Original Article

Evaluation of Seizure Frequency Distribution in Epileptic Patients with Normal and Abnormal Electroencephalogram in Al-Zahra Hospital of Isfahan

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Abstract

Background: Epilepsy is a chronic neurological disorder characterized by seizure recurrence in patients. Electroencephalogram (EEG) has a diagnostic and prognostic role in the management of patients. Studies have shown a significant relation between seizure recurrence and abnormal EEG in newly diagnosed epileptic patients, and people with first episode of unprovoked seizure. The aim of this study is to evaluate seizure frequency in chronic epileptic patients on drug therapy based on normal or abnormal EEG. **Materials and Methods:** This prospective cohort study examined seizure recurrence in 59 epileptic patients (50.8% generalized, 49.2% focal) with normal and abnormal EEG. Data were recorded in patient medical file, and patients were followed by telephone call or visiting by neurologist. **Results:** In this study, 59 patients with a mean age of 29.58 ± 10.37 years were assessed that 42.4% of them were males and 57.6% were females. Seizure frequency in patient with specific abnormal EEG was significantly more than other patients (specific abnormal: 78.9%, nonspecific abnormal: 45.5%, and normal: 31%, $P = 0.005$). Seizure recurrence in patients on polytherapy was significantly higher than others (polytherapy: 76.9% and monotherapy: 27.3%, $P < 0.001$). In patient with abnormal imaging seizure, frequency was more than other patients which was nearly significant ($P = 0.054$). **Conclusion:** Abnormal EEG and number of anticonvulsant drugs have a role in seizure recurrence in epileptic patients.

Keywords: *Electroencephalogram, epilepsy, recurrence*

Introduction

Epilepsy is a chronic neurologic disorder defined by the International League against Epilepsy as repetitive seizures equal or more than two times with more than 24 h between seizures or high probability for repeating seizure (at least 60%) after the first seizure without any specific causes.[1,2] Clinical manifestations of seizures include transient signs and symptoms such as alteration in level of consciousness, motor, sensory, autonomic, and mental manifestation reported by patients or another who observed them.[3] According to international classification, epilepsy has three types based on electroencephalogram (EEG) patterns and clinical manifestations including general, focal, and epileptic spasm that the focal type is more prevalent than others.[4,5] Epilepsy is prevalent in 3.1–5.7 cases in every 1000 individuals all around the world.[6-8]

Epilepsy is diagnosed by taking history, physical and neurological examination, using EEG, and doing imaging such as magnetic resonance imaging (MRI) in some cases. EEG has an important role in epilepsy diagnosis and evaluations. However, having normal or abnormal EEG does not definitely confirm epilepsy diagnosis.[1,9,10] For assessing EEG sensitivity in diagnosing epilepsy, the prevalence of abnormal EEG in epileptic patients was evaluated. In one study on 180 epileptic patients, 55% of them had primary abnormal EEG that 33% of them had abnormal EEG with specific patterns.[10] In another study, the prevalence of abnormal EEG in epileptic patients was 41.9%.[11]

In addition to diagnostic usage, EEG can be an effective modality for evaluating treatment, prognosis, and probability of seizure recurrences.[10] Some studies reported that there is a weak association between abnormal EEG and seizure recurrences, and this association is weaker in controlled and improving epilepsies.[9] In contrast, there

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are other studies demonstrated that there is a significant association between seizure recurrences and having abnormal EEG and presence of high-frequency waves with specific patterns can anticipate seizure recurrences.[12,13]

Despite the important role of EEG in diagnosis and primary evaluation of newly diagnosed epilepsies, the routine EEG usage in chronic epilepsy has controversies.[9] In this study, we aimed to evaluate seizure frequency distribution in epileptic patients with normal and abnormal EEG in Isfahan city as a third populated province in Iran country.

Materials and Methods

This study was a prospective cohort study in epileptic patients who referred to neurology clinics in Al-Zahra Hospital in Isfahan University of Medical Science (IUMS) between 2015 and 2016. Inclusion criteria were as followed: (1) age more than 18 years, (2) presence of documented diagnosis for idiopathic epilepsy, (3) having epilepsy over 1 year, (4) using pharmacological treatment, (5) lack of history of head trauma, brain tumor, asphyxia, mental retardation, cerebral palsy, and other neurologic impairment, (6) lack of history of childhood febrile seizure, (7) having at least one EEG with high quality, and (8) willingness for participating in this study. Patients who did not continue their treatment and those who had lost to follow-up were excluded from the study. This study was approved by the Regional Bioethics Committee of IUMS.

