FREQUENCY AND CAUSES OF BREAKTHROUGH SEIZURES AMONG ADULT PATIENTS WITH EPILEPSY DESPITE ANTIEPILEPTIC TREATMENT

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ABSTRACT

Objective: To determine the frequency and causes related to the precipitation of breakthrough seizures among adult patients with epilepsy despite antiepileptic treatment.

Study Design: Cross sectional analytical study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi, from May 2018 to Oct 2018.

Methodology: The sample population comprised of 161 adult patients of epilepsy reporting to Military Hospital Rawalpindi with the epilepsy using the antiepileptic drugs (AEDs) at least for the past six months. Detailed history and physical examination was carried out for all the patients. Frequency of breakthrough seizures among this population was calculated and relationship were assessed with the precipitation of the breakthrough seizure.

Results: Out of 161 patients of epileptic included in the study, 78 were male and 83 were female. Out of these 80.1% patients had breakthrough seizures. After applying the logistic regression we found that increasing age, marital status, sleep deprivation, total duration of treatment, missing one or two doses of antiepileptic drugs and watching television for long hours were strongly related to the precipitation of breakthrough seizures in our study patients.

Conclusion: There was showed high frequency of breakthrough seizures in our population despite the use of AEDs. Special attention should be paid to the patients with increasing age and living alone. Education of patients regarding proper sleep, stress management, restricting TV hours and strict compliance should be done in order to prevent the phenomenon of breakthrough seizures and achieve a good control over this potentially life threatening condition.

Keywords: Anti-epileptic drugs, Breakthrough seizures, Epilepsy causes.

INTRODUCTION

Break through seizures are the seizures that occur after a period of seizure-free time and depict the inadequate control of disease highlighting the treatment failure. Prescribed dose reductions and inadequate compliance should be excluded before labeling the seizure as break through[1]. It is a prevalent health problem that affects ≈39-75.3% of the patients suffering from epilepsy[2,3]. Breakthrough seizures can occur due to various causes but whatever the cause may be their occurrence is considered as a treatment failure and should alarm the neurophysicians treating the patient[1].

Millions of people suffer from epilepsy worldwide with a wide range of prevalence in different parts of the world. 9.9/1000 people suffer from epilepsy in Pakistan according to the latest survey carried out by the local health professionals[4]. Most of the patients among these belong to rural areas and are inadequately treated, increasing the chances of breakthrough seizures and emergency presentations[4].

A number of previous researches highlight the high prevalence of breakthrough seizures among various populations. 75.3% of the epileptic patients suffered from breakthrough seizures in a study done in Uganda[2]. Another similar study done in our local population showed that 39.3% of the children and 44.1% of the adults suffered from the breakthrough seizures which highlights the magnitude of this understudied phenomenon in our part of the world[3]. Al-kattan *et al* concluded that various precipitating factors are

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linked to the break-through seizures and patients and their caregivers should be educated adequately about these in order to achieve the proper control of this disease[4]. Breakthrough seizures if persists for a long period can lead to various mental health issues and emotional distress[7]. It also causes financial burden on the individual, his family and the state health budget[5,6]. All these factors affect the life of individual in all the domains leading to the compromised quality of life[7,8].

Fever, playing videogames, emotional stress[9], non-compliance, menses among females[2], sleep deprivation and missed doses[4] have been associated with the precipitation of breakthrough seizures among the patients of epilepsy. These factors may cause this precipitation by physiological, psychological or biological reasons.

This study was planned to investigate the frequency of breakthrough seizures among the epileptic patients and to identify the factors related to this precipitation.

METHODOLOGY

This cross sectional analytical study was conducted at Pak Emirates Military Hospital Rawalpindi between May to October 2018. All the patients of idiopathic epilepsy with age between 18 and 60 and on one or more AED for last six months were included in the study. Sample was gathered by using consecutive sampling. Sample size was calculated by using the WHO sample size calculator[5]. Exclusion criteria were the patients, who did not consent to or those with a past or current history of any psychiatric or chronic physical illness (Space occupying lesion of CNS, CVA, CVST, DM, IHD, HTN, RA or other diseases of chronic nature) or with a past or current history of substance use or pseudoseizures. Patients who could not read or perform the questionnaire were also excluded.

