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Outcome of Convulsive Status Epilepticus in Children: A Cross Sectional Study

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Abstract

Background: Convulsive status epilepticus (CSE) is the most common neurological emergency in children and often associated with poor outcome. A prospective cross sectional study was done on 193 north Indian children with CSE, aged one month to 15 years presented in pediatric emergency with primary objective was to record the time taken to control seizure and secondary objective was to find out etiology, laboratory changes, neuroimaging findings. *Methods:* Children (1 month to 180 months) were recruited in study as per protocol. Seizure was managed as per hospital and Indian Academy of paediatrics protocol. Data was entered in predesigned proforma and analyzed for outcomes. *Results:* The mean age of children was 56.7±47.1 months, where as male: female ratio was 2.3:1. Seventy four (38.3%) children belonged to the age group 61-180 months, followed by 13-60 months (34.7%) and 1-12 months (26.9%). Fever; 87 (45.1%) was most common associated symptom followed by vomiting (29.5%), headache (4.7%), and diarrhoea (3.1%). Seizure was clinically controlled (Group-I) in 149 (77.2%), partially controlled (Group-II) in 25 (12.95%), and 19 (9.84%) patients had died (Group-III). The mean duration of CSE at presentation was significantly higher in Group-II and group-III. The mean time taken to control seizure in group-I was 49.7±54.1 minutes, group-II; 135.8±77.7 minutes and in group-III; 118.21±97.5 minutes respectively. The most common CT-scan finding was meningoencephalitis 43 (22.3%), followed by tubercular meningitis 34 (17.6%), bacterial meningitis 33 (17.1%), neurocysticercosis 19 (9.8%) and cerebral infarction (5.2%). CSE was controlled with lorazepam and phenytoin in most of children. *Conclusion:* The duration of CSE at presentation, number of seizure episodes, time taken to control status epilepticus and etiology were the important factors for outcome of status epilepticus.

Keywords: Convulsive Status Epilepticus (CSE); Generalized Tonic Clonic Seizure; Partial Seizure; Prolonged Febrile Seizure; Lorazepam; Phenytoin; Midazolam; Sodium Valproate.

Introduction

Convulsive status epilepticus (CSE) is a common neurological emergency in children, and if continued for long duration may leads to death or long term neurological sequelae [1,2]. CSE requires early expedient management to decrease morbidity and mortality. The incidence of convulsive status epilepticus (CSE) in children range from 10 to 38/100000/year [3,4]. Incidence of status epilepticus in an exclusively pediatric population based study in North London was 18-20/100000/ year. The incidence was highest among children below 1 year of age [5].

In patients younger than 16 years, the most common cause of status epilepticus was fever and/or infection (36%), whereas in adults, this accounted for only 5%. Cerebrovascular disease accounts approximately 3% of status epilepticus in children as against 25% in adults [6]. Shinnar et al. reported more than 80% of status epilepticus in children younger than 2 years and were febrile or acute symptomatic in origin [7]. In contrast, cryptogenic and remote symptomatic causes were more common in older children.

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CSE is associated with various biochemical and hematological changes in blood and include hyperglycemia or hypoglycemia and acidosis (both metabolic and respiratory). Acidosis usually resolves with termination of seizure. Aminoff et al., reported metabolic acidosis and mild leukocytosis in blood and cerebrospinal fluid in some patients with status epilepticus [8].

Neuroimaging has significant contribution in the diagnosis and treatment of patients with CSE. It is even more important for those patients who have medically intractable seizures [9]. MRI is the preferred imaging technique but CT scans has a number of advantages such as lower cost, scan speed, ready accessibility, and easy use, which provide a relatively reliable imaging modality for most patients [10]. It can accurately detect hemorrhage, infarctions, gross malformations, ventricular system pathologies, and lesions with underlying calcification. The sensitivity of CT in patients with epilepsy is not higher than 30% in unselected populations [11].

Prognosis of CSE has strong correlation with the underlying disease. It is poor, when CSE had presented with coma and caused by anoxia/hypoxia. Mortality rates related to CSE have decreased over the last 60 years, probably in relation to faster diagnosis and more aggressive treatment. The probability of death is closely correlated with age [12].

The present prospective cross-sectional study was done with primary objectives to record the time taken to control seizure and secondary objective was to find out etiology, laboratory changes, neuroimaging findings.

Methods

This study was carried out in department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University between September 2011 to April 2014 on 193 patients presented and admitted with convulsive status epilepticus (CSE). Ethics committee of the institute approved the study protocol.

