of patients also have a past history of febrile seizures. This may indicate a genetic link between the two conditions, or a genetic predisposition to febrile seizures at a younger age in patients with BECTS. Some differences in the clinical manifestations of patients with a past history of febrile seizures may suggest that these conditions may be interdependent but with closely linked genes .

As a rule, the patients show normal development and are neurologically normal. However, considering its prevalence, this syndrome may occur in developmentally or neurologically abnormal children .Therefore, the presence of developmental retardation or neurologic deficits does not

preclude its diagnosis.

Higher cerebral functions such as language may be affected by focal sharp waves even in these benign partial epileptic syndromes .Transitory cognitive impairment occurs in association with rolandic spikes, and in some patients interferes with scholastic performance or with general psychosocial functioning (Deonna T,2000)

Recurrent headaches or migraine are frequent symptoms in BECT but may not be significantly more frequent than in control children. Septien et al. (1991) found migraine in 63% of patients with a history of this disorder, on the basis of a long term controlled study, and have concluded that the association of the two conditions is not fortuitous.

SEIZURE MANIFESTATIONS

Seizure manifestations are related to the somatosensory and motor area in the lower rolandic region just above the sylvian fissure, and consist of unilateral paresthesiae involving the tongue, lips, gums and inner cheeks, and unilateral motor phenomena involving the face, lips, tongue, pharyngeal and laryngeal muscles (Watanabe 1996). Difficulty with speech and vocalization is caused by a peripheral type of motor disturbance or dysarthria and occurs irrespective of the laterality of the epileptogenic focus. Sialorrhea, drooling, gurgling sounds from the throat, and a feeling of

suffocation are also common. These orofacial symptoms should not be mistaken for oral automatisms. Speech and oromotor deficits may be an initial or a sole symptom of the disorder. Consciousness is usually preserved unless seizures become secondarily generalized. Failure to respond secondary to arrest of speech should not be mistaken for impaired consciousness. Hemifacial seizures may spread to the upper arm but rarely to the lower limb. Secondary generalization of seizures is rare during wakefulness, but frequent during sleep. In diurnal seizures, somatosensory symptoms may be the only manifestation. The initial focal manifestations of the nocturnal seizures although in fact, secondarily generalized tend to be diagnosed as generalized tonic clonic attacks.

Three types of nocturnal seizures occur (Lerman, 1998):

1. Hemifacial seizures associated with speech arrest and drooling.
2. Seizures similar to the above but with loss of consciousness, usually with gurgling and grunting noises.
3. Generalised convulsions.

However, the presence or absence of consciousness is often difficult to determine in nocturnal seizures in children with speech arrest and uncertain memory. In older children, hemifacial seizures are commoner, whereas in younger ones hemiconvulsive or generalized nocturnal seizures

are more frequent in some series (Beaussart, 1972). Louisse(1993) divided the seizure characteristics into typical and atypical features and tried to correlate the seizure semiology with outcome.

EEG FEATURES

The electroencephalographic features of BECTS has recently been reviewed by Kellaway(2000) .The dominant EEG features of BECTS is a focal surface negative spike with specific biophysical characteristics. The average duration is approximately 74 milliseconds. The average sharpness or degree of curvature of peak is 0.022 microvolt /millisecond. The average amplitude of the spike is 160 microvolt, but some individual spikes may exceed 300 microvolt.

The high amplitude, the relatively prolonged duration and the bluntness of the spike suggest that it is generated by an extensive neuronal pool. When effective drug treatment results in clinical seizure control, these parameters of the spike change: the amplitude and duration of spike decrease and the sharpness increases.

The predominant negative spike may be preceded by a low amplitude sharper surface positive spike. After the large negative spike, there is a trough followed by an after going slow wave. This complex may show two distinct types of potential field (a) Stationary pattern with a negativity in the

inferior Rolandic region and a simultaneous positivity in the frontal region. (b) a non stationary pattern consisting of an initial sharp spike which reaches its maximal negativity in the frontal region before the onset of the ascending arm of the rolandic spike and showing simultaneous positivity in the rolandic region. Predominance of the non-stationary pattern is statistically associated with an increased probability for clinical seizures.

Surface negativity of the rolandic spike in the inferior rolandic area with a simultaneous positivity in the frontal region is taken as the evidence of a true electrical dipole(Gregory and Wong 1992). Kellaway (2000) regards this as an evidence of a virtual dipole , the significance of which is not clear. During the seizure activity a reversal of the dipole is demonstrated.

Single and multiple dipole modeling has been used to determine the number, three dimensional localization and the sources of the elements of the rolandic spike complex. The tangential source appears to be located deeply within the central sulcus , the radial source more superficially involving either the pre or post central gyrus. It is found that the spike and slow waves are constituted by two different dynamic processes.

The focal rolandic spikes may occur only in NREM sleep or if present during awake periods, they are always greatly increased in number and rate in spindle sleep. This is supposed to be due to enhanced thalamocortical

drive.

Shifting spike topography is also described in BECTS. This may be shifting of the rolandic spike focus to the opposite hemisphere or the disappearance of one focus after the appearance of spikes bilaterally. The appearance of independent spike foci in one or more sites in the same or opposite hemisphere along with a typical rolandic spike is also described. These findings suggest that BECTS is not a focal epilepsy in the anatomical sense but that the essential abnormality is widely disseminated throughout the cortex.

