International Journal of Contemporary Pediatrics
Jeergal NA et al. Int J Contemp Pediatr. 2024 Apr;11(4):444-448
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20240734

Original Research Article

Clinical profile, etiological factors and outcome of children with status epilepticus admitted in tertiary hospital: a prospective study

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Received: 23 February 2024
Accepted: 15 March 2024

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ABSTRACT

Background: Status epilepticus (SE) is a medical emergency, and its neurological outcome is a concern to every pediatrician in developing countries. The incidence of convulsive SE in children is approximately 10–27/100,000 per year, with the highest incidence in children less than one year of age. Approximately 30% of patients presenting with status epilepticus are having their first seizure. The objective of the study is to evaluate the clinical and etiological pattern of SE and its outcome in children admitted to PICU.
Methods: This was a prospective study conducted among 50 patients aged 1 month to 12 years presenting with status epilepticus. The study was conducted over a period of one year from April 2022 to April 2023.
Results: A majority of the patients were in the age group of 1-5 years (64%) and higher incidence of male children was observed (74%). Generalized tonic clonic seizure (GTCS) was predominant in 76% of the children and seizure duration was 10-20 minutes in 44% of the children. The most common etiologies were Meningoencephalitis (44%) and febrile seizures (20%). Nearly 70% of the children showed complete recovery with no neurological symptoms and 5 (10%) children died.
Conclusions: Status epilepticus is a life-threatening emergency and timely management is essential to prevent morbidity and mortality. CNS infection is a major etiology and majority of the children showed good response with AED treatment.

Keywords: Status epilepticus, CNS infection, Antiepileptic drugs, Generalized tonic clonic seizure, Mortality

INTRODUCTION

Status epilepticus (SE) is the common neurological manifestation encountered in children and requires immediate emergency care. SE is defined as the continuous or recurrent seizure activity with unable to regain the consciousness, which lasts for more than 5 minutes. Albeit, there is a substantial improvement in the treatment strategies, still SE is associated with significant morbidity and mortality.[1] The estimated annual incidence of SE is 20 per 100,000 children and the neonatal age is the most common risk factor for the development of SE.[2] Despite treatment advances, there is marked increase in the morbidity (28-34%) and mortality (7-22%) during the last decade.[3] Age is an important etiological factor for SE and pattern of disease is significantly different between young and older children. Clinically SE is classified as convulsive which includes (tonic clonic, clonic, tonic or myoclonic and non-convulsive) which encompasses (absence, simple partial, complex partial) seizures respectively.[4] Among the SE patients, around 30% experience the first episode of seizure. SE in highly prevalent in children aged <5 years and with an incidence rate of >100 per 100,000 children. Among the SE children the most common form of etiology is convulsive SE (CSE) which is present 90% of the children. The estimated CSE annual incidence is around 10-73 /100, 00 children and the incidence is higher in children <2 years of age (135-156/100,000 children) respectively.[5] In uncontrolled SE, it leads to various life threatening complications which includes cardiac failure, metabolic alterations, loss of

autonomic functions, pulmonary manifestations and complete neurological damage.[6]

Prolonged activity of SE has negative impact on brain and thus initiation of early treatment is recommended to avert the seizures and its related complications. The SE prognosis in children is influenced by various clinical factors such as seizure duration, type of seizure, etiological causes, children age and the presence of comorbidities.[7] Identification children with higher risk is an emerging area and requires quality care to prevent any neurological complications.[8] Regarding, pharmacotherapy, benzodiazepines (BZD) are the first line therapy to mitigate seizures within 5-10 minutes are the first-line drugs to control seizure within 5-10 minutes of convulsion.[9] If the seizure is not controlled second line drugs such as phenytoin, Levetiracetam and Valproate must be given within 10-20 minutes of seizure.[10] For uncontrollable seizures, third line agents such as anesthetic medications It should be followed by second-line drugs in the next 10-20 minutes. If the convulsion does not get control, third-line drugs such as anesthetic medicines (midazolam, barbiturates) must be administered as continuous infusion within 30-60 minutes.[11] In this backdrop the present study was conducted to evaluate the clinical profile, etiology and outcome of children with status epilectus admitted to pediatric intensive care unit.

METHODS

This was a prospective study conducted among the children aged 1month to 12 years presenting with SE. The study was conducted at Al-Ameen Medical College and Hospital, Vijayapura, Karnataka, India for a period of one year from April 2022 to April 2023 after getting approval from institutional ethical committee.

Inclusion criteria

Children aged 1 month to 12 years who at presentation or during PICU stay had status epilepticus –defined as continuous seizure activity or recurrent seizure activity without consciousness lasting for >5 min.

Exclusion criteria

Children with neonatal seizures and patients in whom the information regarding seizure activity was incomplete or unknown were excluded from the study.

Based on the purposive sampling method, 50 children were included in the study and informed consent was obtained from the parents. Detailed clinical history was collected from the parents/guardians with relevance to the case. Special importance was given to the type of seizure, associated clinical symptoms, birth and perinatal history, family history of seizures, developmental history, vaccination history, history of trauma and similar episodes in the past. Detailed general and systemic examination was done with special emphasis to neurological examination.

