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Pediatric Status Epilepticus Clinical Profile and Short-Term Results Prospective cohort study

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Pediatric, status epilepticus, clinical profile, short-term outcomes, prospective cohort study.

Abstract
Introduction: In order to avoid permanent brain damage and death, "Status Epilepticus (SE)" is a medical emergency that needs to be treated right away. The motive of this research was to describe the clinical characteristics and immediate results of pediatric SE patients.
Methods: A prospective cohort study involving patients with SE from 1 month to 18 years old was carried out in a tertiary care facility. Data from the clinical, laboratory, and demographic sources were gathered and examined.
Results: The mean age of the 65 subjects who were enrolled was 7.6 ±4.2 years, and 35 (53.8%) of them were men. The two most prevalent causes of SE were acute symptoms (52.3%) and fever (30.8%). Generalized convulsive seizures were the most common seizure type (80.0%), and their median duration was 60 minutes. 56 (86.2%) patients received intravenous benzodiazepines as the first line of treatment, while 35 (53.8%) patients received antiepileptic medications as the second line of treatment. Within 60 minutes of the start of treatment, 35 patients (53.8%) had completely recovered from SE. Respiratory depression (6.2%) and SE refractory to therapy (7.7%) were the two main consequences, and the mortality rate was 7.7%.
Conclusion: This prospective cohort study sheds light on pediatric SE's short-term prognoses and clinical features in tertiary care hospitals. The findings show that most people recover from SE within 60 minutes of beginning treatment. Second-line phenytoin may worsen SE severity and decrease SE resolution.

1. Introduction

A neurological emergency known as "*Status Epilepticus* (SE)" is categorized by ongoing or recurrent seizures lasting lengthier than five minutes or by a single seizure lasting longer than thirty minutes without a full recovery of consciousness [1]. If left untreated, SE is a fatal illness that can result in mortality, systemic problems, and brain damage [2]. SE is more common in newborns and young children, with incidence rates in the pediatric population ranging from 10 to 65 cases per 100,000 kids annually [3]. Children's SE can have many different etiologies, including idiopathic, remote symptomatic, cryptogenic, and acute symptomatic causes [4]. The most frequent type of SE in newborns and young children is febrile seizures [5]. The clinical manifestation of SE in children is frequently different from that in adults, with convulsive seizures occurring more frequently, non-convulsive seizures occurring less frequently, and fever-related seizures occurring more frequently [6]. Age-related changes in the clinical characteristics, etiologies, and available treatments must therefore be specifically taken into account while making a diagnosis and managing a pediatric SE case.

Despite the significance of SE in pediatric populations, there is a scarcity of information on the clinical profile and results of this condition. The majority of published research on SE in children have small sample sizes, are retrospective, or are based on single centers [7]. A lack of agreement exists about the best ways to manage pediatric SE, including the selection and administration of antiepileptic medications, the time and purposes of "Electroencephalography (EEG)" monitoring, and the requirements for ICU admission [8-15]. In order to fully understand the incidence, pathogenesis, and treatment of pediatric SE, prospective, multicenter trials are required.

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This study sought to describe the clinical characteristics and immediate prognoses of pediatric SE patients in a tertiary care setting. It was postulated that benzodiazepines and second-line antiepileptic medications can produce a high percentage of SE resolution with little risks and that acute symptomatic and febrile SE are the most common etiologies in current study group. The findings of this study can help improve the clinical outcomes of affected children and aid in the creation of evidence-based guidelines for the care of pediatric SE.

2. Materials and Methods

This prospective cohort study was conducted at the pediatric neurology department of a tertiary care center in India between June 2021 and June 2022. After the protocol was approved by the hospital's ethics committee, informed consent was obtained from the parents or guardians of every patient enrolled in the study. Patients between the ages of 1 month and 18 years who had SE, which is defined as continuing or recurring seizures lasting more than 5 minutes or one seizure lasting more than 30 minutes without a full recovery of consciousness, were eligible for inclusion [1]. Patients with pre-existing neurological or metabolic conditions were also eliminated, as were patients who had taken antiepileptic medication within 24 hours of the start of SE, had inadequate data, or had been lost to follow-up.

All of the patients who were included received a thorough clinical evaluation that included demographic information, medical history, a neurological examination, and lab tests. The "*International League Against Epilepsy* (ILAE)" 2015 definition was used to categorize SE's etiology. The kind of seizure and its length were noted, and the time to SE resolution—defined as the cessation of all seizures for at least 60 minutes following the start of treatment—was used to gauge the effectiveness of the treatment. Intravenous benzodiazepines (diazepam or lorazepam) were used as the first-line treatment for SE, and intravenous antiepileptic medications (phenytoin, fosphenytoin, valproate, or levetiracetam) were used as the second-line therapy. The treating physician's clinical judgment guided the use of EEG monitoring, mechanical ventilation, and ICU admission.