There have been a few documentations of ictal recordings (Dalla Bernardina and Tassinari, 1975). They usually show frequent rhythmic spikes or low voltage fast activity beginning in the centrotemporal region on one side .The paroxysmal discharges increase in amplitude and decrease in frequency, spreading to the adjacent regions and then to the whole hemisphere, evolving to high amplitude rhythmic spikes, and then to spike and waves when secondary generalization occurs. Lerman (1998) recorded a diurnal seizure beginning with focal decremental activity followed by dense spikes in the centrotemporal area during the tonic phase and spike-waves in the clonic phase with no spread and no postictal slowing. Guiterrez, Brick and Bodensteiner (1990) recorded a subclinical seizure with

paroxysmal discharges showing a dipole reversal relative to the interictal discharges, and postulated the origin of the seizure discharges to be deep in the sylvian fissure in areas within cortical folds.

PATHOPHYSIOLOGY

Both clinical seizure manifestations and the location of EEG foci suggest that the epileptogenic focus is in the part of the lower rolandic cortex representing the face and the oropharynx. The bluntness of the spikes and the frequent association with slow waves may suggest a true focus, deep in the sylvian fissure.

Only a fraction of patients with typical rolandic sharp waves have clinical seizures. Factors, which contribute to the expression of clinical epilepsy, have not been elucidated. Heijbel et al (1975) postulated the existence of an inhibitory factor, capable of preventing seizures, which can be breached by external or internal factors. Lerman (1998) suggested that a precipitating factor was needed to convert the inherited trait into the overt disease. The marked age dependency of symptoms and almost regular disappearance of seizures and EEG abnormalities at puberty may suggest a hereditary impairment of brain maturation(Watanabe,1996).

The fact that patients with typical rolandic spikes may develop

occipital spikes typical of benign occipital epilepsy, while patients with typical occipital spikes may develop typical rolandic spikes and generalized spike-wave typical of idiopathic generalized epilepsy, strongly suggests that there are close links between these disorders (Panayiotopoulos, 1993). He considered the terminology of seizure susceptibility syndromes for these disorders compared to the term epilepsy.

INVESTIGATION

Neuroimaging procedures are usually considered unnecessary in this benign syndrome, but may be indicated in cases with atypical features such as persistent seizures and/or long duration of active epilepsy. Ambrosetto (1992) reported unilateral rolandic macrogyria in a patient with BECT- like epilepsy. Typical rolandic sharp waves may be seen in children with tumors and other organic lesions.

Visual and somatosensory evoked potentials have been reported to be of high amplitude with no changes in morphology and latency. Overnight sleep recordings in children with BECTS do not show significant modifications in sleep organization . Laub et al. (1992) found localized hypoperfusion in about 40% of the patients using single photon emission computed tomography (SPECT) with technetium-99m hexamethyl propyleneamine oxime (HMPAO). The significance of their findings is

unknown because of the absence of correlation between the localization of the EEG focus and the site of the hypoperfused area.

TREATMENT

In view of the benign nature of the condition, intensive therapy is unnecessary. Treatment should not be instituted after the first seizure. There were no differences in seizure frequency, recurrence or duration of active epilepsy between untreated and treated patients with BECT in some studies(Ambrosetto and Tassinari, 1990). The parents' opinion about treatment may be particularly relevant in this type of epilepsy, because of the low morbidity and bettr long term prognosis(Bourgeois 2000). Side effects of anticonvulsants may be more harmful than seizures. All the primary AEDs are equally effective. Carbamazepine was considered the drug of first choice, but a possible worsening of seizures and atypical evolutions have been reported with this medication. Valporate have been reported equally effective and is emerging as the first line AED in this syndrome. Once daily administration at bedtime may be sufficient in the case of nocturnal seizures. Once-daily administration of a low dose of clonazepam was also found to be highly effective in some cases (Watanabe 1996). Although most patients respond to a low dose of a single drug, a few are highly drug-resistant. In such cases, monotherapy at a moderate dose with some persisting seizures

may be better than high dose polypharmacy with neurotoxic side effects (Loiseau, 1993). The duration of treatment may be shorter in some cases than in epilepsy in general, in keeping with the spontaneous disappearance of rolandic spikes between 12 and 15 years of age. Some authors advocate continuance of anticonvulsant therapy until the age of 14-16 years (Loiseau, 1993). Anticonvulsants may be successfully discontinued in patients with normal EEGs who have been seizure-free for more than 2 years. Some 80% of patients become seizure-free, and remains so for at least 6-12 month when drug therapy was discontinued after 2 years of treatment. It is more important to give the parents a full explanation of the benign nature of the disorder, in order to avoid unnecessary psychologic reactions than to prescribe drugs (Lerman, 1998).

Spike discharges typically seen in benign partial epilepsies of childhood can also be observed in nonepileptic asymptomatic children with symptoms such as headache, abdominal pain, cyclic vomiting, etc. Such children should not be treated with antiepileptic drugs (Lerman ,1998)

PROGNOSIS

Seizures eventually disappear and EEGs normalize irrespective of treatment. The duration of active epilepsy is longer in patients with earlier ages of onset (Loiseau et al., 1988). Seizures are more easily controlled in

patients with secondarily generalized seizures than those with only partial seizures. Rarely (in 1-2 % of patients), partial or generalized tonic-clonic seizures recur during adolescence or adulthood, which may represent another form of idiopathic epilepsy rather than a relapse of the same syndrome (Loiseau, 1993). The absence of typical EEG sharp waves and seizure characteristics of this syndrome in adults also indicates that this syndrome improves before adulthood.