Convulsive status epilepticus was defined, for the purpose of the study, as a single clinical seizure lasting more than 30 minutes or repeated seizures over a period of more than 30 minutes without intervening recovery of consciousness, but for practical standpoint, treatment was considered by 5–10 minutes, or when at least two seizures have occurred back-to-back without an intervening return to consciousness.

Inclusion Criteria

The study population included all infants and children aged above 1 month to 15 years admitted in pediatric emergency, ward or pediatric intensive care unit with CSE. The enrolled patients were treated as per recommended protocol of Indian Academy of Paediatrics.

Exclusion Criteria

Patients with hepatic or uremic encephalopathy with convulsive status epilepticus were excluded from study.

Complete blood count, blood glucose, serum calcium, arterial blood gas analysis, cerebrospinal fluid study, renal function tests and imaging (CT-scan/MRI-scan or both) of cranium were done in all patients. Tandom mass screening (TMS) for metabolic diseases was done as needed to find out etiology. Findings of enrolled patients were recorded in a pretested performa and collected data was analyzed by SPSS version [16].

Results

One hundred ninety three (193) children with CSE, presented to pediatric emergency and admitted in paediatrics ward were taken for this prospective hospital-based observational study. Children were divided in three groups based on control of seizure activity: Group-I: Seizure controlled (149), Group–II: Seizure uncontrolled (25) and Group-III: death (19) patients.

The basic characteristics of enrolled children in the study are mentioned in Table 1. The mean age of the children was 56.71±47.1 months (1 month to 15 years). The maximum number of children belonged to the age group 61-180 months i.e. 74 children (38.3%) followed by 13-60 months (34.7%) and 1-12 months (26.9%). In the present study 69.9% were male, and male to female ratio was 2.3:1.

They were further categorized into three groups: Status of generalized tonic clonic seizure (GTCS), status of partial seizure, and status of febrile seizure. 164 (85%) had status of GTCS, 24 (12.4%) had status of partial seizure, and 5 (2.6%) had status of febrile seizure. Eighty nine (46.1%) children had presented with history of more than 4th seizure episode, 14 (7.3%) had 4th episode, 24 (12.4%); third episode, 29 (15%); second episode, and 37 (19.2%); first episode. Fever (45.1%) was most common associated symptom, followed by fever with vomiting (29.5%), fever with headache (4.7%) and

fever with diarrhoea (3.1%). The family history of seizure was present in 11 (5.7%) children.

The hematological and biochemical changes in children with status epilepticus are mentioned in Table 2. Of 193 children, 6 children had died before their CT-scan, 72 (37.3) had normal study. The most common CT-scan finding was meningoencephalitis 35 (18.1%), followed by tubercular meningitis with hydrocephalus; 27 (13.9%), neurocysticercosis 19 (9.8%), cerebral infraction 10 (5.2%), and hypoxic ischemic 6 (3.1%). Other less common findings are mentioned in Table 3.

Table 1: Basic characteristics of children with Status epilepticus

	Group-I (n=149) (Mean±S.D.)	**group-II (n=25) (Mean±S.D.)**	**group-III (n=19) (Mean±S.D.)**	**Total (%) (Mean±S.D.)**
Age (Mean±S.D.)	56.7±47.2	60.6±49.1	51.4±45.1	56.7±47.1
1month-12monthS	41(78.8)	7(13.5)	4(7.7)	52(26.9)
13months-60months	51(34.2)	7(10.4)	9(13.4)	67(34.7)
>60 months	57(77)	11(14.9)	6(8.1)	74(38.3)
Sex: Male	104(77)	18(13.3)	13(9.6)	135(69.9)
Types of S.E.				
S.E of GTCS	131(79.9)	16(9.8)	17(10.4)	164(85)
Partial S.E	13(54.2)	9(37.5)	2(8.3)	24(12.4)
Febrile SE	5(3.4)	0(0.0)	0(0.0)	5(2.6)
Episode of S.E				
First episode	34(22.8)	2(8)	1(5.3)	37(19.2)
Second episode	24(16.1)	2(8)	3(15.8)	29(15)
3rd episode	22(14.8)	1(4)	1(5.3)	24(12.4)
4th episode	10(6.7)	2(8)	2(10.5)	14(7.3)
>4th episode	59(39.6)	18(72)	12(63.2)	89(46.1)
Associated symptoms				
Fever	72(48.3)	6(24)	9(47.4)	87(45.1)
Fever+vomiting	41(27.5)	8(32)	8(42.1)	57(29.5)
Fever+headache	6(4)	2(8)	1(5.3)	9(4.7)
Fever+vomiting+headache	7(4.7)	0(0.0)	1(5.3)	8(4.1)
Fever+vomiting+diarrhea	3(2)	0(0.0)	0(0.0)	3(1.6)
None	17(11.4)	5(20)	0(0.0)	22(11.4)
Family history of seizure	8(5.6)	2(8)	1(5.3)	11(5.7)

Table 2: Laboratory findings in children with status epilepticus (n=193).

