



A CROSS SECTIONAL ANALYTICAL STUDY OF BREAK THROUGH SEIZURES IN EPILEPTICS IN A TERTIARY CARE CENTER

Neurology

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ABSTRACT

Introduction: Epilepsy is a chronic disease affecting millions of patients worldwide. However, it continues to be a highly stigmatized and disabling chronic condition. Breakthrough seizures are seizures that occur in a person who had previously good consistent control of epilepsy documented in the medical records and then gets another seizure. Breakthrough seizures may result from forgotten prescriptions, under dosing, and use of recreational drugs, alcohol sleep deprivation etc. **Methods:** All the patients with epilepsy attending the OPD of Tirunelveli medical college between April 2021 and March 2023 were enrolled for the study. Those fitting in break through seizure were given a structured proforma. **Results:** A total of 380 patients with epilepsy were considered for the study. Nearly half the patients (50%) had breakthrough seizures. Factors precipitating break through seizures like alcohol, screen time, sleep deprivation and menstruation in females were all significant with p value <0.05. However other factors like drug changes due to non availability, missed doses and increasing number of doses per day were statistically very significant with a p value of <0.0001. **Conclusions:** The prevalence of breakthrough seizures can be amenable to change if we take measures to ensure the drug availability thereby leading to decrease in medication change and missed doses. Education helps to impart more knowledge of disease and helps in compliance and decrease the stigma associated with the disease.

KEYWORDS

Break through seizure, Epilepsy, Treatment failure

INTRODUCTION:

Epilepsy is a non communicable disease which does not respect any age boundaries. It has been described since ancient times. As per the 2023 data compiled by the World health organization the global prevalence of epilepsy is 50 million. The middle income and low income countries constitute 80% of people living with epilepsy. The proper diagnosis and availability of drugs can help decrease the morbidity and mortality of 70% of these people. Around three quarters of people living in low income countries do not get the required treatment (1) India contributes to one -sixth (12 million) of the global burden (2). With the ever increasing population the numbers won't see a decline any soon unless a specific targeted approach is taken up by the government and health care workers in creating public awareness.

A breakthrough seizure is defined as the first seizure after a minimum of 12 months seizure freedom while on treatment (3). Chawla et al had defined seizure control as seizure free interval of at least 6 months (4). The International League Against Epilepsy (ILAE) had identified breakthrough seizures separately from treatment failure after ruling out poor treatment compliance and planned dose reductions (5).

Seizures occurring in any individual who was in epilepsy control with proper drug compliance is to be considered as breakthrough seizures and cause needs to be evaluated (6). Some of the common causes of breakthrough seizures are missed medications, anti seizure medications (ASM) below therapeutic levels and use of generic drugs (7). Excessive watching of Television and screen time, sleep deprivation, stress and some of the few factors leading to breakthrough seizures (8). Yirga Legesse Niriayo, et al. 2019 reported that non compliance and neglect was the most common cause of non adherence (9). Even a single breakthrough seizure in a well controlled patient can cause social and economical implications in form of increased stigma, loss of working hour, costs of hospitalization, employment etc (10). Though inadequate compliance was a risk factor for break through seizure, we tried to find out the reasons for the same.

METHODOLOGY:

This multifactorial analytical study was carried out in Tirunelveli medical college, Tamilnadu from April 2021 to March 2023 (2 years). A through history and clinical examination was carried out in all epilepsy patients who had an episode of seizure while on medications. Imaging and EEG was done in all patients with seizures. Before the onset of study we had obtained the institutional ethical committee clearance and scientific advisory committee clearance.

We could enroll 189 adult patients aged between 18 years to 75 years

with a clear cut diagnosis of breakthrough seizures for the study. Patients with history of hemiplegia, space occupying lesion, children less than 18 years, ladies with confirmed pregnancy, those without any proper records and those who didn't give the written consent were excluded from the study.

We had a standard proforma in which the basic demographic details like age, sex, seizure semiology etc was determined. Duration of treatment was assessed by noting down the date when the drugs were first dispensed and the duration was divided as less than 6 months, 6 months to 1 year, 1-5 years and more than 5 years. Number of drugs taken and the number of times these drugs were taken were also noted as 1, 2, >2 and 1, 2, 3 respectively. A detailed in depth questioning was done to find out the missed doses. We then probed to find out the reason for the lack of compliance and their knowledge of the disease by a simple yes/no question and scores were provided. The number of hours slept was divided into less than 8 hours and more than 8 hours. Duration of screen time was subdivided into <1 hours per day, 1-4 hours per day and >4 hours per day. For female patients they were asked whether seizures worsened during menstruation. Routine blood investigations, x ray, CT scan were done for all the patients requiring admission and a thorough examination for focus of infection was searched. The patients with epilepsy was managed as per the ILAE criteria (11).