In patients followed up for long periods, temporal changes in the EEG often make allocation into discrete syndromes impossible. The electroclinical patterns overlap and the determining factor for prognosis is not the location but the morphology of the sharp waves.

Morikawa, Seino and Yagi (1992) conducted a longitudinal study of children with partial seizures and rolandic discharges and found that rolandic discharges disappeared in an age-related manner in idiopathic patients, but tended to persist in the symptomatic ones. They concluded that the presence of rolandic discharges was not a hallmark of a benign outcome, but the presence of sylvian seizures indicated a favourable prognosis.

Recent reports have also shown that significant disabilities can occur in BECTS. Mean intellectual abilities were also found to be lower in BECTS cohorts compared to control groups. But these dysfunctions are found only

on detailed neuropsychological evaluation, the clinical relevance of which is not clear. It can be argued that only a small subgroup of children with BECTS develop complications. These cognitive impairments were never correlated, with individual EEG or clinical features. Krammer et al (2001) reports transient oromotor deficits in children with BECTS ,the significance of which is also not clear.

MATERIALS &METHODS

Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) is a tertiary referral center for neurological and cardiac disorders in South India. Nearly 10,000 persons with epilepsy are enrolled in the Comprehensive Epilepsy Care program of this Institute. EEG services of this Institute perform about 2000 EEG every year. All the reports on EEGs performed in this Institute between 1994-2000 were screened to identify those with centrotemporal spikes. The EEGs of children below 18 years which satisfied the following criteria were initially identified.

1. Normal background activity
2 High amplitude biphasic spikes followed by prominent slow waves in mid temporal(T3,T4) and central(C3,C4) areas with marked activation during sleep

The presence of a classical electrical dipole across the frontocentral region with a simultaneous frontal positivity and centrotemporal negativity was not mandatory for inclusion in the study group.

The medical records of these children were carefully scrutinized to identify those who satisfy the following criteria.

1. They should have one or more clinical seizures.

2. They should have normal intelligence

The Exclusion criteria were

1. Presence of significant developmental delay
2. Presence of major neurological deficits

Learning disability and minor impairment in scholastic performance were not considered as exclusion criteria. All children who satisfied these criteria were invited to come to the clinic for re-evaluation. Only those patients, who were assessed by the principal investigator, were included in the final analysis.

The evaluation included

1. A detailed history emphasizing on the seizure semiology, perinatal history, detailed developmental history, psychosocial problems, learning abilities and scholastic achievement.
2. A detailed neurological examination was conducted stressing on oromotor functions and minor neurological dysfunctions as defined by Touwen (1979).
3. Parental opinion about academic performance with emphasis on learning disabilities
4. Assessment of neuropsychological, language and scholastic performance was by a team of child psychologist and speech

pathologist in the Institute of Cognitive and Communicative Neurosciences (ICCONS), Trivandrum, India in multiple sessions.

Attention and frontal lobe tests were tested according to the age and educational standards of the children The IQ was assessed using the Malins Intelligence scale for Children (MISC), which is a standardized Indian adaptation of the Weschler Intelligence Scale for Children (WISC). Praxis evaluation included items for nonrepresentational movements, facial praxis, ideational apraxia, intransitive and transitive movements. Standardized memory test for children was administered in detail. Visuomotor ability was tested using Seguin form board test and social functioning was assessed by Vineland social maturity scale.

Language evaluation included screening for hearing and oral-motor speech skills. Receptive and expressive languages were assessed using a standardized scale. The articulation was tested according to a non-standardized test of articulation, which included the main sounds of the local language, Malayalam.

All patients had a detailed EEG evaluation using a 10-20 system of electrodes, with both waking and sleep EEGs. Focal epileptiform activities over the centrotemporal region were identified and the characteristics of the discharges were studied. The reactivity of the epileptic activity was tested

by sensory stimulation. Other possible extrarolandic foci were looked for.

Radiological evaluation was not mandatory for inclusion in the study.

Table I - Items of assessment

Minor neurological dysfunction

1. Astereognosis
2. Agraphesthesia
3. Adiado chokinesia
4. Dysarthria
5. Oromotor apraxia
6. Sialorrhea
7. Change in Jaw reflexes
8. Change in deep tendon reflexes
9. Asymmetric deep tendon reflexes
10. Asymmetric associated movements
11. Hypokinesia
12. Motor coordination defects
13. Changes in muscle tone
14. Tremor
15. Choreiform movements
16. Nystagmus
17. Strabismus
18. Frontal lobe tests

Neuro psychological tests

1. Malins intelligence scale for children
2. Bender Gestalt test
3. Complex figure test
4. Memory test for children
5. Benton visual retention test
6. Seguin form board
7. Vineland social maturity scale

Language evaluation

1. Receptive expressive emergent language scale
2. Malayalam language test
3. Malayalam articulation test
4. Reading readiness test.

RESULTS

A total of 13,462 EEGs were done during the study period (1994-2000) on which the EEG reports were available. 112 EEG reports were identified which satisfied the inclusion criteria . After going through the case records, 4 patients without clinical seizures and 6 patents with severe neuro developmental delay were excluded. The remaining 102 patients were invited to the clinic for a re evaluation. Of the 52 children who came for the reevaluation, 2 were excluded in view of significant developmental retardation with focal deficits.

