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ELECTROENCEPHALOGRAPHIC PATTERN AND OTHER DETERMINANTS OF SEIZURE FREEDOM IN IDIOPATHIC GENERALIZED EPILEPSY WITH GENERALIZED TONIC CLONIC TYPE OF SEIZURES IN CHILDREN

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ABSTRACT

Background: Patients with idiopathic generalized epilepsy have varied response to antiepileptic drugs. Determinants of seizure freedom in Idiopathic generalized epilepsy with generalized tonic-clonic type of seizure in children was least studied. We sought to determine few clinical and EEG pattern associated with poor control of seizure. **Methods:** We retrospectively studied risk factors including EEG pattern by classifying it in the atypical abnormal, Typical abnormal, normal in pediatric patients less than 12 years with idiopathic generalized epilepsy having generalized tonic-clonic type of seizures from the onset of epilepsy. Relationship between risk factor and seizure freedom were analyzed. **Result:** 126 patients were included, with male: female ratio 1.1:1, with a median age of 5 years. 69 % patients had good control seizure. 57.1% had age at onset less than 6 year, 15.9% had family history of epilepsy, and both were risk factor for poor control of seizure with p-value 0.039, 0.0021 respectively. Most patients had typical abnormal EEG pattern (39.7%), followed by atypical abnormal pattern (36.5%). Atypical abnormal pattern in EEG was a determinant of poor control of seizure. (p-value: 0.0003). **Conclusions:** Majority of children attained seizure freedom with appropriate anti-epileptic drugs. Atypical abnormal pattern in EEG, early onset and family history of epilepsy are associated with poor seizure freedom.

INTRODUCTION

Approximately 40% of people with epilepsy have seizures defined by the International League Against Epilepsy as generalized at onset. 1These patients experience various types of seizures including absences, myoclonic seizures, and generalized tonic–clonic seizures. Although idiopathic generalized epilepsies are thought to be relatively easy to control with antiepileptic drugs, up to 30% of patients with idiopathic generalized epilepsies have poor response to treatment with antiepileptic drugs.[2]

The reasons for medication resistance in patients with Idiopathic generalized epilepsies have been shown to include poor compliance to medication regimens, 3 early age at epilepsy onset,4 and presence of generalized tonic–clonic seizures.5 Studies examining treatment resistance in Idiopathic generalized epilepsies have been with less sample size6, were conducted before newer Antiepileptic drugs became available2,6 and focused on clinical7,8or EEG9,10 aspects of Idiopathic generalized epilepsies, other studies without fullydescribing EEG abnormalities.[5,6]

Fernando-Dongas et al. reported that EEG asymmetries are associated with antiepileptic drug resistance.6Therefore; the main aim of this retrospective study was to explore EEG pattern and other determinant of seizure freedom in idiopathic generalized epilepsy with generalized tonic clonic semiology in pediatric age group of less than 12 years. The main hypothesis was that patients who respond to antiepileptic drugs are havinggood control of seizure shows typical abnormal EEGpattern, whereas patients with poorly controlled epilepsies have atypical patterns in EEG.

METHODS

This retrospective observational study approved by institutional ethical committee. Patient seen during November 2017 to November 2018 in epilepsy clinic of a tertiary care hospital in western India, were eligible to participate. Study subject identified with health records kept in institution for the purpose of follow up.
Inclusion criteria were all pediatric patients less than 12 years with idiopathic generalized epilepsy having generalized tonic clonic type of seizures from the onset of epilepsy completed 6 months of follow up with all medical records including neuroimaging and EEG before starting treatment. All patients with poor compliance, other type of seizure at the onset or later, comorbidities like mental retardation, cerebral palsy, symptomatic epilepsy, patients with abnormal neuroimaging were excluded from study.

A total 189 patients reviewed 126 patients included in the study, 12 patients excluded for multiple seizure semiology during the course of follow up, 32 were excluded because they had the presence of comorbidities.13 patients excluded because didn't have a EEG recording before starting antiepileptic drug, since Antiepileptic drugs might have impact on EEG pattern, 11 4 patients had poor drug compliance, 2 patients with abnormal neuroimaging or absence of neuroimaging at the time of study. The remaining 126 patients were enrolled and completely reviewed their health records.

Data collection and definitions:

All details extracted from patients using standardized case format including seizure onset, type of seizures, and family history of epilepsy, antiepileptic drugs, EEG, neuroimaging, and outcome.