Fifty-nine epileptic patients were selected based on inclusion and exclusion criteria for participating in this study after filling out consent letter. Diagnosis of epilepsy was documented for each patient by an expert neurologist in this study based on international criteria.[1,2] All patients were under pharmacological treatment categorized in two groups include monotherapy and polytherapy. EEG was taken for all patients and reported by expert neurologist in EEG sciences. If more than one EEG were taken from patients in this 1-year time period, the best one in quality was evaluated in this study. All EEGs were taken by one electroencephalogram instruments and one operator.

Data about each patient were extracted from their records including demographic data (age, gender, marital status, and educational level), treatment regimen, EEG, and imaging reports. EEG reports were classified into two groups: abnormal EEG and normal EEG. Abnormal EEGs were categorized into two subgroups: specific and nonspecific. Specific pattern defined as the presence of epileptogenic waves which are specific for epilepsy including sharp show wave, slow spike wave, polyspike, spike wave, and other special changes for epilepsy.[9,14] Nonspecific patterns include abnormal waves which decrease seizure threshold including asymmetric or asynchronous background, slow background, irregularity, and theta and delta activity which can be seen not only in epilepsy but also in other disease and are not specific for epilepsy.[9,14]

Imaging abnormality contains nonspecific patterns such as diffuse signal alternation or slight atrophic changes and other unspecific changes[15] which are not compatible with secondary causes such as brain tumor, stroke, hematoma, ischemia, and abscess.

After collecting these data, patients were divided into two groups including normal and abnormal EEG. Both groups were followed for 1 year simultaneously. Patients were followed every 3 months by visiting in neurology clinic or phoning them. Seizure recurrences were diagnosed by patient's reports or their caregiver observation reports. The number of seizure attacks in 1-year duration was recorded in special forms for each patient and for seizure recurrences' patients defined as with and without recurrences.

Data analysis

Data about all participants were analyzed with SPSS software version 20 (SPSS Crop., Chicago, IL, USA). For reporting quantitative and qualitative reports, we used mean ± standard deviation and number or percent, respectively. Variables were compared between groups using independent *t*-test and Chi-square test. A two-sided α level of 0.05 was used to assess statistical significance. For omitting the effect of age, gender, and treatment, linear regression model was used.

According to recursive matter of epilepsy, the mean interval between seizures was measured, and for the analysis, generalized linear model (Poisson logistic linear) was used. The mean interval was entered in the Poisson model as a covariate factor in seizure recurrence.

Results

In this study, 59 epileptic patients with a mean age of 29.58 ± 10.37 years (18–57 years) were evaluated for seizure recurrences. Among all patients, 50.8% of them (n = 30) were without seizure relapses and 49.2% (n = 29) had experienced seizure relapses. The mean age in the first group was 30.45 ± 9.77 years and in the second one was 28.73 ± 11.02 years (P = 0.53). About 42.4% of participants were males and 57.6% were females. The mean number of seizure frequency was 3.51 ± 3.70 times during 1 year. The mean duration of disease was 11.03 ± 9.34 years and 50.8% had general type and 49.2% had focal type of seizure.

Evaluating EEG reports showed that 32.2% of patients had abnormal EEG with specific patterns, 18.6% had abnormal EEG with nonspecific patterns, and 49.2% had normal EEGs. Chi-square test showed that relapses were significantly more prevalent in patients with abnormal EEG especially those with specific patterns (abnormal EEG with a specific pattern: 78.9%, abnormal EEG with nonspecific pattern: 45.5%, normal EEG: 31%, P = 0.005). Comparing relapses between patients with normal EEG and abnormal EEG with specific patterns showed that relapses were more prevalent in those with abnormal

EEG (P = 0.003). Comparing relapses between those with normal EEG and abnormal EEG with nonspecific patterns showed that recurrences were more prevalent in those with abnormal EEG but not significantly (P = 0.46), and comparing seizure relapses between two subgroup of patients with abnormal EEG showed that recurrences were more prevalent in patients with abnormal EEG with specific patterns, but these differences were not statistically significant (P = 0.10).