50 children were finally included in the study. Male to female ratio was 29:21. The age of onset of seizures ranged from 4-13 years (mean age 7.84 yrs). 12 children (24%) had typical febrile seizures before the onset of epilepsy. Adverse perinatal events, like prematurity, minimal birth asphyxia and neonatal jaundice were reported, in 10 children (20%). None of the children had, significant developmental delay; but delayed language development (DLD) was seen in 15 children (30%). 13 children (26%) gave a family history of epilepsy, but further characterization of the type of the epileptic syndrome was not possible in the majority.

TABLE- II **BASE LINE CHARACTERISTICS**	
M:F ratio	29:21
Mean age of onset of seizure	7.84
Adverse parinatal events	10(20%)
Delayed language development	15(30%)
Presence of family seizures	12(24%)
Family history of epilepsy	13(20%)

18 (36%) children had nocturnal generalized seizures, 5 (10%) children had only pure daytime partial seizures and the rest had a combination of the two, as classically described. Majority of children had typical seizure semiology. Atypical/rare features were described only in 16 children (32%). None of the children had status epilepticus or todd paresis.

TABLE-III **SEIZURE SEMIOLOGY**	
Nocturnal generalized seizures	18(36%)
Pure diurnal seizures	5(10%)
Diurnal & nocturnal seizures	27(54%)
Atypical features	16(32%)

Detailed neurological examination did not show any major neurological deficits in the subjects. Soft neurological signs as described above were seen in 12 children (24%). Neuroimaging, either CT/MRI were available only 20 children (40%), all of them were normal.

All patients had at least one EEG characteristic of BECTS. 22 (44%) had left centrotemporal spikes and 8 (16%) had right centrotemporal spikes. 20 had bilateral discharges.

Generalized spike and wave discharges were seen in 20 children (40%). Detailed analysis of the spike foci showed a tangential dipole across the fronto central region with frontal positivity and central and temporal negativity in 8 children (16%), Another focus apart from the typical Centro temporal focus was found in seven patients (14%).

TABLE-IV	
EEG CHARACTERISTICS	
Lateralisation	Left- 22 (44%)
	Right –8(16%)
	Bilateral-20 (40%)
Generalised Spike and waves	20(40%)
Extrarolandic focus	7(14%)
True electrical frontocentral dipole	8(16%)

A detailed assessment of the type of antiepileptic drugs used and the response to treatment with respect to be seizure frequency and severity and the EEG findings was not done. An overall analysis showed that all the patients were controlled on monotherapy with the first AED. 18 children (36%) were on Carbamazepine, 11 on Valporate and 11 on phenobarbitone. 6 children were not on treatment at the last contact.

When the seizure frequency at the time of evaluation was considered ,the children belonged to two separate categories ; Older children who were seizure free for several years and younger children with active epilepsy. All the patients had well-controlled epilepsy and seizure frequency score as assessed by the Engel Score ranged from 01-05.

27 children (54%) were reported to have learning problem and poor scholastic achievement, by parental interview. There was a significant correlation between the self-reported learning problems and absence of the frontocentral dipole in the EEG ($p < 0.001$).

TABLE V	
NEURO PSYCHOLOGICAL PROFILE	
Number of children who under went detailed neuropsychology	23
IQ	
Normal	20
Border line	3
ADHD	9
Expressive language problem	9(18%)
Learning disability	19/23

Detailed neuropsychological and language assessment could be completed in only 23 children (46%). IQ was normal in 20; borderline MR

was seen in 3 children. 9 children showed features of attention deficit hyperactivity disorder. No correlation could be found out between the presence of ADHD and the seizure semiology, EEG characteristics or the type of AED used. Detailed language assessment showed abnormalities in language, mainly in the form of expressive language in 9 children (18%). There was a significant correlation between atypical seizure semiology, abnormal speech ($p = 0.021$), and developmental language delay ($p= 0.047$).

Learning disability was found in 19/23 children who underwent detailed assessment. There was a significant correlation between parentally reported learning problem and poor scholastic achievement and the learning disability detected by neuropsychological assessment. ($p=0.003$). A statistically significant correlation was not obtained between the seizure semiology, EEG features and the presence of learning disability.

DISCUSSION

This cross sectional study tried to assess the clinical, electroencephalographic and neuropsychological profile of children with BECT attending a tertiary care epilepsy center. We chose EEG as the primary diagnostic criterion , in order to identify possible cases of BECTS for the following reasons.

1. Practically all children with epilepsy undergo EEG examination in this center.
2. The defining characteristic of BECTS is the presence of centrotemporal spikes in the EEG, while all other characteristics can be variable.
3. BECTS is often misdiagnosed for other conditions until EEG is performed.

This methodology was similar to the Turkish study by Gunduz et al (1999).

Although the prevalence of EEGs with centrotemporal spikes (112/13,462; 0.84%) in this highly selected group from a tertiary epilepsy center was not comparable to the population based data , other demographic parameters like the sex ratio & age of onset were similar to the population based study from Iceland (Astradson et al, 1998). Majority of the children had both nocturnal and diurnal seizures(54%). Atypical seizure

characteristics apart from the classical description was seen in a significant group 32% and this was associated a poor language outcome. This finding is in accordance with the observation by Louisse et al (1996).