Seizure freedom was the outcome measure; absence of seizure for 6 month from onset with antiepileptic drugs taken as good control, patient with history seizures with antiepileptic drugs was taken as poor control. Age of onset was the first age at which seizure occurred. Very first EEG taken at the seizure onset was chosen for assessing the pattern of EEG. (11) EEG was classified in to 3 patterns 12(1) Normal (2) typical abnormal (3) Atypical abnormal.

The following details in EEG were noted; state of arousal, type of discharge (spike-wave, polyspike, polyspike-wave), frequency of discharges, site of amplitude maximum, amplitude symmetry, paroxysm organization, paroxysm morphology, paroxysm onset and offset (focal/generalized).[13,14]

Typical abnormal EEG includes a generalized spike and wave discharge or polyspike and wave discharge bisynchronous fashion.
We defined the following epileptiform EEG abnormalities to be "atypical abnormal";

(1) Amplitude asymmetry of paroxysms and fragments (2) Focal onset, offset, or abnormal morphology of paroxysms (3) Focal discharges (4) Generalized paroxysmal fast rhythm (GPFR).[15]

Statistical analysis

Data presented in frequencies and percentages, groups were compared using chi-square test with level of significance was set at p value less than 0.05.All data management and analyses were performed using Microsoft excel 2016 and SPSS version 17.0.2.

RESULT

Demographic characteristics.

A total of 66 (52.4 %) out of 126 patient were males, remaining 60 (47.6 %) were female. Their age ranged from 2 year to 12 year, with a median age of 5 years. Table 1 summarizes the age and gender distribution of the study participant.

Table 1: Distribution of age and gender.

Gender	Age category (years)			Total
	1-4 Years	4-8 years	8-12 years	
Male	19 (15.1%)	30 (23.8%)	17 (13.5%)	66 (52.4%)
Female	11 (8.7%)	21 (16.7%)	28 (22.2%)	60 (47.6%)
Total	30 (23.8%)	51 (40.5%)	45 (35.7%)	

Variables and seizure freedom.

87 (69 %) patients out of 126 had good control of seizures, 39 (31%) patients had poor control. 71.2 % males and 66.7 % females had good control, while 28.8% males and 33.3% females had poor control of seizures. There was no statistically significant difference in seizure freedom based on gender (p-value: 0.0581).

57.1% had first episode of seizure less than 6 years of age, 43.9% had after 6 years of age. The median age of onset of seizure was 4 years. 55 (76.4%) out of 72 patient with age of onset of seizure less than 6 years had good control of seizure, meanwhile 40.7% patient with age of onset more than 6 years had poor control of seizures. Early onset of seizures that is less than 6 years was found to be a risk factor for poor seizure freedom with p-value0.039.

15.9% patient had family history of epilepsy, out of which 60% had poor control of seizure. A positive family history of epilepsy is a risk factor for poor control of seizures. (P-value: 0.0021). Table 2 summarizes the relationship of variables with seizure freedom in study participants.

Table 2: Relationship between the variables and seizure freedom.

Variable	Seizure freedom		Total
	Good control	Poor control	
Gender			
Male	47 (37.3%)	19 (15.1%)	66 (52.4%)
Female	40 (31.7%)	20 (15.9%)	60 (47.6%)
p value : 0.581			
Age of onset of seizure			
Less than 6 years	55 (43.6%)	17 (13.5%)	72 (57.1%)
More than 6 years	32 (25.4%)	22 (17.5%)	54 (42.9%)
p value : 0.039			
Family history of epilepsy			
Yes	8 (6.4%)	12 (9.5%)	20 (15.9%)
No	79 (62.7%)	27 (21.4%)	106
p value : 0.0021			

Pattern of EEG and seizure freedom

Most of the patients had typical abnormal pattern of EEG (39.7%), followed by atypical abnormal pattern (36.5%), least were normal pattern of EEG (23.8%). 42(84%) out of 50 patient with typical abnormal EEG pattern had good control of seizure, meanwhile 76.7% of normal pattern of EEG also had good control of seizure. 52.2 % patient with atypical abnormal pattern of EEG had poor control of seizure. This wasstatistically significant with a p-value 0.0003. (Table 3)

Table 3: Patterns of EEG and seizure freedom

Pattern of EEG	Seizure freedom		Total (126)
	Good control	Poor control	
Normal	23 (76.7%)	7 (23.3%)	30 (23.8%)
Typical abnormal	42 (84%)	8 (16%)	50 (39.7%)
Atypical abnormal	22 (47.8%)	24 (52.2%)	46 (36.5%)
p value : 0.0003			