In advanced Poisson model analysis with considering the seizure interval as a covariate, the seizure recurrences were significantly higher in patients with abnormal EEG comparing with normal EEG group (β: 0.289, 95% confidence interval [CI]: −0.022–0.600, P: 0.049), also comparing the specific abnormal EEG subgroup with normal EEG group showed a significant higher relapses in specific abnormal EEG group (β: 0.433, 95% [CI]: 0.097–0.769, P: 0.012).

The linear regression model after blocking the age, gender, and treatment effect showed more seizure relapses in patient with abnormal EEG, but the differences were not significant (odds ratio: 1.059, 95% [CI]: 0.959–1.168, P: 0.25).

Among all, 55.9% and 44.1% had received monotherapy and polytherapy, respectively. Chi-square test showed that seizure recurrences were more prevalent in patients with polytherapy regimen (monotherapy: 76.9%, polytherapy: 27.3%, $P < 0.001$). About 48 patients from 59 participants had imaging reports that 89.6% of them were normal and 10.4% were abnormal. Seizure recurrences were more prevalent in patients with abnormal imaging that this difference was nearly significant (normal imaging: 100% and abnormal imaging: 48.8%, P: 0.054). All data about seizure relapses in epileptic patients are shown in Table 1 in details.

Table 1: Distribution in epileptic patient with or without recurrence

Variable	Without recurrence, *n* (%)	With recurrence, *n* (%)	*P*
Gender			
Male	15 (60)	10 (40)	0.29
Female	15 (44.1)	19 (55.9)	
Marital status			
Single	15 (57.7)	11 (42.3)	0.43
Married	15 (45.5)	18 (54.5)	
Education			
Noneducated	1 (50)	1 (50)	0.84
Primary school	3 (75)	1 (25)	
Under diploma	5 (45.5)	6 (54.5)	
Diploma	14 (56)	11 (44)	
Bachelor	9 (60)	6 (40)	
Master and above	1 (50)	1 (50)	
Seizure type			
Generalized	18 (60)	12 (40)	0.19
Focal	12 (41.4)	17 (58.6)	
Type of treatment			
Monotherapy	24 (72.7)	9 (27.3)	<0.001*
Polytherapy	6 (23.1)	20 (76.9)	
Imaging			
Normal	22 (51.2)	21 (48.8)	0.054
Abnormal	0	5 (100)	
EEG			
Specific abnormal	4 (21.1)	15 (78.9)	0.005*
Nonspecific abnormal	6 (54.6)	5 (45.5)	
Normal	20 (69)	9 (31)	
Total	30 (50.8)	29 (49.2)	

The Chi-square test showed that rate of recurrence was significantly higher in patient with polytherapy and patient with abnormal EEG. EEG: Electroencephalogram, *$P \geq 0.05$

Discussion

In this study, 59 patients with idiopathic epilepsy were evaluated, and the association between seizure relapses and demographic factors, type of seizure, type of treatment, imaging, and EEG were assessed. This study demonstrated that relapses were more prevalent in those with abnormal EEG with specific patterns, significantly. Using EEG for diagnosing abnormalities after the first seizure attacks was important.[16] Research showed that in patients with long-term treatment, presence of abnormal EEG before and after antiepileptic treatment is a prognostic factor for increasing the risk of recurrences.[17] Several studies reported that in patients with abnormal EEG, seizures were poorly controlled which leads to more seizure recurrences.[3] In Western studies, there was an association between seizure recurrences and presence of abnormality in EEG in epileptic patients.[18-20] Review studies showed that there are two factors strongly associated with increasing the risk of seizure recurrences including abnormal EEG with specific patterns and abnormal neurologic examination, and seizure recurrences were more prevalent when both factors are present simultaneously.[21] However, there are other studies that did not show any relations between seizure relapses and EEG reports.[4] One study evaluated risk factors of seizure recurrence in epileptic patients, abnormal EEG did not predict seizure recurrences, and the etiology of disease and age of disease onset were associated with seizure recurrence.[22] The role of EEG in predicting seizure recurrences has controversy and arise this question that which aspect of EEG has an important role in epileptic patients.[9] Most of the studies in different region demonstrated that presence of abnormality especially those with specific patterns is associated with increasing risk of recurrences and this association in newly diagnosed cases were more obvious. This study showed that specific abnormal EEG is predicting more seizure recurrences not only in newly diagnosed patients but also in patients who were known case of epilepsy and receiving drug treatment.