Statistical Analysis:

The socio demographic data of the full sample of subjects participating in the research was entered in a structured Proforma. Drug compliance was assessed using Morisky adherence scale.

All statistical analysis was performed using SPSS. Characteristics of participants their demographic details were described by using the descriptive statistics. Frequency was calculated for the basic characteristics of the patients enrolled in the study. Univariate analysis was done for the categorical data.

Chi square was done to identify the relationship between anti seizure medications and breakthrough seizures.

p value of <0.05 was considered significant

RESULTS:

A total of 380 patients with well documented seizures were enrolled for the study. One hundred and eighty nine (189) patients who fulfilled the inclusion criteria for breakthrough seizures were included in the study. The majority of the patients were females 65%. The lower limit for age

was taken as 18 years and upper limit as 75 years. The demographics and basic characteristics of the study population are entered in Table 1. There was a uniform prevalence of breakthrough seizures throughout the age band with maximum prevalence across 31-50 year age group. Generalized tonic clonic seizure (GTCS) was the most common semiology with a prevalence of 59% (111/189). Most of the patients had been taking medications for a long time with 69% (131/189) patients taking treatment for more than an year. A single drug could control seizures in 54% of patients. Phenytoin was the most common drug dispensed, followed by Carbamazepine with a 53% patients having to take more than 2 doses per day. This imputed nearly half the patients (48%) to miss more than 3 doses of asm. Only 23% of patients developed breakthrough seizures without even missing a single dose.

Sleep deprivation was significant in patients with breakthrough seizure (p value 0.05) with almost 77% (146/189) patients reporting inadequate sleep. There was a significant association of alcohol misuse and breakthrough seizures with a p value of 0.001. Stress was the most common factor which precipitated alcohol misuse in males. Screen time also had a significant association with breakthrough seizures with a p value of 0.002 with more than 83% of patients using screen more than an hour.

Drug unavailability was an important reason with 115/189-61% of patients citing unavailability of drugs many a times. To validate that point, their records were checked with the dates of drug unavailability and medication changes. There was a very significant association with medication changes and drug unavailability with break through seizures with a p value of <0.001. Knowledge of the disease was another novel factor that was assessed in this study and we could find that only 44% of patients knew about the perils of the disease they were suffering from. This could be one reason for the lack of seriousness regarding the care and need for proper compliance.

Females at the time of menstruation had a significant increase in breakthrough seizures with a p value of 0.001

Infection was not a major contributor in this study as we did not take into consideration many patients in ICU

Table 1: Basic Characteristics Of Patients Enrolled In The Study

Basic characteristics	N	Percentage
Age mean, median, SD	42,40,16	
Age group		
18-30 years	55	29
31-50 years	76	40
51-75 years	58	30.6
Sex		
Males	66	34.9
Females	123	65.1
Marital status		
Married	147	77.8
Unmarried	42	22.2
Level of education		
Illiterate	44	23.3
Primary school	51	27
Secondary school	24	12.7
High school	14	7.4
College	56	29.6

Table 2: Factors Precipitating Breakthrough Seizures

Factor	F value	p value
Knowledge of disease	5.87	0.016
Duration of treatment	7.56	0.0001
Number of drugs taken	3.275	0.04
Doses missed	25.6	0.0001
Non availability of drugs	8.686	0.004
Hours slept	3.688	0.05
Screen time	6.64	0.002
Alcohol use	6.64	0.002
Drug abuse	4.48	0.036
Menstruation	234.84	0.0001

Table 3: Relationship Between Anti Seizure Medication And Breakthrough Seizures

Factor	N	P value
Drug availability	74	0.001

Knowledge of disease	83	0.001
Medication change	103	0.01
Duration of treatment		0.02
<6 months	33	
6 months to 1 year	25	
1 to 5 years	94	
>5 years	37	
Number of times/day		0.0001
1	4	
2	85	
3	100	
Doses missed		0.02
None	44	
3 doses or less	54	
>3 doses	91	

DISCUSSION:

The incidence of breakthrough seizures were reported to be around 50% in our hospital which was well in accordance with other internationally published studies who had reported an incidence between 35 to 75% (5)(12)(13). Around 60% of our patients received inadequate treatment. Many factors have been implicated in causing breakthrough seizures. In 1988 WHO had reported that an estimated 80% of epileptic patients in world receive inadequate or no treatment at all (14). So we can safely infer that over a span of 25 years there has been a 20% improvement in compliance.