Reported data showed unilateral centrotemporal spikes in 60% of children and bilateral spikes in the rest with marked activation during drowsiness and sleep.(Watanabe 1996) . A similar rate was seen in the present study. Drury and Beydun (1991) found an extra focus outside the centrotemporal area in 20% of children with BECTS. A number of authors have mentioned the coexistence of other foci, multiple independent sharp wave foci, shifting of the location of sharp waves from a posterior to a centrotemporal location, and vice versa. There was no correlation between the presence of extra rolandic focus and the final seizure and cognitive outcome in these studies. The present study also confirmed these observations.

According to the classic definition of BECTS, absence of neurological and neuropsychological defects was a mandatory criterion. But recent reports have shown that significant disabilities can occur in BECTS (Deonna T et al, 2000). Mean intellectual abilities were also found to be lower in BECTS cohorts compared to control groups (Gunduz E et al, 1999, Weglage.J 1997). But these dysfunctions are found only on detailed

neuropsychological evaluation, the clinical relevance of which is not clear. It can be argued that only a small subgroup of children with BECTS develop complications. These cognitive impairments were never correlated with individual EEG or clinical features.

The existence of the clinical syndrome of BECTS is also questioned by recent studies showing significant deficits and atypical evolutions (Fejerman N 2000). Some authorities consider this as a broad continuum of brain maturation disorders with a marked phenotypic variability; for others they represent fundamentally distinct conditions.

This study showed that a significant number of children with BECTS had learning disability and poor scholastic achievement. These could not be accounted for by the burden of clinical seizures, as the seizures were mainly nocturnal and minor.

Learning disability in epilepsy is divided primarily into two states; a) state dependant b) permanent (Cornaggia,2001)

The possibility of the simultaneous presence of both types cannot be excluded. The extract prevalence of state dependant or permanent learning disorders in is not delineated till now (Lhatoo SD &Sander JWAS, 2001). Permanent learning disability is associated with brain damage or stable brain dysfunction (Holmes.GL, 2001). State dependant learning disorders may be

the result of the effect of epilepsy itself or the medication used to treat it. These may also be due to mood disorders, low level of self-perception or expectation or reduced learning opportunities.

Various situations in epilepsy can cause a state dependant learning disability.

1. Ictal changes – Unrecognized non-convulsive status epilepticus which can continue for months.
2. Peri-ictal changes: when the subjects have multiple seizures per day, so that they do not have time to recover from one to another.

Transitory cognitive impairment (TCI) can occur due to the presence of frequent subtle seizures and the direct effects of interictal EEG epileptiform discharges. TCI can occur in association with focal/ generalized specific EEG discharges, which is better brought about by appropriate psychological tests. Focal epileptic discharges can produce specific errors: left sided discharges are more likely to produce errors in verbal tasks, where as right sided discharges may involve non-verbal activities.

Subclinical discharges may be accompanied by disruption of educational skills in children, but this needs further evaluation. The extent to which such subtle manifestations affect learning and behavior remains unknown. It has also been suggested that, if allowed to continue for a long

time, state dependent learning disorders can lead to permanent deficits. Eg. Landau- Kleffner syndrome (LKS), Electrical status epilepticus in slow wave sleep (ESES).

The relative contribution of AEDs towards the production of learning disability is also not well defined. A large number of studies have been published, with no conclusive evidence. Tentatively, Lamotrigime, Carbamazepine, and Valporate were less often implicated, where as phenobabital and phenytoin were more commonly suspected with learning problems.

The effect of AED on the cognitive and scholastic achievement can be double edged. They can improve learning by reducing the number of discharges or the frequency of seizures, but at the same time, they may impair learning as a result of the direct side effects like sleepiness, slowed reactions, attention deficit etc. This may be of particular importance in a syndrome like BECTS, where the seizure burden is very small and the seizures are generally nondisabling and nocturnal. The decision to start AEDs should be based not only on the number of seizures, but also on the cognitive and scholastic performance of the child. Some authorities recommend withholding of AEDs if the seizures are nondisabling and nocturnal. Some others put the arbitrary figure of 4-5 seizures before

starting the AEDs.(Watanabe,1996). The clinical course of the syndrome, which is characterized by frequent seizures and spontaneous remission in adolescence, should be kept in mind while initiating AEDs(Bourgeois 2000).

There are no definite guidelines for the choice of AEDs in BECTS. The seizures respond well to all the standard antiepileptic drugs. But recently, there are a few reports slowing atypical evolutions in BECTS, possibly related to specific AEDs. CBZ and Phenytoin were implicated mainly (Aldenkamp A.P,2001). But a recent study, conclusively show that the incidence of CBZ induced complications in BECTS is very small (Corda D et al 2001).

The present study was not designed primarily to look into the efficacy and safety of AEDs in BECTS. Superficial analysis shows good seizure control on all the primary AEDs. There were no episodes of clinical exacerbation in seizures or neuropsychological decline on a particular AED except for the development of atonic spells in a child on phenytoin, which disappeared after withdrawal of the offending drug. This study did not show any significant difference between the AEDs on the seizure outcome, changes in EEG and cognitive and scholastic performance.

We tried to correlate the EEG features with the cognitive and scholastic performance. There are reports suggesting different EEG

parameters predictive of the atypical evolution. The laterality of the discharges is said to be one of the features. Predominant left sided discharges were associated with impairment in verbal tasks and right-sided discharges were associated with nonverbal tasks.