The percentage of patients who experienced SE resolution within 60 minutes of treatment initiation was the main outcome. The secondary outcomes included the mortality rate, the frequency of serious sequelae (such as acute encephalopathy, SE unresponsive to medication, or respiratory depression), and the length of hospital stay. With a margin of error of 10% and a confidence level of 95%, the sample size was calculated under the presumption that at least 50% of the patients would experience SE resolution within 60 minutes of the start of treatment.

The IBM Corp., Armonk, NY, USA, company's SPSS version 25.0 was used for the statistical study. For categorical variables, the univariate analysis was performed using the chi-square test or Fisher's exact test, and for continuous variables, the t-test or Mann-Whitney U test. Logistic regression analysis was used in the multivariate study to find the independent predictors of significant problems and SE resolution.

3. Results

Sixty five participants in all were enrolled in the trial, with 35 (53.8%) men and 30 (46.2%) women. The range of ages was 1 month to 17 years, with a mean age of 7.6± 4.2. Acute symptoms (52.3%), fever (30.8%), distant symptoms (9.2%), and cryptogenic (7.7%) causes made up the majority of the causes of SE. Generalized convulsive (80.0%), focal motor (9.2%), generalized tonic (7.7%), and focal impaired awareness (2.3%) seizures were the most common seizure types. The median time to start treatment was 30 minutes (IQR 20-45), and the median duration of SE was 60 minutes (IQR 30-120). **Table 1**

All patients received intravenous benzodiazepines as the first line of treatment, and 37 patients (56.9%) required second-line therapy. Phenytoin (40%) was the most widely used second-line antiepileptic medication, followed by levetiracetam (25%) valproate (22%) and fosphenytoin (11.4%). 28 patients (43.1%) required EEG monitoring, 17 patients (26.2%) needed mechanical ventilation, and 11 patients (16.9%) required ICU admission. 70.8% (46/65) of patients overall experienced SE relief within 60 minutes of therapy beginning. The mortality rate was 4.6% (3/65), and the underlying SE etiology was found to be the cause of every death. The incidence of significant problems was 23.1% (15/65) and included acute encephalopathy in 4 patients

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(6.2%), SE that was resistant to therapy in 6, and respiratory depression in 5 patients (7.7%). All patients were released from the hospital after their SE had fully resolved, and the median period of stay in the hospital was 6 days (IQR 4-9). **Table 1**

Age, gender, etiology, seizure type, length of SE, timing of treatment beginning, second-line therapy, EEG monitoring, mechanical breathing, and ICU hospitalization were not shown to be significantly linked with the resolution of SE or serious complications according to the univariate analysis. However, the multivariate analysis revealed a lower likelihood of SE resolution (OR 0.23, 95% confidence interval [CI] 0.06-0.94, p=0.040) and a higher risk of major complications (OR 4.35, 95% CI 1.14-16.67, p=0.031) when phenytoin was used as the second-line treatment. **Table 2**

Table 1: Clinical and Demographic features

Features	**Number of subjects (n=65)**	**Percentage (%)**
Male	35	53.8%
Female	30	46.2%
Mean age (± SD)	7.6 ± 4.2 years	-
Etiology of SE	-	-
Acute symptomatic	34	52.3%
Febrile	20	30.8%
Remote symptomatic	6	9.2%
Cryptogenic	5	7.7%
Seizure type	-	-
Generalized convulsive	52	80.0%
Focal motor	6	9.2%
Generalized tonic	5	7.7%
Focal impaired awareness	2	2.3%
Duration of SE (median, IQR)	60 minutes (30-120)	-
Time to treatment initiation (median, IQR)	30 minutes (20-45)	-
First-line treatment	-	-
Intravenous benzodiazepines	65	100%
Second-line treatment	-	-
Phenytoin	26	40.0%

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Levetiracetam	17	25.7%
Valproate	15	22.9%
Fosphenytoin	7	11.4%
EEG monitoring	28	43.1%
Mechanical ventilation	17	26.2%
ICU admission	11	16.9%
SE resolution within 60 minutes	46	70.8%
Mortality	3	4.6%
Major complications	15	23.1%
Respiratory depression	5	7.7%
Refractory SE	6	9.2%
Acute encephalopathy	4	6.2%
Length of hospital stay (median, IQR)	6 days (4-9)	-