The precipitants in breakthrough seizures is multifactorial. Addressing these factors goes a long way in tackling this menace which is a burden on the public health system. There is an important need to address the factors like drug availability, to increase patient knowledge of the disease, thereby increasing the compliance. In view of heavy patient load in government settings like ours we need to either take time to explain to patient regarding compliance or train other para medical staff to educate patients regarding adequate compliance (5).

Our study comprised of 65% females and 35% males. Of these 77% were married. Epilepsy prevented many women, especially those located near forest areas from carrying out their daily chores. Marital strife was evident in the form of more people with epilepsy coming for medications alone. However in our opd setting we were not able to probe further into patients interpersonal life due to time constraints. This was in concordance with a study in Calcutta by Das et al in 2006 (15).

A lot of patients were concerned about their children getting the disease. Many believed that their seizures had a lot to be done with spiritual scourge and considered it to be a type of punishment from God. Some of our patients had consulted local shamans and taken traditional medicines before coming to us. This had an effect on the recall ability of the patients to describe the correct semiology. Studies and data has shown that these beliefs were rooted out from western culture decades ago (16)(17). In India we still have a long way to go in achieving this goal (18).

Education played an indirect role in seizure remission. About 44 participants (23.3%) in our study were illiterate and 27% of our patients were educated only up to primary school. A chi square analysis between level of education and knowledge of disease showed a significant association, p value 0.03. Though those with education also missed their drug doses there was a significant association p-0.02 in those who were illiterate. This resonates with the lack of seriousness to the disease.

In another South Indian study, education helped in removal of apprehension of side effects of asm and helps in proper compliance (19).

A univariate analysis between break through seizures and various factors leading to breakthrough seizures showed a very significant association. In our study there was a significant interplay between patient factors and policy factor. Drug availability (policy factor) p value-0.001, medication changes p value-0.01 and changes in number of doses p value 0.0001 which stemmed from the non availability of drugs leading to missed doses p value 0.02 were all very significant.

Polytherapy was a risk factor to non adherence with a p value of

0.0001, which was in stark contrast to the study by Samsonsen. C from Norway who couldn't find any significant association. (20) This could be explained by the study by Lee JW who said that proper communication of the ASM by the treating neurologist could help prevent non-compliance. (19) However the study done by Mason et al in Cambridge stated that polytherapy has a negative correlation with drug compliance. (22)

The other precipitating factors leading to poor compliance like alcohol abuse p value 0.002, drug abuse p value 0.036, screen time p value 0.002, lack of sleep p value 0.05, all had a significant role in precipitating breakthrough seizures. This was in perfect synchrony with the study by Lin YY who concluded that those with children with screen time of more than an hour per day had increased incidence of epilepsy and decreased sleep. (23) Duration of treatment also had a significant effect on seizures. Majority of our patients were on treatment for more than an year, p value-0.002. This is in contrast to the study in Uganda (5) who reported better outcome in those with longer duration of treatment. This difference could be attributed to the fact that once patient becomes seizure free coupled with lack of knowledge of disease stops treatment by themselves leading to recurrence. Seizures occurring just before, during or after menstruation was very significant with a p value of 0.0001. This was in tune with other studies from developing countries. (5) Unavailability of drugs in small primary health centre could also be another reason as patients have to travel as long as 100km to reach a medical college. This means a loss of days wages and financial constraints. Patients with multiple co morbidities were found to be lesser compliant to treatment. This was also seen in another Ethiopian study done 2016 (24).

Semiology of the event as described by the bystander and the patient were different leading to diagnostic and treatment dilemma. Self reporting done by some patients were inconsistent with the EEG findings, leading us to reconsider the diagnosis. Some patients had depressive features and did not fully disclose their marital acrimony. Alcoholism in males, screen time, and decreased sleep stood out among all patients with breakthrough seizures across all age groups which were significant confounders. Government medical colleges in state of Tamilnadu are usually frequented by the less affluent sections of the society, hence this study cannot be extrapolated across all the sections of the society where the well to do people with better education might have a better compliance. This study coincided with the second wave of covid and hence we had a limitation in travel facilities due to lockdown causing many to stop medications.

CONCLUSION:

Breakthrough seizures are still the most common cause of epilepsy. There is an urgent need from the policy makers to make sure that the drugs are available all the time. Health workers should take more time to explain to the patients regarding the need for regular drug intake. While dispensing ASM it has to be made sure to write down the dosage and timing of medications so as to avoid missing of doses. Proper education should be imparted to avoid the stigmata of the disease. Regular psychiatry counseling should be given so as to prevent patients from going into depression and helping them tide over their personal crisis.

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