Research Article

Clinical Profile of Patients with Status Epilepticus from Rural Area

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ABSTRACT

Status epilepticus (SE) is a neurological emergency associated with significant morbidity and mortality, if not treated effectively in time. An attempt was made to generate the baseline data regarding the etiologies and clinical profile of SE. A total of 50 patients diagnosed on clinical grounds as SE were analyzed for different parameters. SE was found more common in males and in the age group 21-40 years. Most common etiology was acute symptomatic (68%). Seven patients subjected to lumbar puncture and CSF analysis revealed TB meningitis (three), viral etiology (three) and pyogenic meningitis (one). Of the 50 patients, 44 (88%) responded to the first-line drugs and six (12%) patients required second-line drugs. Five patients (10%) succumbed to death due to massive intra-cerebral bleeding (two), endosulfan poisoning (one), Japanese encephalitis with refractory SE (one) and primary epilepsy with intractable seizures (one). Age, gender and etiology of SE were found to be non-significant. Results indicate that SE can occur in epileptic as well as non-epileptic individuals. Early recognition, good knowledge of various etiologies, prompt initiation of therapy and availability of ventilatory facility as well as ICU care is of paramount importance in the management of SE.

KEY WORDS: clinical profile, rural area, status epilepticus

INTRODUCTION:

Status epilepticus (SE) is a major neurological emergency, which can cause significant morbidity and mortality, if not treated effectively in time. SE is a term used to describe a prolonged and self-sustaining seizure that may have overt, subtle, or almost no behavioural manifestations. It may be regarded as the most extreme form of epilepsy, or as an expression of an acute and often life-threatening brain disorder,such as stroke or encephalitis.

The diagnosis of SE is not difficult when motor signs are overt. However, these motor signs are seen in some of the patients only and other clinical types still pose serious diagnostic challenges such as subtle SE, complex partial SE and Non-convulsive status-epilepticus. Age-specific incidence rates of SE show a U-shaped curve with a bimodal distribution peaking in very young and the elderly.[1]

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Its aetiology varies among the different age groups. The aetio-pathologies may be heterogeneous, which may vary with time, cultural and environmental factors.[2] A periodic analysis is therefore necessary to know the current trends of the aetiology of SE. Due to the dearth of information on aetiologies, response to current treatment guidelines and outcome of SE; this study was conducted to generate the baseline data which pertained to the aetiologies and the clinical profile of SE in our region.

MATERIALS AND METHODS:

The present study was carried out in a tertiary care hospital. The study protocol was approved by ethical committee of Govt. Medical College, Latur. A total of 50 cases admitted in Emergency Ward and ICU, diagnosed on history and clinical grounds as status epilepticus were included in the study, after taking informed and written consent from close relative. The patients with non- convulsive status epilepticus, pseudoseizures and patients below 12 years of age were excluded from the study. The patients with continuous seizure of more than five minutes duration or two or more discrete seizures of five minutes duration between which there was an

incomplete recovery of consciousness were subjected to a detailed recording of their history, neurological examinations and routine investigations which included a haemogram, renal and liver function tests, blood sugar level, arterial blood gas analysis and a metabolic profile assessment including serum calcium and magnesium. Lumbar puncture were done after controlling the seizures. All the patients were treated with intravenous lorazepam and phenytoin according to the protocol- intravenous lorazepam (0.1 mg/kg), followed by the intravenous loading of phenytoin (20 mg/kg) as the first-line drug treatment. If the seizure did not stop within 30 minutes of the starting of the loading dose of phenytoin, the patients were given additional intravenous phenytoin (5 mg/kg). Patients already on valproate therapy were given loading dose of valproate (25-30mg/kg). The second line drugs were given when no response was observed with the above drugs in the first hour. The second line drugs were- an intravenous loading dose of valproate (25-30 mg/kg) (if not given earlier) or phenobarbitone (20 mg/kg) as the loading dose, followed by a maintenance drip (60 mg/min) till the seizures were under control or till one hour, whichever was earlier. If the seizures could still not be controlled after one hour (refractory seizures), thiopentone (10-20 mg/kg) as a loading dose, followed by an infusion (0.5-1.0 mg/kg/hr) was given along with mechanical ventilatory support. In addition, the patients received appropriate treatment for the underlying disease. Those patients who failed to respond to the initial lorazepam and the loading dose of phenytoin were defined as non-responders.