In our study, there was a nearly significant association between imaging and recurrences. In one study in 150 newly diagnosed epileptic patients, abnormal MRI findings were associated with more seizure relapses.[23] Studies on factors related to seizure relapses showed that abnormal EEG and imaging modalities were associated to increasing recurrences.[24] In other study in patients with epilepsy, the presence of abnormality in computed tomography (CT) was associated with increasing seizure recurrences.[18]

In this study, recurrence rate was more in patients who received polytherapy treatment. Epileptic patients need the long-term use of medications, but after controlling disease, seizure recurrence is common special when the dosage of medications was reduced.[25] Studies reported that patients with abnormal EEG had more uncontrolled disease situation that may lead to more recurrences and causes needs for polytherapy treatments.[26,27] The effects of epilepsy treatment on seizure recurrences were evaluated in limited studies. There is not any specific algorithm for evaluating definite seizure recurrences and determining the risk and time of recurrences.[28] In study evaluated predisposing factors of response to epileptic treatment, patients with seizure recurrences were those who received polytherapy treatment and suggested patients who received polytherapy treatment had poorer disease control which causes more recurrences in these patients and epilepsy in those with monotherapy medication regimen is likely controlled, and recurrences are uncommon among these epileptic patients.[29] Study on 130 patients with generalized seizures evaluated patients in two groups including those who received monotherapy and polytherapy and showed that there were not any differences in recurrences and number of seizures in these two groups.[30] These differences between studies are maybe because of this fact that patients who received polytherapy treatment may have severe seizure recurrences due to other etiologies and maybe patients who received monotherapy treatment are those who received polytherapy regimen previously. For accurate evaluation of this association for generalizing these findings to society, further researches are needed to evaluate patients initially after starting epileptic treatment.

This study does not show any association between recurrences and demographic factors including gender, marital status, and educational level. There are other studies with similar findings that did not show any relation between gender and recurrence risks in epileptic patients.[13,18] In this study, the proportion of female was more than male that maybe affected our findings. For assessing the exact effect of demographic factors on seizure recurrences, more researches with greater sample size are needed.

One of the strengths of this study is following patients for 1 year repeatedly in Iranian population that cohort study in this population is limited. In addition, most of researches in this population were in newly diagnosed cases, but this study evaluated epileptic patients who started their treatment at least 1 year ago. In this study, patients divided into two groups including with and without recurrences had not differences between demographic factors that reduce study biases. One of the important limitations of this study was its small population that is not efficient for generalizing our findings to society. This study evaluated patients in a wide range of ages, (18-57 years) and it is better to assess patients in the same age group separately. Further researches with greater sample size and similar age groups are needed.

Conclusion

This study showed that presence of abnormal pattern in EEG and also number of anticonvulsant drugs can have a role in seizure recurrence in epileptic patients.

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Conflicts of interest

There are no conflicts of interest.

References

1. Iliescu C, Craiu D. Diagnostic approach of epilepsy in childhood and adolescence. Maedica (Buchar) 2013;8:195-9.
2. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, *et al.* ILAE official report: A practical clinical definition of epilepsy. Epilepsia 2014;55:475-82.
3. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, *et al.* Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46:470-2.
4. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, *et al.* Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE commission on classification and terminology, 2005-2009. Epilepsia 2010;51:676-85.
5. Berg AT, Shinnar S, Levy SR, Testa FM. Newly diagnosed epilepsy in children: Presentation at diagnosis. Epilepsia 1999;40:445-52.
6. Serrano-Castro PJ, Mauri-Llerda JA, Hernández-Ramos FJ, Sánchez-Alvarez JC, Parejo-Carbonell B, Quiroga-Subirana P, *et al*. Adult prevalence of epilepsy in Spain: Epiberia, a population-based study. Scientific World J 2015;2015:602710.
7. Sayehmiri K, Tavan H, Sayehmiri F, Mohammadi I, Carson KV. Prevalence of epilepsy in Iran: A meta-analysis and systematic review. Iran J Child Neurol 2014;8:9-17.
8. El-Tallawy HN, Farghaly WM, Rageh TA, Shehata GA, Metwally NA, Badry R, *et al.* Spectrum of epilepsy – Prevalence, impact, and treatment gap: An epidemiological study from Al-Quseir, Egypt. Neuropsychiatr Dis Treat 2016;12:1111-8.
9. Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry 2005;76 Suppl 2:ii2-7.
10. Pillai J, Sperling MR. Interictal EEG and the diagnosis of epilepsy. Epilepsia 2006;47 Suppl 1:14-22.
11. Hughes JR, Gruener G. The success of EEG in confirming epilepsy-revisited. Clin EEG Neurosci 1985;16:98-103.
12. Hauser WA, Rich SS, Annegers JF, Anderson VE. Seizure