DISCUSSION

In this retrospective study we explored EEG pattern and few other risk factor associated with seizure freedom in pediatric patients with idiopathic generalized epilepsy having generalized tonic clonic type of seizures. Our main finding is that atypical abnormal EEG pattern is associated with decreased chance of seizure freedom. Although these findings are not surprising as they are supported by literature.[12, 13, 14, 15] But our study is differ from other literature is by two reasons, that are study population is children less than twelve year age group, and clinical scenario is idiopathic generalized epilepsy having generalized tonic clonic type of seizures. Other studies included all type of idiopathic generalized epilepsies and patients with varied age groups.[15, 16, 17]

Risk factor associated with drug resistance in patients with idiopathic generalized epilepsies with generalized tonic clonic type of seizures is less studied. Our study shows family history of epilepsy and early age of onset less than 6 years associated with poor seizure freedom, same time gender didn't found to be a risk factor. Study by J P Szaflarski et al. shown that age of onset, family history of seizure, gender are not risk factor for poor control of seizures.[17]It may because of difference in inclusion parameter in the study.Idiopathic generalized epilepsies are considered to be of primarily genetic origin but specific abnormalities have not identified many patients. Such genetic abnormalities may also be the cause of difference in seizure freedom in those patients with family history of epilepsy, likely we would expect these patients might have atypical abnormal EEG pattern.[18,19]

Similar to our study Nicolson et al found that younger age at onset of seizure was associated with poor outcome.[20].

The presence of focal discharges in idiopathic generalized epilepsies similar to atypical abnormal pattern of EEG in our study has been previously reported. Literature review by Seneviratne U et al. found EEG focalities ranging from 16% -56%reported in differentpublications.21. Study by LE Betting et al included idiopathic generalized epilepsies with generalized tonic clonic seizure in awakening and generalized tonic clonic seizure only as categories, shown most patients had normal followed by atypical EEG patterns, which contrasts our study.12 This wide range and difference from LE Betting et al can be explained by heterogeneous patient population and methodology. Proportion of patients showing atypical abnormal EEG pattern in our study also falls in the above range.

Several studies evaluated electroencephalographic pattern and seizure freedom in patients with idiopathic generalized epilepsy. In concordance with our study Wolf et al, Fernando-Dongas MC et al, Leutmezer F et al, also noted asymmetries and focal abnormalities are associated with poor control of seizure. [5, 6, 13] But they included all idiopathic generalized epilepsies mainly absence and juvenile myoclonic epilepsy. All idiopathic generalized epilepsies having same location of generalized slow wave discharge generator should respond to appropriate antiepileptic drugs well. But in patients with atypical abnormal EEG pattern shown poor response to antiepileptic drugs, at least theoretically not supportive to above evidence of same location of generalized slow wave discharge generator that is thalamo-cortical network as show by functional magnetic resonance imagingevaluation. [22] So that varied location of seizure generation, focal neuronal metabolic abnormalities can be considered as a cause. [17,23]

Limitations of this study should be noted. Serial EEG was not considered; therefore we cannot exclude the possibility that some serial EEG with focal features were missed. Second, as in all retrospective studied selection bias may have lead in inclusion of patients who are more likely to be referred to a tertiary epilepsy clinic, that is patient with poorly controlled idiopathic generalized epilepsies, but this seems to be unlikely as the proportion of patient in seizure freedom is similar those in other literatures.

In summary our study showed that atypical abnormal pattern of EEG, early onset and family history of seizure are associated with poor seizure freedom with appropriate anti-epileptic drugs in pediatric patients with idiopathic generalized epilepsy having generalized tonic clonic type of seizure.