STATISTICAL ANALYSIS:

In univariate analysis, age was analysed as a continuous variable, and the etiology, sex, response to treatment were analysed as categorical variables. The variables studied for statistical significance included age, sex, duration of SE, etiology, response to first line treatment and 30 day mortality.

RESULTS:

In this study, maximum number of cases were found in the age group 21-40 years (n=24) followed by 11-20 years age group (n= 8). The youngest patient was 13 years old and oldest was 75 years old. Mean age was 40 years ±17.2 years. Out of the 50 cases, 23 (46%) were female and 27 (54%) were males. Male to female ratio was found to be 1.2:1.

The etiology was acute symptomatic in 68% patients, remote symptomatic in 6 % patients and cryptogenic in 4 % patients. Eleven patients were identified as established epileptics with poor drug compliance. Amongst these five patients missed the anti-epileptic drug (AED) treatment due to forgetfulness. Four had financial limitations in continuing the drugs and two stopped the medicines due to ignorance. In the acute symptomatic SE patients, CNS infections were the commonest etiology (n=19 patients). Neurocysticercosis (NCC) was found to be the most frequent infection, followed by meningo-encephalitis. In the vascular etiology of symptomatic SE, haemorrhagic stroke was found to be the commonest cause (n=5). One patient had cerebral venous sinus thrombosis. Six patients had SE due to metabolic disorders. Hyperglycaemia (n=1), hyponatraemia (n=1), endosulfan poisoning (organochlorine insecticide) (n=1), organo-phosphorus poisoning (n=1), alcohol withdrawal (n=1) and hypoxic brain injury (n=1) (Table 1).

Out of 50 patients, seven clinically indicated patients who had the clinical signs of meningeal irritation were subjected to lumbar puncture and CSF analysis was done. Out of these seven patients, one had findings which were suggestive of pyogenic meningitis, whereas three had TB meningitis. Three patients had mild lymphocytic pleocytosis with a mild increase in proteins, which was suggestive of viral etiology (Graph 1).

Of the 50 patients with SE, 44 (88%) responded to the first-line drugs and six (12%) patients required second-line drugs. The variables which were studied to predict the response to the first-line drugs included etiology and the duration of SE. The non-responders in acute symptomatic SE were 14.7% as compared to 6.3% in other etiologies. The duration of SE and the delay in starting the treatment in all of the non-responders were more than 24 hours. None of the patients who presented after 48 hours of duration of SE responded to first line AEDs. Thus, the statistically significant predictor of non-responsiveness to 1st line AEDs in patients with SE was duration of status epilepticus. Etiology of SE was found to be non-significant (Table 2).

In the present study, mortality was 10% (n=5). Four out of five deaths were seen in the acute symptomatic group, two of them being cases of massive intra-cerebral bleeding, one patient of endosulfan poisoning and one had Japanese encephalitis with refractory SE. The fifth death fell into the established epilepsy group whose SE was of

Table 1: Etiologies of SE

Etiology	No. of patients	Subgroup	Disease
Acute symptomatic	34	CNS infections (19)	Neurocysticercosis :NCC (10) Meningencephalitis(5) Tuberculoma /TBM(3) Pyogenic meningitis (1)
		Vascular (9)	Haemorrhagic CVA (5) Non- haemorrhagic infarct (3) Cerebral venous sinus thrombosis (1)
		Metabolic (6)	Poisoning (2) Hypoglycaemia (1) Hyperglycaemia (1) Alcohol intoxication (1) Hypoxia (1)
Remote symptomatic	3	--	Old stroke with gliosis (2) Small calcific lesion (1)
Established epilepsy	11	--	--
Cryptogenic	2	--	--

