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Research Article

A COMPARATIVE STUDY OF FIRST EPISODE STATUS EPILEPTICUS AND MULTIPLE EPISODES OF STATUS EPILEPTICUS IN EMERGENCY DEPARTMENT OF TERTIARY HOSPITAL OF BUNDELKHAND REGION, CENTRAL INDIA

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ABSTRACT

Objective: Status epilepticus (SE) is a medical emergency that necessitates prompt and intensive treatment to prevent damage to the brain and other complications. SE can occur in any age group, but it is most observed in infants and the elderly. The diagnosis of convulsive SE is primarily clinical, but neuroimaging and laboratory studies are required to identify the underlying cause when convulsion is subsided. Bundelkhand region is a proposed state, located between Uttar Pradesh and Madhya Pradesh in central India, has a population of approximately 18 million, with around 14 million residing in rural areas (Census 2011). This region is infamous for its backward healthcare and education systems. This study aims to compare the outcomes of individuals experiencing their first episode of SE versus those with multiple episodes in terms of seizure control or progression to refractory or super-refractory status, considering the underlying causes.

Methods: A total of 100 participants were selected for the study at MLB Medical College, Jhansi, between March 2020 and November 2021. Before participation, written informed consent was obtained after explaining the study's objectives and procedures in detail. Data were recorded on an Excel sheet and analyzed using the Statistical Package for the Social Sciences software, applying appropriate statistical tests when necessary.

Results: Among the 100 patients with SE, the common etiological factors were anticonvulsant drug withdrawal (33%) and central nervous system (CNS) infections (33%), followed by metabolic encephalopathy (17%), cerebral vascular accidents (12%), and hypoxemic encephalopathy (5%). The patients were managed according to standard protocols and drug availability. The outcomes were categorized as seizure control, hospital death, or development of refractory or super-refractory status. Among the patients, 35% developed refractory SE, and within that group, 29% progressed to super-refractory status.

Conclusion: The fatality rate of SE was 14.0%. Predictors of higher mortality rates included the first episode of SE, patient's age, lack of response to initial antiepileptic drugs, duration of convulsions, and untreatable underlying causes. Etiologies such as CNS infections and anticonvulsant drug withdrawal were considered preventable and have better outcomes.

Keywords: Status epilepticus, Episodes of SE, Seizures, Etiology.

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INTRODUCTION

A seizure is a manifestation of abnormal synchronous hyperactivity in a group of cortical neurons [1]. Epilepsy, on the other hand, is defined as the occurrence of at least two unprovoked or reflex seizures more than 24 h apart. Status epilepticus (SE) was previously defined as a seizure lasting 30 min or longer, or a series of seizures without recovery of normal mental status in between [2]. However, the Neurocritical Care Society guidelines from 2012 revised the definition to include seizures lasting 5 min or more with continuous clinical and/or electrographic activity, or recurrent seizures without recovery [3]. SE can be of multiple types such convulsive or non-convulsive, with convulsive SE characterized by tonic-clonic movements and mental impairment, while non-convulsive SE is identified through seizure activity on an electroencephalogram without accompanying movements [4]. The incidence of SE shows a bimodal age distribution, with peaks in infancy and the elderly. The incidence rate ranges from 7 to 40 cases per 100,000 persons per year, with a higher prevalence in males. While most patients with SE have a history of epilepsy, it can also occur in individuals without epilepsy. Short-term mortality rates within 30 days range from 7.6% to 22%, with higher rates observed among the elderly [5-7].

Objectives

This study aims to compare the demographic distribution, etiology/risk factors, outcomes, mortality, and prognosis between individuals experiencing their first episode of SE and those with multiple episodes.

METHODS

This observational and descriptive cross-sectional study was conducted at M.L.B Medical College, Jhansi in the Neurology Department of Medicine over a period of 18 months. Patients' legally authorized representative who agreed to participate in the study provided written informed consent. SE diagnoses were made by treating physicians. Patients with first episode SE and patients with multiple episodes of SE were grouped separately. Data on demographic variables (age, sex, and educational level), type of SE, seizure duration, and etiological history were collected. SE cases due to metabolic disturbances such as dyselectrolytemia, hypoglycemia, uremic encephalopathy, and hepatic encephalopathy were included in the study. The collected data were entered into an Excel sheet and managed according to guidelines and medication availability.