Gregory and Wong (1992) reported that a true electrical dipole in EEG across the fronto central region with frontal positivity and central and temporal negativity was associated with a good neuropsychological and seizure outcome. Recently, a large prospective study has demonstrated five qualitative and one quantitative interictal EEG patterns associated with occurrence of atypical evolutions in BECTS, namely intermittent slow wave focus, multiple asynchronous spike-wave foci, long spike-wave clusters, generalized 3 C/S absence like spike-wave discharges, conjunction of interictal paroxysms with positive and negative myoclonia, abundance of interictal abnormalities during wakefulness and sleep (Massa R et al,2001). The present study shows a significant association with the presence of fronto central dipole and cognitive outcome. In a majority of children whose parents reported significant learning problems, EEG showed absence of the fronto central dipole ($P < 0.001$). This association could not be established statistically after the neuropsychological evaluation, which may be related to the small sample size.

There was no correlation between the learning problems with the presence of extrarolandic or generalized discharges. The presence of atypical features in the clinical semiology was another factor, which was found to be correlating well with a worse neuro psychological outcome. This has been documented by some earlier studies also.

CONCLUSIONS

BECTS represents a well defined pediatric epileptic syndrome with an excellent seizure outcome. The affected children generally have normal intelligence and normal neurological examination. But a significant proportion of them develop neuropsychological and learning impairment, leading to poor scholastic achievement. It may be possible to identify the children at risk for development of scholastic problems by careful clinical evalution at the first contact itself. A typical seizure semiology and presence of classical electrical dipole across the frontocentral region in the EEG may be some of the good prognostic features. Larger, population based prospective studies are needed for further validation of these results.

REFERENCES

1). Aicardi, J. Benign partial epilepsy of childhood. In: Epilepsy of Children. 2nd Edition (Ed. J. Aicardi). International Review of child Neurology Series. New York, Raven Press, 1994:pp.139-145

2). Aldenkamp AP,Effects of antiepileptic drugs on cognition, Epilepsia 2001,42,Suppl1,46-49

3). Ambrosetto G, Tassinari CA. Antiepileptic drug treatment of benign childhood epilepsy with Rolandic spikes: is it necessary? Epilepsia 1990; 31:802-5

4). Ambrosetto, G. Unilateral opercular macro-gyria and benign childhood epilepsy with centro-temporal (rolandic) spikes: report of a case. Epilepsia 1992, 33, 499-503

5). Astradsson A, Olaffson E,Ludvigsson P et al. Rolandic Epilepsy: An incidence study in Iceland , Epilepsia,39(8) : 884-886,1998

6). Beaussart M. Benign epilepsy of children with rolandic (centro-temporal) paroxysmal foci. A clinical entity. Study of 221 cases. Epilepsia 1972; 13:795-811

7). Bourgeois BF,Drug treatment of benign focal epilepsies of childhood, Epilepsia 2000,1057-58

8). Commission on Classification and Terminology of the International League Against Epilepsy, Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia, 1989, 30, 389-99

9). Corda D,Gellise P,Genton P,Dravet C et al,Incidence of Drug induced aggravation in BECTS, Epilepsia,2001,42, 754-759

10). Cornaggia CM, Gobbi G,Learning disability in Epilepsy :Definitions and classification Epilepsia,2001,42, S1 2-5

11). Dalla Bernardina B, Tassinari CA, EEG of a nocturnal seizure in a patient with BERS, Epilepsia 1975,497-501

12). Deonna T, Zesiger P, Davidoff V et al, Benign partial epilepsy of childhood: a longitudinal neuropsychological and EEG study of cognitive function,Dev medicine and child neurology,2000,42,595-603

13). Drury I and Beydoun A (1991) Benign partial epilepsy of childhood with monomorphic sharp waves in centrotemporal and other locations Epilepsia, 32,662-7

14). Fejerman N, Caraballo R, Tenembaum S ,Atypical evolutions of benign localization-related epilepsies in children: are they predictable? Epilepsia 2000; 41,380-390

15). GalanoPoulou as,Bojko A,Lado F et al . The spectrum of neuropsychiatric abnormalities associated with electrical status epilepticus in sleep, Brain& Development,2000,279-295

14) Gregory DL, Wong PK, Cinical relevance of dipole field in rolandic spikes, Epilepsia 1992,33,36-44

15) Guiterrez AR, Brick,JF,BodensteinerJ,Dipole reversal :an ictal feature of benign partial epilepsy with centrotemporal spikes,Epilepsia,1990,31,544-8

16) Gunduz E, Demirbelek V, Korkmaz B. Benign rolandic epilepsy: neuropsychological findings. Seizure 1999; 8:246-249

17) Heijbel J, Bohman M. Benign epilepsy of children with centrotemporal EEG foci: intelligence, behavior, and school adjustment. Epilepsia 1975; 16:679-87

18) Holmes GL. Benign focal epilepsies of childhood, Epilepsia 1993; 34 suppl 3: S49-61

19) Holmes GL Clinical spectrum of benign focal epilepsies of childhood, Epilepsia 2000,1051-52

20) Holmes GL,Pathogenesis of learning disabilities in epilepsy, Epilepsia 2001,42 S1 13-15

21) Kellaway P. The electroencephalographic features of benign centrotemporal (rolandic) epilepsy of childhood. Epilepsia 2000; 41:1053-1056

22) Krammer U,Benzeev B,Harel S,Kivity S,Transient Oromotor deficits in Children with BECTS, Epilepsia 2001,42,616-620

23) Laube MC,Funke R,Kirsch CM et al BECT: Comparison of cerebral blood flow imaging,neuropsychological testingand long term EEG monitoring ,Epilepsy Research,1992,suppl 6,95-98

24) Lerman P. BCECTS. In : Engel J, Pedley TA, eds. Epilepsy: a comprehensive textbook. Philadelphia: Lippincott-Raven, 1998:2307-14.