The diagnosis of epilepsy was made on the witness account or the electro-encephalogram findings as per the International League against Epilepsy (ILAE) definition[10].

The seizure in a person with previously controlled epilepsy despite the use of prescribed regimen of AEDs[1]. These were the factors related directly with the onset of the seizure. Patient, witness and the neurologist were convinced that

Table-I: Characteristics of the study group and frequency of breakthrough seizures.

Socio demographic factors Total	Subjects without breakthrough seizures n (%) 32 (19.9)	Subjects with breakthrough seizures n (%) 129 (80.1)	*p*-value
Age			
≤45	26 (81.2)	115 (89.1)	0.222
>45	06 (18.8)	14 (10.9)	
Gender			
Male	12 (37.5)	66 (51.2)	0.166
Female	20 (62.5)	63 (48.8)	
Fever			
No	18 (56.3)	82 (63.6)	0.445
Yes	14 (43.7)	47 (36.4)	
Psychological stress			
No	27 (84.4)	83 (64.3)	0.029
Yes	05 (15.6)	46 (35.7)	
Sleep deprivation			
No	20 (62.5)	84 (65.1)	0.78
Yes	12 (37.5)	45 (34.9)	
Flickering lights			
No	27 (84.4)	93 (72.1)	0.153
Yes	05 (15.6)	36 (27.9)	
No of AEDs			
One	28 (87.5)	111 (86.1)	0.941
>1	04 (12.5)	18 (13.9)	
Total duration of treatment			
<5 years	30 (93.7)	127 (98.4)	0.80
>5 years	02 (6.3)	02 (1.6)	
Changed brand of antiepileptic drug			
No	26 (81.2)	111(86)	0.495
Yes	06 (18.8)	18 (13.9)	
Missed one or two doses			
No	10 (31.2)	23 (17.8)	0.092
Yes	22 (68.8)	106 (82.2)	
Marital status			
Married	14 (43.7)	71 (55.1)	0.143
Widow, single or divorced	18 (56.3)	51 (44.9)	
Watching television			
<4 hours	28 (87.5)	84 (65.1)	0.013
>4 hours	4 (12.5)	45 (34.9)	

these factors were the cause of precipitation of the seizures[11].

Patients were provided with a detailed description of the study and were inducted into the study after written informed consent. Patients with confounding variables like presence of chronic physical, neurological or mental illness or pseudoseizures were identified by detailed history taking and excluded from the study. The study questionnaires were administered to the patients and were asked to answer the questions according to their experience. Socio demographic variables were also collected. Variables in the study included age, gender, marital status, watching television for long hours, fever, sleep deprivation, psychological stress, flickering lights, change of brand of AEDs, total no of drugs, total number of years of treatment and missing of one or two doses of AEDs. The socio demographic data of the full sample of subjects participating in the research was entered in a structured Performa.

All statistical analysis was performed using SPSS-21. Characteristics of participants and the presence or absence of breakthrough seizures were described by using the descriptive statistics. Binary logistic regression analysis was done to evaluate factors related to the presence of breakthrough seizures. Chi Square & Fisher test were used for qualitative data. Differences between groups were considered significant if *p*-values were ≤0.05.

RESULTS

A total of 200 patients of epileptic were approached to participate in the study. Nine refused participation and 20 were ineligible due to exclusion criteria (2 gave history of pseudo seizures, 3 had space occupying lesion in brain, 2 had CVA, 5 had clinical depression and 8 had DM). After being consented, an additional 10 did not provide complete data at baseline, leaving 161 participants who had participated in the complete study. Out of 161, 19.9% had good control of epilepsy and were seizure free while 80.1% reported the breakthrough seizures. Characteristics of the study participants were mentioned in the table-I. Table-II showed increasing age, marital status, sleep deprivation, total duration of treatment, missing one or two doses of AEDs and watching television for long hours were strongly associated with the precipitation of the breakthrough seizures when regression analysis was done.