Sample size

This was 100 patients.

Inclusion criteria

Age >18 years with a clinical diagnosis of SE was excluded from the study.

Exclusion criteria

The following criteria were excluded from the study:

- Age <18 years

- Seizure episodes due to head injury
- Eclampsia.

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences statistics version 22. Descriptive values such as mean and standard deviation (SD) were calculated for quantitative data. Chi-square was applied for assessing the independence of proportions. $p<0.05$ is considered significant. Mean±SD and percentages were used to express numerical and categorical parameters, respectively. The Chi-square test was applied to analyze categorical variables.

RESULTS

Mean age of participants was 41.24±16.71 and majority of the patients having first and multiple episodes were found in 18–30 years of age groups, that is, 41 (41%) followed by 51–50 years of age group, that is, 22 (22%). Minimum patients were found in >60 years of age group, that is, 11 (11%). Mortality was higher in 51–60 years of age group in first episode SE group while there was no such preponderance in multiple episodes of SE.

As per found data in Table 2, majority of patients were found male, that is, 60 (60%) and rest were female, that is, 40 (40%). Ratio of M: F is 1.5:1. Male patients have higher numbers of both types of SE and higher deaths as compare to females.

Out of 100 patients, 54 (54%) patients controlled at early stage of SE, and rest 46 progressed in further stage in which 11 (11%) patients controlled at established stage and 35 (35%) land up in the refractory SE in which 23 (23%) patients controlled at refractory SE and 12 (12%) patients super refractory to the treatment.

Maximum mortality rate associated with the super refractory SE which out of 14 patients 8 (57%) patients were expired followed by refractory SE 5 (35.71%). SE controlled at early stage have better prognosis. There is no death in initial stages of SE in multiple episodes group while higher mortality was recorded in later stages of 1st episode of SE group.

Anticonvulsant drug withdrawal (ACDW) in the preexisting epileptic patients (33%) and central nervous system (CNS) infection (33%) are the leading cause of SE followed by metabolic disturbance (Dyselectrolytemia, Hypoglycemia, Uremic encephalopathy, and Hepatic encephalopathy) and Cerebrovascular accident (12%), and Complete hanging (hypoxic encephalopathy) is 5%. ACDW has highest numbers of multiple episodes of SE while CNS infections have highest numbers of 1st episode of SE.

This table shows maximum mortality associated with the complete hanging and cerebrovascular accident, that is, 5 (35.71%) followed by CNS infection 2 (14.29%), anticonvulsant drug withdrawal, and metabolic disturbance, that is, 1 (7.14%). The highest mortality is found in hanging cases all of which have 1st episode of SE followed by cases of cerebrovascular accident (CVA).

DISCUSSION

In 100 patients of our study, 60% were male and rest 40% were female, the similar finding was in Ozdilek *et al.*, study in 2013 where 53% were male and 47% patients were female [8]. While Treiman *et al*. found 82.3% male patients in total 518 participants of SE in 1998 [9].

In our study, the age group ranged from >18 years of age, 41% cases were in the age group of 18–30 years followed by 51–60 years of age (22%), 31–40 years of age (14%), and 41–50 years of age (12%) then >60 years of age group 11%. Mean age was 41.24±16.71 years, the similar result was found in Verma *et al*., (2018) study done in North India where the mean age was 41.71±19.72 years. Moreover, majority of the patients belonged to the age group of 21–30 years [10], while the studies done by Treiman *et al*. (1998) and Horváth *et al*. (2019)