After initial management investigations sent were blood glucose, blood gas analysis haematological, biochemical and microbiological study of blood *viz.* urine and cerebrospinal fluid (CSF) where needed, brain imaging *viz.* magnetic resonance imaging (MRI) brain, computed tomography (CT) scan, and electroencephalogram (EEG).

Seizures was treated according to the standard guidelines.[12] Detailed treatment, response, and outcome were also noted.

Data analysis

The data were analysed using statistical package for the social sciences (SPSS) v 23. Quantitative variables were represented as mean and SD and categorical variables as frequency and percentage. Interdependent student t test was used for the continuous variables and Chi-square test for the categorical variables.

RESULTS

In this study 50 children meeting the inclusion criteria were recruited for the study. The demographics and clinical characteristic of the children was shown in Table 1.

Male preponderance was observed with 37 (74%) were males and 13 (26%) were females respectively. The mean age of the children was 4.12±0.87 years. Regarding age wise distribution majority of the children were in the age groups 1-5 years (32, 64%), 6-12 years (15, 30%) and <1 year (3, 6%) respectively. Regarding seizure type majority of children had generalized tonic clonic seizure (GTCS) (38, 76%) and focal seizure in 12 (34%). Majority of the children, 22 (44%) had seizure 10-20 mins followed by <10 mins in 17 (34%) of children, 21-30 in 7 (14%) and >30 mins in 4 (8%) children respectively. Family history of seizure was present in 11 (22%) children.

Distribution of clinical symptoms and clinical signs was shown in Table 2. Regarding clinical symptoms, 45 (90%) had fever, 39 (78%) had altered sensorium respectively. The most common clinical signs was low Glasgow coma scale (GCS) in 25 (50%) children, papilledema in 10 (20%) and meningeal signs in 12 (24%) of the children respectively.

The biochemical profile among the SE children was shown Table 3. Anemia was present in 28 (56%) of children. Increased CRP level was present in 32 (64%) of the children, deranged liver function test (LFT) in 7 (14%), deranged renal function test in 4 (8%) and hyponatremia in 13 (26%) of the children respectively.

The distribution of children according to etiology was shown in Table 4. In this study the major etiology was meningoencephalitis in 44% of children followed by febrile seizures in 20% and epilepsy in 14% of the children respectively.

Table 1: Demographic and clinical features of the study participants.

Variables	Frequency (%)
Age distribution (years)	
<1	3 (6)
1-5	32 (64)
6-12	15 (30)
Gender	
Male	37 (74)
Female	13 (26)
Seizure type	
GTCS	38 (76)
Focal	12 (34)
Seizure duration (minutes)	
<10	17 (34)
10-20	22 (44)
21-30	7 (14)
>30	4 (8)
Family history of seizure	
Present	11 (22)
Absent	39 (78)

Table 2: Clinical symptoms and signs among the status epilepticus children.

Variables	Frequency (%)
Clinical symptoms	
Fever	45 (90)
Altered sensorium	39 (78)
Lethargy	30 (60)
Irritability	25 (50)
Vomiting	20 (40)
Loose stools	13 (26)
Headache	5 (10)
Clinical signs	
Low GCS	25 (50)
Papilledema	10 (20)
Meningeal signs	7 (14)
Hepatomegaly	3 (6)
Splenomegaly	2 (4)
Pallor	2(4)
Icterus	1 (2)

The EEG and neuroimaging findings of the children were as follows. Out of 50 children, 35 underwent EEG and 18 (51.4%) had GTCS and 10 had focal (28.6%) and 7 has normal finding (20%). Out of 50 children, 32 underwent neuroimaging modality and the major finding was cerebral edema in 12 (37.5%) children, neurocysticercosis (3, 9.4%), acute disseminated encephalomyelitis (3, 9.4%), dysembryoplastic neuro-epithelial tumour (3, 9.4%), exudates at basal ganglia (2, 6.2%), infarcts (2, 6.2%) and normal in 7 (21.9%) respectively.

The patterns of antiepileptic drugs (AED) were shown in Table 5. In this study majority of the children were treated with two AED in 24 (48%), followed by 1 AED in 16 (32%) of children. Midazolam infusion was given in 3 (6%) children.

Table 3: Biochemical profiles among the status epilepticus children.

Biochemical parameter	Frequency (%)
Anemia	28 (56)
Leukocytosis	22 (44)
Thrombocytopenia	15 (30)
Increased ESR	9 (18)
Increased CRP	32 (64)
Deranged LFT	7 (14)
Deranged RFT	4 (8)
Hyponatremia	13 (26)
Hypokalemia	5 (10)

Table 4: Distribution of etiology among the status epilepticus children.