25) Lhatoo SD,Sander JWAS,The epidemiology of epilepsy and learning disability, Epilepsia 2001,42,S1-6-9

26) Louisse P, Benign focal epilepsies of childhood (in)Wyllie E(ed),The Treatment of Epilepsy--Principles and Practice,1993,503-12

27) Loiseau P, Duche B, Cordova S, Dartigues JF, Cohadon S. Prognosis of benign childhood epilepsy with centrotemporal spikes: a follow-up study of 168 patients. Epilepsia 1988; 29:229-35

28) Massa R,deSaint Martin A,Carcangiu R,Rudolf G et al EEG criteria predictive of complicated evolution in idiopathic Rolandic epilepsy, Neurology 20001,57,1071-79

29) Morikawa T,Seino M,YagiK,Is Rolandic discharge a hallmark of benign partial epilepsy of Childhood, Epilepsy Research,1992,suppl 6,59-69

30) Panayiotopoulos CP. Early-onset benign childhood seizure susceptibility syndromes. Epilepsia 1997; 38:285-93.

31) Septien L,Pelletier JL ,Brunotte F ,Migraine in patients with centotemporal epilepsy of childhood ,a Hm PAO SPECT study,Cephalagia,1991,281-4

32) Touwen, B.C. Examination of the Child with minor Neurological Dysfunction. 2nd Edition. Clinics in Developmental Medicine No. 71. Oxford, Spastics International Medical Publications, 1979:pp.125-137.

33) Watanabe K. Benign partial epilepsies (in) Wallace S(ed) Epilepsy in children, Chapman & Hall, 1996

34) Weglage J, Demsky A, Pietsch M, Kurlemann G. Neuropsychological, intellectual and behavioral findings in patients with centrotemporal spikes with and without seizures. Developmental Medicine & Child Neurology, 1997 39:646-51.

APPENDIX

NATURAL HISTORY OF BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

INVESTIGATORS: ***Dr. VINAYAN. K. P, Dr. SANJEEV. V. THOMAS***

1.NAME: _____

2.AGE AT REGISTRATION: ☐☐

3.SEX: ☐

4.HOSPITAL NO: ☐☐☐☐☐☐☐

5.DISTRICT ADDRESS: ☐☐

Thiruvananthapuram	01	Thissur	08
Kollam	02	Palakkad	09
Alappuzha	03	Malappuram	10
Pathanamthitta	04	Kozhikode	11
Kottayam	05	Wayanad	12
Idukki	06	Kannur	13
Ernakulam	07	Kasargode	14

Other states 21

6.AFS Age at onset of seizures in years ☐☐

SEIZURE SEMIOLOGY

7.Aura-somatosensory- 1,others (specify)- 2 ☐

8.Seizure type: Frequency

1. ☐
2. ☐
3. ☐

nocturnal=1,diurnal=2,both=3

SPECIAL FEATURES

yes-1,no-2

9.SPEARR speech arrest ☐

10. SALIVA salivation ☐

11.PARTOL	paresthesias over tongue & lips	☐	
12.HEMCON	hemiconvulsions	☐	
13.FEESUF	feeling of suffocation	☐	
14.BRFASE	brachiofacial seizures	☐	
15.HEMIFA	hemifacial seizures	☐	
16.GUTSOU	guttoral sounds	☐	
17.TOUTRE	tongue trembling	☐	
18.TEECHA	teeth chattering	☐	
19.CON JAW	contraction of jaw	☐	
Rare Features			
20.LEGSIG	leg signs(clonic jerks, weakness, pain , prickling)	☐	
21.BODSIG	unilateral body signs (paresthesias, atonia)	☐	
22.EPGAPA	epigastric pain	☐	
23.BLINDS	blindness	☐	
24.FLASHS	flashes of light	☐	
25.TORSON	lateral torsion of body	☐	
Past History			
26.FEBRIL	febrile seizures	☐	
27.ANTNAT	antenatal complications	☐	specify—
28.PERNAT	adverse perinatal events	☐	specify—
29.DEVDEL	developmental delay	☐	global-1,motor-2,mental-3 absent-4
30.LANGUA	language	☐	normal-1,delay-2
31.LEARDI	learning disability	☐	yes-1, no-2

32.SCHOLA	scholastic achievement	☐ good-1,fair-2,poor-3
Family History		yes-1, no-2
33.FAFEBR	febrile seizures	☐
34.FAEPIL	epilepsy	☐
33.FABECT	BECT	☐
34.FAAEEG	abnormal EEG	☐

Treatment

	yes-1,no-2	Duration(yrs)
35.PHENO	☐	☐
36.PHENY	☐	☐
37.CBZ	☐	☐
38.VPA	☐	☐
39.OTHERS(specify)	☐	☐

40.CURTRE	current treatment	☐ pheno-1,pheny-2,cbz-3, vpa-4,others-5
General Examination		yes-1, no-2
41.GENEUC	neurocutaneous markers	☐
42.GEDYSM	dysmorphic features	☐
43.GEHEMI	hemiatrophy	☐
44.GECONG	congenital anomalies	☐ specify-
Neurological Examination		
45.NEUREX	major neurological defects	☐