Table-II: The correlated factors relating to precipitation of breakthrough seizures in the binary logistic regression.

	β	*p*-value	OR (95% CI)
Age (ref. is 45 years or less)	-1.600	0.061	0.202 (0.038-1.077)
Gender (ref. is male)	-0.796	0.120	0.451 (0.165-1.229)
Fever (ref. is no fever)	-2.879	0.742	0.056 (0.008-0.414)
Psychological stress (ref. is no stress)	-0.895	0.171	0.409 (0.114-1.472)
Sleep deprivation (ref. is no sleep deprivation)	0.161	0.005	1.175 (0.450-3.068)
Flickering lights (ref. is no flickering)	-2.690	0.171	0.068 (0.006-0.832)
No of AEDs (ref. is >1 AED)	-0.963	0.074	0.382 (0.133-1.097)
Duration of treatment (ref. is >05 years)	2.265	0.008	9.626 (1.820-50.923)
Changed brand of AEDs(ref. is not changed)	0.465	0.486	1.593(0.430-5.899)
Missed one or two doses (ref. not missed doses)	-2.545	0.003	0.078 (0.015-0.423)
Marital status (ref. is married)	-1.796	0.039	0.166 (0.030-0.913)
Watching television (ref. is <4 hours)	1.556	0.032	4.741 (1.145-19.629)

DISCUSSION

Breakthrough seizures among the patients of epilepsy on AEDs have been reported in various studies done in the past[2,3,5]. Assessing the patients of epilepsy reporting in neurology department of our hospital we found that 80.1% of our patients reported the presence of breakthrough seizures

despite using the routine prescribed medication which is in a bit higher as compared to the studies done in the past on this phenomenon[2,3,12]. Some of the factors that may precipitate the breakthrough seizures among epileptics have been reported as sleep deprivation, psychological stress, poor compliance and long duration of illness. Reason behind these may be related to increased neuronal activity in response to these or fall in the AED levels in the blood either due to improper compliance or drug interactions[13-16].

Sleep deprivation and provocation of seizures have a strong correlation in the studies done in the past[5,9]. Sleep is such a complex biological function with physiological, psychological and social dimensions that its soundness requires a total well being of an individual. Therefore detailed briefing on this aspect should be given to the patient while starting him on the AEDs. Our study showed similar results and sleep deprivation emerged as a strong predictor for precipitation of breakthrough seizures. Psychological stress was found related when chi-square was applied but found unrelated on logistic regression. Stress can have a direct effect on neuronal activity and it can also exert its effect by exerting the effect on sleep as sleep problems and psychological problems have a positive correlation[17].

Increasing age has not been a consistent correlate with breakthrough seizures among epileptic patients in studies done in past[2,5]. Results in our study were different and increasing age was strongly related to the presence of breakthrough seizures among the epileptic patients. Reason might be decreased care or resistance towards treatment due to long standing nature of illness.

Missing one or two doses of AEDs was also strongly associated with the precipitation of breakthrough seizures among our target population. This finding is in accordance with the existing literature[18,19]. This is the reason for which all measures should be applied on these patients to improve the compliance.

The use of questionnaire for assessing the compliance. Ideally drug levels should have been done in all the cases to confirm the compliance. Another limitation was the chance that the subject may under or over report symptoms on self-administered questionnaires. We suggest further studies on a broader based and a more representative sample size in order to generalize the results.

CONCLUSION

There was a frequency high frequency of breakthrough seizures in our population despite the use of AEDs. Special attention should be paid to the patients with increasing age and living alone.

RECOMMANDATION

Education of patients regarding proper sleep, stress management, restricting TV hours and strict compliance should be done in order to prevent the phenomenon of breakthrough seizures and achieve a good control over this potentially life threatening condition.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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