Table 1: Distribution of patients according to their age

Age (in years)	1st Episode of SE				Multiple episodes of SE				Total Number of patients
	n	%	Deaths	% of Death	n	%	Deaths	% of Death	
18–30 years	24	58.54	1	4.17	17	41.46	0	0.00	41
31–40 years	8	57.14	1	12.50	6	42.86	0	0.00	14
41–50 years	7	58.33	3	42.86	5	41.67	1	20.00	12
51–60 years	14	63.64	4	28.57	8	36.36	1	12.50	22
>60 years	7	63.64	2	28.57	4	36.36	1	25.00	11
Total	60	60.00	11	18.33	40	40.00	3	7.50	100

SE: Status epilepticus

Table 2: Gender distribution of patients

Gender	1st Episode of SE				Multiple episodes of SE				Total number of patients	Chi-square	p-value
	n	%	Deaths	% of Death	n	%	Deaths	% of Death			
Male	38	63.33	6	15.79	22	36.67	2	9.09	60	0.300	0.581
Female	22	55.00	5	22.73	18	45.00	1	5.56	40	0.154	0.695

SE: Status epilepticus

Table 3: Stages of status epilepticus

Parameters	Status epilepticus (n=100)*				Expired (n=14)*			
	1st episode of SE	%	Multiple Episodes of SE	%	1st episode of SE	%	Multiple episodes of SE	%
Early	31	51.67	23	57.50	0	0.00	0	0.00
Established	7	11.67	4	10.00	2	18.18	0	0.00
Refractory	14	23.33	9	22.50	3	27.27	1	33.33
Super Refractory	8	13.33	4	10.00	6	54.55	2	66.67
Total	60	100.0	40	100.0	11	100.0	3	100.0

SE: Status epilepticus

Table 4: Distributions of cases according to etiology

Etiology	1st episode of SE		Multiple episodes of SE		Total	Chi-square	p-value
	n	%	n	%			
CNS infection	21	63.64	12	36.36	33	19.591	<0.001
Anticonvulsant drug withdrawal	10	30.30	22	69.70	32		
Cerebrovascular accident	12	92.31	1	7.69	13		
Others*	17	77.27	5	22.72	22		

*Dyselectrolytemia, Hypoglycemia, Uremic encephalopathy, Hepatic encephalopathy, Complete hanging (hypoxic encephalopathy), CNS: Central nervous system

Table 5: Correlation of mortality with the etiology

Etiology	1st Episode of SE		Multiple episodes of SE		p-value
	Death	%	Death	%	
CNS infection	1	4.76	1	8.33	<0.001
Anticonvulsant drug withdrawal	0	0.00	1	4.35	0.004
Cerebrovascular accident	4	33.33	0	0.00	<0.001
Metabolic disturbance	1	8.33	1	20.00	0.003
Complete hanging (hypoxic encephalopathy)	5	100.00	0	0.00	0.003

CNS: Central nervous system

have higher mean age as compared to our study. Their mean age was 58.6±15.6 years and 64.1±13.9 years, respectively [3,9].

Treatment of SE often requires ICU facilities where assessment and management of airway, breathing, and circulation is top priority. An IV line is secure to give injectable medicines, high flow oxygen is given because seizure causes anoxic injury to brain. Next step is to give seizure abortive drug treatment (i.e., short-acting benzodiazepine) and to find out the underlying cause of SE. Loading dose of antiepileptic drug (AED) following administration of benzodiazepines is given in all patients who present with SE, unless the immediate cause of SE is known and definitively corrected (e.g., severe hypoglycemia). The 54% patients controlled at early stage (<30 min), 46% patients remain refractory to first-line treatment in which 11% controlled at established stage (32–120 min) and remained 35% land up in the refractory SE stages (>120 min), in which 12% patients progressed in the super-refractory SE (>24 h). A similar result was found in Ozdilek *et al*., (2013) in which 31% of a total SE were remain refractory to the treatment [8].

In our study, we found that the predominant etiological factors are anti-convulsant drug withdrawal/non-compliance to medicines in the pre-existing epileptic patients (33%) and CNS infection (33%) followed by the metabolic disturbance (Dyselectrolytemia, hypoglycemia, uremic encephalopathy, hepatic encephalopathy (17%), and cerebrovascular accident (12%), and complete hanging (hypoxic encephalopathy)) 5% case of SE. Similar result found in Verma *et al*., (2018), study in which not taking AEDs as prescribed was responsible for 34.9% of the cases of SE followed by CNS infection in 24.1% participants was the precipitating factor of SE [10]. Trinka *et al*. (2015) also found low antiepileptic drug levels accounting for at least one fourth of SE. In older adults, stroke is the major cause of SE (about 36%). The other common causes of SE are alcohol and other substance withdrawal; CNS tumors, traumatic brain injury, and drug overdose are not encountered in our study [11].