Minor Neurological Dysfunction

46.MNDAST	astereognosia	☐
47.MNDAGR	agraphesthesia	☐
48.MNDADI	adiadochokinesia	☐
49.MNDDYS	dysarthria	☐
50.MNDORO	oromotor apraxia	☐
51.MNDSIA	sialorrhea	☐
52.MNDJAR	change in jaw reflexes	☐
53.MNDDTR	change in DTR	☐
54.MNDADT	asymmetric DTR	☐
55.MNDAAM	asymmetric associated movements	☐
56.MNDHYP	hypokinesia	☐
57.MNDCOR	motor coordination defects	☐
58.MNDTON	changes in muscle tone	☐
59.MNDTRE	tremor	☐
60.MNDCHO	choreiform movements	☐
61.MNDNYS	nystagmus	☐
62.MNDSTR	strabismus	☐
63.MNDPRA	limb apraxia	☐
Investigations		normal-1, abnormal-2
64. NEINCT	CT head	☐
65.NEINMR	MRI brain	☐

EEG in BECT

No: Date: Medicine:

Code:

Background Activity

Frequency: Amplitude:

Transients

Maximum amplitude:
micro volts-
milliseconds-

Electrodes: UL/BL
1.
2.
3.

1) Pseudorhythmic
2)Polymorphic slow waves
3)Synchronous
4) 3Hz spike& wave
5)Other locations-
PGV/Post.temporal

Phases:

Dipole: +ve/ -ve

Extrarolandic: yes-1, no-2 ☐

Activation: eye opening/eye closure

Hyper ventilation

Photic stimulation

Drowsiness

Sleep:
stage I
stage II
stage III &IV

Somatosensory evoked potentials:

Checklist for Diagnosis of BECT(tick)

Clinical:

1.Absence of neurological and mental deficits

2.Family history positive for BECT

3. Onset above infancy and below puberty.

4.Brief partial seizures

5.Secondary generalization during sleep.

6.Good response to medication

7.No mental deterioration.

8.Remission in second decade.

EEG:

1.Normal background activity.

2.Charecteristic morphology.

3.Tendency for discharges to shift and be multifocal.

4.Coexistence of generalized spike and wave discharges.

5.Activation of discharges by sleep.

6.Remission of typical discharges before adolescence

NEUROPSYCHOLOGICAL EVALUATION

Attention

Digit Span: DF: DB: Attention Span:

Memory Test for Children

Sub Tests	Scores
Personal information	-
Mental control	-
Sentence repetition	-
Logical memory	
a. Story recall immediate	-
b. Story recall delayed	-
Word recall meaningful	-
Word recall nonmeaningful	-
Delayed response learning	-
Picture recall	-
Benton Visual Retention Test	-
Paired associate learning	-

Wechsler Memory Scale-Form2

Personal and current information	-
Orientation	-
Mental control	-
Logical memory A.	-
B.	-

Digits forward - Digits backward - Digits total -

Visual reproduction 1 - 2 -

3-L - 3-R - Total -

Associate learning	Easy 1	-	Hard 1	-
	2	-	2	-
	3	-	3	-
	Total(A)	-	Total(B)	-
	A/2+B	-		

Visuo- motor ability

			Yes-1, No-2
Bender Gestalt Test -	Perseveration	-	☐
	Omission	-	☐
	Distortion	-	☐
	Integration	-	☐
	Rotation	-	☐
	Any other signs if any	-	☐

Malin's Intelligence Scale for Children

Verbal Tests		Score	Performance Tests		Score
Information	-		Picture completion	-	
Comprehension	-		Block design	-	
Arithmetic	-		Object assembly	-	
Analogies & similarities	-		Coding	-	
Vocabulary	-		Maze	-	
Digit Span	-				
Verbal IQ	-		Performance IQ	-	
FIQ	-				

Seguine Form Board

Mental age	-	
IQ	-	

Vineland Social Maturity Scale

Social age -

Social quotient -

{Adequate-1, Impaired-2}

Fine motor abilities - ☐

Gross motor abilities- ☐

Language Evaluation

{Adequate-1, Impaired-2}

Fluency - ☐

Comprehension - ☐

Naming - ☐

Reading - ☐

Writing - ☐

Spelling - ☐

Articulation

{Yes-1, No-2}

Sluttering - ☐

Nasaliting - ☐

Learning disability - ☐

Quality of Life

MEDICAL:

66.QOLSEZ seizure frequency score in the 12 months before last review ☐☐

	Engel score
Seizure free off AED	01
Seizure free need for AED not known	02
Seizure free require AED to remain so	03
Non disabling simple partial seizures only	04
Non disabling nocturnal seizures only	05
1-3 per year	06
4-11 per year	07
1-3 per month	08
1-6 per week	09
1-3 per day	10
4-10 per day	11
>10 per day	12

67.QOLAAD adverse drug reactions nil-1,mild-2,severe-3 ☐

68.QOLPSY psychological problems ☐

69.QOLSOC social problems ☐

70.QOLEDU educational problems ☐

71.QOLECO economic problems ☐

72.QOLPHA physical activities normal-1,limited-2 ☐

73.QOLBEH behaviour appropriate-1,inappropriate-2 ☐

74.QOLGHE perception about general health good-1, fair-2,poor-3 ☐