	Group-I (n=149) (mean±S.D.)	group-II (n=25) (mean±S.D.)	group-III (n=18) (mean±S.D.)	p-value		
				I vs. II	I vs. III	II vs. III
Hemoglobin(gm/dL)	10.5±2.03	10.7±2.2	10.5±2.5	0.708	0.988	0.824
TLC(cells/mm3)	13884.6± 8194.1	15126.2± 13113.5	18405.6±6996.4	0.526	0.026	0.340
Neutrophil(%)	65.7±14.1	61.9±13.1	71.1±13.5	0.218	0.121	0.031
Lymphocyte(%)	28.4±13.3	30.2±10.6	21.7±11.5	0.537	0.041	0.017
Platelet count (cells/mm3)	279597.9± 161496.3	257640.2± 139651.9	327116.7± 186581.2	0.523	0.248	0.170
Random blood glucose(mg/dL)	110.6±7.6	93.6±16.5	125.8±54.4	0.184	0.322	0.009
Total calcium (mg/dL)	10.6±7.6	10.4±0.8	9.5±1.7	0.868	0.545	0.036
Ionized Calcium (mmol/L)	1.06±0.19	1.08±0.12	0.96±0.23	0.556	0.050	0.034
pH	7.39±0.08	7.36±0.09	7.37±0.13	0.048	0.342	0.671
Hco3(mmol/L)	22.3±5.4	20.9±5.4	19.7±7.1	0.334	0.109	0.556
BE	-2.01±5.3	-2.9±5.9	-4.2±6.9	0.439	0.114	0.520
Na+(mmol/L)	132.4±7.4	135.6±11.5	130.2±8.1	0.064	0.258	0.095
K+(mmol/L)	4.2±0.8	4.4±0.9	4.1±0.9	0.097	0.822	0.249
Urea(mg/dL)	40.4±36.2	50.8±64.4	53.8±49.5	0.245	0.157	0.870
Creatinine(mg/dL)	0.84±0.5	0.92±0.8	1.2±1.7	0.500	0.034	0.448

Table 4 showed the time period of CSE, time taken to control seizure and duration of hospital stay. Mean time of CSE at presentation to our emergency in Group-I, Group-II and Group-III were 67.18±55.97, 108.8±84.17, and 136.05±96.93 minutes respectively. The mean time taken to control CSE in group-I was 49.7±54.1 minutes, whereas in group-II; 135.8±77.7 and group-III; 118.2±97.5 minutes. The time taken to control CSE is more in group-II, and group-III than group-I and were statistically significant. The mean time of hospital stays in group-I was 10.2±4.1 days, group-II: 13.9±8.1 and group-III: 3.57±5.6 days.

Table 5 showed the number of antiepileptic drug used in CSE. Three children with febrile status got controlled with lorazepam and others required additional antiepileptic. CSE got controlled in majority with lorazepam and phenytoin in Goup-I, whereas others needed either midazolam or valproic acid or both and in combination with propofol infusion. Most of patients in Group-II required multiple antiepileptics including propofol infusion but not achieved complete control of seizure. The duration and number of episodes of CSE, time taken to control and underlying etiology were important contributing factors for outcome of status epilepticus.

Table 3: Findings of CT-scan of brain in children with convulsive status epilepticus (n=193)

	Group-I (n=149)	group-II (n=25)	group-III (n=19)	Total (%) (n=193)
Normal study	61(40.9)	8(32)	3(15.8)	72(37.3)
Meningoencephalitis	29(19.5)	2(8)	4(21.1)	35(18.1)
Tubercular meningitis with hydrocephalus	18(12.1)	6(24)	3(15.8)	27(13.9)
Neurocysticercosis	14(9.4)	4(16)	1(5.3)	19(9.8)
Cerebral infarction	9(6.1)	1(4)	0(0.0)	10(5.2)
Cerebral atrophy	4(2.7)	2(8)	0(0.0)	6(3.1)
Periventricular Leukomalacia	4(2.7)	2(8)	0(0.0)	6(3.1)
Subdural effusion	3(2.01)	0(0.0)	0(0.0)	3(1.6)
Brain abscess	3(2.01)	0(0.0)	1(5.3)	4(2.1)
Intra-cranial hemorrhage	1(0.7)	0(0.0)	1(5.3)	2(1.03)
Hydrocephalus	2(1.3)	0(0.0)	0(0.0)	2(1.03)
Corpus callosum agenesis	1(0.7)	0(0.0)	0(0.0)	1(0.52)
Not done	0(0.0)	0(0.0)	6(31.6)	6(3.1)

Group-I: Seizure controlled, Group-II: Seizure uncontrolled, Group-III: Death.