In our study of 100 patients of SE, the case fatality rate 14% (n=14), among the expired patients, hypoxemic encephalopathy accounted for the predominant etiological factor associated with the mortality 35.71% followed by CVA (35.75%) CNS infection (14.29%), metabolic disturbance 7.1%, and ACDW 7.14%. A similar study of Verma *et al*., (2018) showed mortality rate 16% (n=26), in which CVA (10 cases), CNS infection (11 cases), metabolic disturbance (2 cases), and AEDs non-compliance (1 cases). The numbers of episodes did not have a significant difference in terms of mortality [10].

In our study, 14 patients expired and among expired patients, 57% were super refractory to the treatment, 35.71 were in refractory SE, and 7.14% were in established SE. Similar study of Misra *et al*., (2017) in which SRSE occurs in 13% patients with SE and 43% of them died [12].

In our study, predictors of mortality are age, duration of seizure, lack of response to first-line drug, and non-treatable etiology such as CVA and hypoxemic encephalopathy, associated with the high mortality rate. The patients who have controlled in the early stage and with the treatable etiology such as CNS infection and metabolic disturbance have less mortality rate. Similar study of Verma *et al*., (2018) showed predictor of mortality were low GCS (odd ratio [OR]=9.64, 95% CL=2.064–45.02) and lack of response to first-line drug (OR=0.019, 95% confidence interval=0.003–0.11) were associated with significant mortality. Mortality was due to convulsive status epilepticus per SE in eight cases, while, in the remaining, it was due to underlying diseases [10].

CONCLUSION

The study titled "A comparative study of first episode SE and multiple episodes of SE in the emergency department of a tertiary hospital in the Bundelkhand region, central India" was a hospital-based cross-sectional study. Its objective was to compare the distribution of first episode SE with multiple episodes of SE in terms of demographic groups, etiology/risk factors, outcomes, mortality, and prognosis. A total of 100 patients above 18 years of age were included in the study. The following conclusions were drawn from the analysis: SE was found to be more common in males than females, particularly in the age group of 18–30 years. The common etiological factors for SE were anticonvulsant drug withdrawal (33%) and CNS infection (33%), followed by metabolic encephalopathy (17%), cerebrovascular accident (12%), and hypoxemic encephalopathy (5%). About 35% of patients developed refractory SE, with 12 patients (29%) progressing to super-refractory SE. The highest mortality was observed in hanging cases, all of which had their first episode of SE. Cases of CVA also showed higher mortality. Mortality was more pronounced in the 51–60 years age group. No deaths occurred in the initial stages of SE in the multiple episodes group, while higher mortality was recorded in the later stages of the first episode SE group. Factors associated with a higher mortality rate included patient age, lack of response to first-line drugs, longer duration of convulsion, and non-treatable etiology. Treatable etiologies such as CNS infection and anticonvulsant drug withdrawal were found to have better prognosis.

Recommendations

Prompt intervention is recommended in high-risk group patients with SE, after evaluating the etiological factors. Early initiation of AED treatment is advised in cases of CNS infection, as it is a major cause of SE. Patients on AED drugs should not discontinue treatment without guidance from their treating doctor, especially those at risk of anticonvulsant drug withdrawal.

Limitations

The study design was observational and not a randomized controlled trial, which may have introduced selection bias and affected the results. The study did not include cases of alcohol and other substance withdrawal, CNS tumors, traumatic brain injury, and drug overdoses, which could have led to a low number of cases for subgroup analysis. Some data relied on patient reports, which may be subject to recall bias.

CONFLICTS OF INTEREST

Nil.

SOURCE OF FUNDING

Nil.

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