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DECLARATIONS

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REFERENCE

1) Shah KN, Rajadhyaksha SB, Shah VS, Shah NS, Desai VG. Experience with the International League Against Epilepsy classifications of epileptic seizures (1981) and epilepsies and epileptic syndrome (1989) in epileptic children in a developing country. Epilepsia. 1992 Nov;33(6):1072-7.
2) Gelisse P, Genton P, Thomas P, Rey M, Samuelian JC, Dravet C. Clinical factors of drug resistance in juvenile myoclonic epilepsy. Journal of Neurology, Neurosurgery & Psychiatry. 2001 Feb 1;70(2):240-3.
3) Baykan B, Altindag EA, Bebek N, Ozturk AY, Aslantas B, Gurses C, Baral-Kulaksizoglu I, Gokyigit A. Myoclonic seizures subside in the fourth decade in juvenile myoclonic epilepsy. Neurology. 2008 May 27;70(22 Part 2):2123-9.
4) Berg AT, Shinnar S, Levy SR, Testa FM, Smith–Rapaport S, Beckerman B. Early development of intractable epilepsy in children: a prospective study. Neurology. 2001 Jun 12;56(11):1445-52.
5) Wolf P, Inoue Y. Therapeutic response of absence seizures in patients of an epilepsy clinic for adolescents and adults. Journal of neurology. 1984 Oct;231(4):225-9.
6) Fernando-Dongas MC, Radtke RA, VanLandingham KE, Husain AM. Characteristics of valproic acid resistant juvenile myoclonic epilepsy. Seizure 2000;9:385–8.
7) Panayiotopoulos CP, Chroni E, Daskalopoulos C, Baker A, Rowlinson S, Walsh P. Typical absence seizures in adults: clinical, EEG, video-EEG findings and diagnostic/syndromic considerations. J NeurolNeurosurg Psychiatry 1992;55:1002–8.
8) Sadleir LG, Scheffer IE, Smith S, Connolly MB, Farrell K. Automatisms in absence seizures in children with idiopathic generalized epilepsy. Arch Neurol 2009;66:729–34.
9) Sadleir LG, Farrell K, Smith S, Connolly MB, Scheffer IE.Electroclinical features of absence seizures in childhood absence epilepsy. Neurology 2006;67:413–8.
10) Sadleir LG, Scheffer IE, Smith S, Carstensen B, Farrell K, Connolly MB. EEG features of absence seizures in idiopathic generalized epilepsy: impact of syndrome, age, and state. Epilepsia 2009;50:1572–8
11) Konishi T, Naganuma Y, Hongou K, Murakami M, Yamatani M, Okada T. Effects of antiepileptic drugs on EEG background activity in children with epilepsy: initial phase of therapy. Clinical Electroencephalography. 1995 Apr;26(2):113-9.
12) Betting LE, Mory SB, Lopes-Cendes I, Li LM, Guerreiro MM, Guerreiro CA, Cendes F. EEG features in idiopathic generalized epilepsy: clues to diagnosis. Epilepsia. 2006 Mar;47(3):523-8.
13) Leutmezer F, Lurger S, Baumgartner C. Focal features in patients with idiopathic generalized epilepsy. Epilepsy Res 2002;50:293–300.
14) Porter RJ, Penry JK. Responsiveness at the onset of spike–wave bursts. ElectroencephalogrClinNeurophysiol 1973;34:239–45.
15) Seneviratne U, Hepworth G, Cook M, D'Souza W. Atypical EEG abnormalities in genetic generalized epilepsies. Clinical Neurophysiology. 2016 Jan 1;127(1):214-20.
16) Dragoumi P, Tzetzi O, Vargiami E, Pavlou E, Krikonis K, Kontopoulos E, Zafeiriou DI. Clinical course and seizure outcome of idiopathic childhood epilepsy: determinants of early and long-term prognosis. BMC neurology. 2013 Dec;13(1):1-2.
17) Szaflarski JP, Lindsell CJ, Zakaria T, Banks C, Privitera MD. Seizure control in patients with idiopathic generalized epilepsies: EEG determinants of medication response. Epilepsy & Behavior. 2010 Apr 1;17(4):525-30.
18) Delgado-Escueta AV, Greenberg D, Weissbecker K, et al. Gene mapping in the idiopathic generalized epilepsies: juvenile myoclonic epilepsy, childhood absence epilepsy, epilepsy with grand mal seizures, and early childhood myoclonic epilepsy. Epilepsia 1990;31(Suppl. 3):S19–29. [39]
19) Durner M, Keddache MA, Tomasini L, et al. Genome scan of idiopathic generalized epilepsy: evidence for major susceptibility gene and modifying genes influencing the seizure type. Ann Neurol 2001;49:328–35.
20) Nicolson A, Appleton RE, Chadwick DW, Smith DF. The relationship between treatment with valproate, lamotrigine, and topiramate and the prognosis of the idiopathic generalized epilepsies. J NeurolNeurosurg Psychiatry 2004;75:75–9
21) Seneviratne U, Cook M, D'souza W. Focal abnormalities in idiopathic generalized epilepsy: a critical review of the literature. Epilepsia. 2014 Aug;55(8):1157-69.
22) Gloor P. Generalized epilepsy with bilateral synchronous spike and wave discharge. New findings concerning its physiological mechanisms.Electroencephalography and clinical neurophysiology. Supplement. 1978 Jan 1(34):245-9.
23) Serles W, Li L, Dubeau F, Andermann F, Gotman J, Arnold D. NAA/Cr is decreased in the temporal lobes of patients with primary generalized epilepsy. InFourth International Congress on Epilepsy, Florence 2000.