recurrence after a 1st unprovoked seizure: An extended follow-up. Neurology 1990;40:1163-70.
13. Scotoni AE, Guerreiro MM, De Abreu HJ. First epileptic crisis. Analysis of risk factors for recurrence. Arq Neuropsiquiatr 1999;57:392-400.
14. Betting LE, Mory SB, Lopes-Cendes I, Li LM, Guerreiro MM, Guerreiro CA, *et al.* EEG features in idiopathic generalized epilepsy: Clues to diagnosis. Epilepsia 2006;47:523-8.
15. Betting LE, Mory SB, Lopes-Cendes I, Li LM, Guerreiro MM, Guerreiro CA, *et al.* MRI reveals structural abnormalities in patients with idiopathic generalized epilepsy. Neurology 2006;67:848-52.
16. Schreiner A, Pohlmann-Eden B. Value of the early electroencephalogram after a first unprovoked seizure. Clinical EEG Neurosci 2003;34:140-4.
17. Yang LH, Jiang LY, Lu RY, Zhong JQ, Liu SQ, Tao EX, *et al*. Correlation between the changes in ambulatory electroencephalography findings and epilepsy recurrence after medication withdrawal among the population in Southern China. Neurol Med Chir 2013;53:12-6.
18. Lamdhade SJ, Taori GM. Study of factors responsible for recurrence of seizures in controlled epileptics for more than 1½ years after withdrawal of antiepileptic drugs. Neurol India 2002;50:295-300.
19. Hawash KY, Rosman NP. Do partial seizures predict an increased risk of seizure recurrence after antiepilepsy drugs are withdrawn? J Child Neurol 2003;18:331-7.
20. Winckler MI, Rotta NT. Clinical and electroencephalographic follow-up after a first unprovoked seizure. Pediatr Neurol 2004;30:201-6.
21. Kim LG, Johnson TL, Marson AG, Chadwick DW; MRC MESS Study Group. Prediction of risk of seizure recurrence after a single seizure and early epilepsy: Further results from the MESS trial. Lancet Neurol 2006;5:317-22.
22. Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics 2012;129:256-64.
23. Arthur TM, deGrauw TJ, Johnson CS, Perkins SM, Kalnin A, Austin JK, *et al.* Seizure recurrence risk following a first seizure in neurologically normal children. Epilepsia 2008;49:1950-4.
24. Giza CC, Kutcher JS, Ashwal S, Barth J, Getchius TS, Gioia GA, *et al.* Summary of evidence-based guideline update: Evaluation and management of concussion in sports: Report of the guideline development subcommittee of the American Academy of Neurology. Neurology 2013;80:2250-7.
25. Khan RB, Onar A. Seizure recurrence and risk factors after antiepilepsy drug withdrawal in children with brain tumors. Epilepsia 2006;47:375-9.
26. Kalita J, Vajpeyee A, Misra UK. Predictors of one-year seizure remission – A clinicoradiological and electroencephalographic study. Electromyogr Clin Neurophysiol 2005;45:161-6.
27. Verrotti A, Latini G, Giannuzzi R, Cutarella R, Trotta D, Morgese G, *et al.* Factors associated with poor control in partial complex epilepsy. J Child Neurol 2004;19:262-4.
28. Berg AT. Risk of recurrence after a first unprovoked seizure. Epilepsia 2008;49 Suppl 1:13-8.
29. Verrotti A, Trotta D, Salladini C, Morgese G, Chiarelli F. Risk factors for recurrence of epilepsy and withdrawal of antiepileptic therapy: A practical approach. Ann Med 2003;35:207-15.
30. Deckers CL, Hekster YA, Keyser A, van Lier HJ, Meinardi H, Renier WO. Monotherapy versus polytherapy for epilepsy: A multicenter double-blind randomized study. Epilepsia 2001;42:1387-94.