Etiology	Frequency (%)
Meningoencephalitis	22 (44)
Febrile seizures	10 (20)
Epilepsy	7 (14)
Intra cranial hemorrhage	3 (6)
Head trauma	3 (6)
TB meningitis	2 (4)
Malaria	2 (4)
Hepatic encephalopathy	1 (2)

Table 5: Patterns of antiepileptic drugs to status epilepticus patients.

Response of AED	Frequency (%)
1 AED	16 (32)
2 AED	24 (48)
≥3 AED	7 (14)
Midazolam infusions	3 (6)

The final outcome of status epilepticus children was shown in Table 6. Among the 50 children, 35 (70%) recovered without any neurological manifestations, 7 (14%) recovered with neurological manifestation, 5 (10%) had died and 3 (6%) discharged against medical advice.

Table 6: Final outcome among the status epilepticus children.

Final outcome	Frequency (%)
Recovered without any neurological manifestations	35 (70)
Recovered with neurological sequel	7 (14)
Mortality	5 (10)
Discharged against medical advice	3 (6)

DISCUSSION

SE in children is an emergency situation and requires prompt treatment to prevent the morbidity and mortality. In the present study mean age of the children was of the children was 4.12±0.87 years and majority of the children in the age groups 1-5 years encompassing 64%. Similar to our report in a study done by Maytal et al the mean age was 5 years and in Dasgupta et al study the mean age of SE children was 3.81±2.49 years.[13,14] The first episode of seizures is due to the immature mechanism of seizure control in younger children which leads to neuronal function disruption and development of status epilepticus.[6]

In our study, male preponderance was observed which includes 74% of children. Likewise, in a study done by Das et al 64.9% of children were males.[15] Wide range of studies shows that male children are more vulnerable to the development of SE as compared to females.[16]

In the present study, GTCS was the major seizure type observed in 76% of the children. Likewise, in Dasgupta et al study GTCS was the predominant seizure type in SE children accounting for 74% followed by focal seizures in 18% of children.[14] The seizure duration was 10-20 mins in majority of the children (44%). Similar to our report, in Dasgupta et al study 40% of the children had seizure duration 10-19 mins.[14] Previous report indicates that prolonged seizure more than 10 minutes can cause neuronal death.[17] Further, longer convulsion state before the intervention of AEDs is difficult to manage and it can lead to permanent brain damage in children.[18]

In our study, the major clinical symptoms of SE were fever, altered sensorium and lethargy. Likewise in a study done by Prashanthi et al the major symptoms in SE children were fever, headache, vomiting, and altered sensorium.[19] In children with seizures, fever is an important symptom and particularly in developing countries like India, where the CNS related infection due to malaria, meningitis is more common. Febrile seizure is a widely encountered condition and it is generally associated with fever in children aged between 6 months to 5 years. Fever in association with lethargy and altered sensorium reflects the meningitis and meningoencephalitis.

Laboratory measurement of biochemical parameters is a routine diagnostic modality in patients admitted with status epilectus. In our study, 56% had anemia, leukocytosis (44%) thrombocytopenia (30%), increased CRP (64%) and hyponatremia (26%) respectively. Previous study done by Zareifar et al showed significant association between iron status and febrile seizures in children with mean hemoglobin level of 10.8 g/dl and decreased ferritin level (20 ng/dl) in 56.6% of children.[20] Muzafar et al reported that in children with acute symptomatic seizures 7.7% of cases had hyponatremia.[21]

In our study, the major etiology for the development of status epilectus is meningoencephalitis in 44% and febrile seizures in 20% of the children respectively. The etiological cause of SE in developing countries is different when compared to developed countries. In developing countries CNS infections accounted for 28–67% of etiological spectrum and this higher in the paediatric age group.[22]

Regarding anti-epileptic drug therapy (AED) most of the children were treated with two AED in 48% of cases and 3 children with refractory SE were treated with midazolam infusions. The benzodiazepines (BZD) including diazepam, lorazepam, and midazolam are the preferred primary agents for the management of SE in children. BZD elicits rapid action with good potency, in addition they inhibit sustained repetitive neuronal firing similar to carbamazepine and phenytoin.[23] Phenytoin rapidly control the seizures with prolonged effects and it is usually administered when initial treatment with BZD fails in controlling the seizures.[23] The recent status epilepticus guideline considers midazolam as a refractory treatment option (class IIA, level B evidence).[24]

Regarding the final outcome in the present study, majority of the children (70%) recovered without any neurological manifestation and 5 (10%) died. Similarly, in a study done by Amonkar et al the mortality rate among the SE children was 8.9%.[25] However, in a study done by Das et al the overall mortality was higher 29.78%, as compared to the present study.[15]

CONCLUSION

SE is a commonly encountered neurological emergency in children. Younger age children are more susceptible to SE. In our study SE operational definition of 5 minutes is useful in the early treatment. CNS infection is the major etiology identified and majority of the children showed good response and recovered without any neurological abnormalities.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Jeergal NA, Lahari DSS, Thobbi AN. Clinical profile, etiological factors and outcome of children with status epilepticus admitted in tertiary hospital: a prospective study. Int J Contemp Pediatr 2024;11:444-8.