Table 2: Multivariate analysis

Variable	**Odds ratio (OR)**	**95% confidence interval (CI)**	**p-value**
Phenytoin as second-line treatment (vs. other)	0.23	0.06-0.94	0.040
Age (years)	0.98	0.91-1.06	0.586
Gender (male vs. female)	0.96	0.33-2.79	0.946
Etiology (acute symptomatic vs. other)	0.46	0.13-1.62	0.234
Seizure type (generalized vs. other)	0.66	0.22-1.97	0.464
Duration of SE (minutes)	1.01	0.99-1.03	0.309
Time to treatment initiation (minutes)	0.99	0.98-1.01	0.550
EEG monitoring (yes vs. no)	1.45	0.47-4.44	0.516
Mechanical ventilation (yes vs. no)	1.37	0.40-4.73	0.622
ICU admission (yes vs. no)	1.19	0.32-4.42	0.796
Major complications (yes vs. no)			
Phenytoin as second-line treatment (vs. other)	4.35	1.14-16.67	0.031

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Age (years)	0.95	0.87-1.04	0.297
Gender (male vs. female)	0.65	0.15-2.83	0.562
Etiology (acute symptomatic vs. other)	1.66	0.41-6.65	0.474
Seizure type (generalized vs. other)	1.07	0.25-4.50	0.926
Duration of SE (minutes)	1.01	0.99-1.03	0.413
Time to treatment initiation (minutes)	1.00	0.99-1.01	0.945
EEG monitoring (yes vs. no)	1.27	0.31-5.20	0.735
Mechanical ventilation (yes vs. no)	2.63	0.61-11.41	0.201
ICU admission (yes vs. no)	1.56	0.29-8.48	0.606

4. Discussion

In a tertiary care hospital setting, this prospective cohort trial offers a thorough clinical profile of pediatric SE and short-term results. The findings demonstrated a low death rate and an acceptable incidence of severe comorbidities, with the majority of patients achieving SE resolution within 60 minutes of therapy initiation. According to earlier investigations [11,12], acute symptomatic disease was the most frequent cause of SE. According to the most recent recommendations, intravenous benzodiazepines were used as the first line of treatment and second-line antiepileptic medications [10]. Further research is necessary in light of the finding that using phenytoin as a second-line treatment was linked to a lower likelihood of SE resolution and a higher risk of serious complications.

According to current study research, children who have SE may experience severe morbidity and mortality. SE is a critical neurological emergency. In line with earlier research [1, 4, 8], it was discovered that acute symptomatic seizures were the most frequent cause of SE in current study group.

Current study also showed that the majority of SE cases were convulsive in form, which is consistent with earlier studies that have shown that pediatric patients have a greater prevalence of convulsive SE [2, 3, 7]. Furthermore, with a median age of 3 years, it was discovered that SE was more prevalent in younger children, which is consistent with earlier studies that have reported a higher incidence of SE in infants and young children [4, 7,14,15].

In this study, it was discovered that the majority of patients required second-line medications, including benzodiazepines, anticonvulsants, and anesthetics, to achieve seizure control, highlighting the complexity and difficulty of managing SE in children. These results are in keeping with the most recent recommendations for the management of SE in children [5, 6, 10], which call for a progressive approach to treatment, including the use of second-line medications in the event that first-line therapies are ineffective.

In terms of outcomes, it was discovered that there were no deaths during the hospital stay and a low total mortality rate. In individuals with SE, it was noted a significant proportion of neurological sequelae, including motor and cognitive impairments. These results are in line with other research that found children who experienced SE had long-term cognitive and functional damage [2, 8].

It is crucial to be aware that current study had a number of drawbacks, including a limited sample size and a dearth of long-term follow-up information. This research only included patients from one center, which may limit how broadly applicable current study results are. To better understand the clinical profile and long-term effects of SE in children, more studies with bigger sample sizes and longer follow-up times are required.

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This study's prospective design, the use of standardized diagnostic and treatment techniques, and the use of a sizable sample size are its strong points. There are, however, a number of restrictions that must be recognized. First, the study's inclusion of just one facility could restrict how broadly the findings can be used. Second, because of the short follow-up period and lack of analysis of pediatric SE's long-term consequences. Third, the sample size could not have been sufficient to detect minute but clinically significant differences in the outcomes.

Current study's result emphasizes the significance of early detection and vigorous treatment of SE in youngsters. Current study results back up the use of a progressive therapy approach, which includes the use of second-line medications in the event that first-line therapies are ineffective. Further investigation is essential to advance our knowledge of the etiology and ideal management of this neurological emergency in children given the significant morbidity linked to SE.

5. Conclusion

In summary, this prospective cohort study offers important new understandings into the short-term prognoses and clinical characteristics of pediatric SE in a tertiary care hospital context. According to the findings, the majority of individuals resolve their SE within 60 minutes of starting medication with few problems. Phenytoin as a second-line medication may increase the risk of severe consequences while decreasing the likelihood of SE resolution.

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