Table 4: Time period of status epilepticus, time take to control seizure and duration in hospital stay (n=193).

	Group-I (n=149) (mean±S.D.)	group-II (n=25) (mean±S.D.)	group-III (n=18) (mean±S.D.)	p-value I vs II	I vs III	II vs III
Time period of SE(min)	67.2±55.9	108.8±84.2	136.1±96.9	0.002	<0.001	0.325
Time take to control seizure(min)	49.7±54.1	135.8±77.7	118.2±97.5	<0.001	<0.001	0.509
Duration of hospital stay(day)	10.2±4.1	13.9±8.1	3.57±5.6	<0.001	<0.001	<0.001

*min-minutes,*SE-status epilepticus. *Group-I Seizure controlled,* Group-II Seizure uncontrolled,* Group-III Death.

Table 5: Anti-epileptic drug used in study subjects

Anti-epileptic drug	Group-I (n=139)	Group-II (n=25)	Group-III (n=19)	Total (%)
LZP alone	3	0	0	
LZP+ PHT	92	2	4	98
LZP+PHT+MDZ	25	4	3	32
LZP+PHT+MDZ+VPA	23	9	7	39
LZP+PHT+MDZ+VPA+LEV	0	5	1	6
Multiple doses of LZP+PHT+VPA+LEV+propofol	6	5	4	15
I.V calcium gluconate	15	0	4	19
Pyridoxime	1	1	0	2

Group-I: Seizure controlled, Group-II: Seizure uncontrolled, Group-III:Death

LZP-Lorazepam, PHT-Phenytoin sodium, MDZ+Midazolam infusion (2-15 mcg/kg/minute), VPA- Sodium valproate, LEV-Levetiracetam

Discussion

Convulsive status epilepticus is pediatric emergency with good outcome at most of centres. Maximum children belonged to 5-15 years age group. GCTS was the most common presentation. Seizure recurrence of more than four episode was seen in 89 children. This can be attributed to poor drug compliance, choice of antiepileptic, poor follow up. Fever triggered seizure was the most common presentation. Acute symptomatic seizure like menigoencephalitis, tubercular meningitis, bacterial meningitis, necurocysticercosis was the most common etiology in study population. The same finding has been reported in previous studies from developing countries [13-17].

The time taken to control seizure was 49.7±54.1 minutes in group I. whereas this duration was high in group II and Group III, leading to poor outcome and even death. So, aggressive treatment with best supportive care is the need of hour for managing such cases in emergency. Kumar et al. also recorded the similar finding in his group of patients [17].

Intravenous lorazepam and phenytoin were common antiepileptics used for control of seizure in most of patients. Second line atiepiletics used were: valproate, midazolam infusion, propofol infusion. These groups of patients (group II and group III) required supportive care and management in PICU.

Mortality rate was 9.8%, which is comparable to other studies where it ranged from 10.8 to 28% [18,19]. Mortality was found higher in some other studies as high as 30% [17,20]. Low morality rate is attributed to better health facility, proper referral, protocol based management at tertiary care hospital like ours.

Limitations

Our study could further delineate causes for metabolic cases. We could not do neuroimaging with MRI. This might have caused missing of some diagnosis like neurodegenerative disorders, metabolic disorders. Further follow up was not done.

Conclusion

Study highlights important burden of an important medical emergency at a tertiary centre hospital. 5-15 years is the most vulnerable group with GCTS as most common presentation of CSE. Acute symptomatic seizure was the most common group. Seizure were well controlled in most of children with protocol based management and utilization of best supportive care. Intravenous lorazepam and phenytoin were found be most effective drugs in controlling seizure. Had the MRI facility were available easily, we could have diagnosed more metabolic and neurodegenerative cases. Even though, this data had brought important point: etiological diagnosis, duration of status epilepticus, seizure episode, time take to control status epilepticus, anti-epileptics used, and other supportive treatment are the important contributing factors for outcome of status epilepticus.

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