Table 2: Response to AEDs in SE

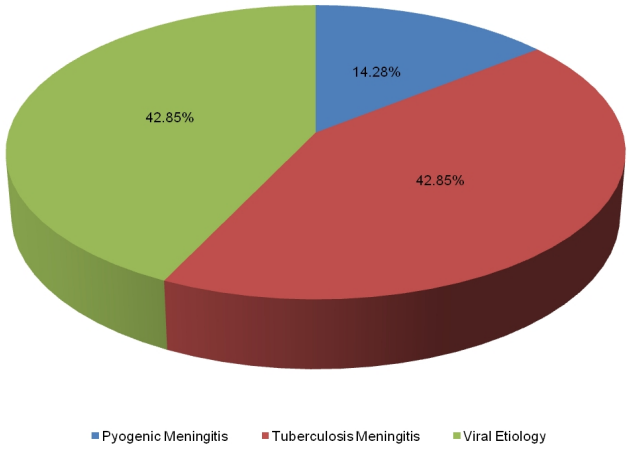
Variable	Responders to first line AED	Non-responders to first line AED	X^2	*p*- value
Etiology				
Acute symptomatic	29 (85.3)	05 (14.7)	0.737	> 0.05 (Not significant)
Other etiologies	15 (93.7)	01 (6.3)		
Duration of SE				
< 24 hours	38 (100)	00	35.795	<0.001 (Highly significant)
25 - 48 hours	06 (75)	02 (25)		
49 - 72 hours	00	04 (100)		

Note - Figures in parenthesis indicate percentages

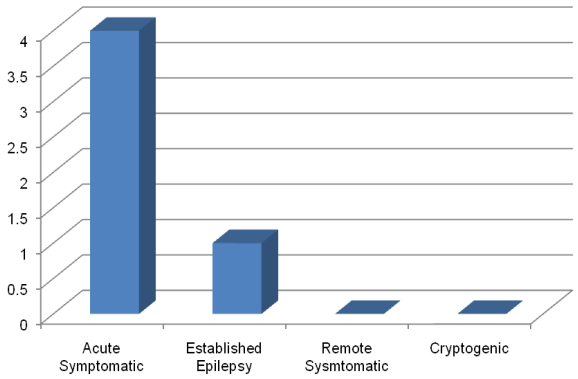
36 hours duration and he had primary epilepsy with intractable seizures, which caused acute renal failure and metabolic acidosis as terminal events (Graph 2).

Amongst the five patients who died, three were between 51-80 years of age. Out of five deaths, four were male and one was female. Five non-responders (83.34%) succumbed to death, whereas there was no mortality amongst the patients who responded to 1st line therapy. Two out of four (50%) patients who presented after 48 hours and three out of eight (37.5%) patients who presented between 25 to 48 hours died, whilst there was no mortality amongst the patients who presented within 24 hours of onset of convulsions. The statistically significant predictors of mortality in patients with SE were duration of status epilepticus and response to 1st line antiepileptic therapy. Age, Gender and etiology of SE were found to be non-significant (Table 3).

Graph 1: CSF Profile in SE.



Graph 2: Mortality



DISCUSSION:

Status epilepticus is a common medical emergency which accounts for 1% – 8% of all the hospital admissions for epilepsy.[3] The duration of SE and its etiology have been the important predictors of its outcome. In the developed countries, pre-hospital treatment protocols are available for the paramedics to reduce the duration of SE and to improve its outcome. However, no such protocols are available in developing countries like India.

The mean age of the patients with SE was 40 ± 17.2 years (13–75 years), 16% were in the younger age group (11-20 years) and 48% fell into the young adult group (21-40 years). These findings are in agreement with earlier studies from the developing countries, wherein a higher proportion of the patients with SE were either children or young adults (20–40 years) [4,5]. However, in the developed countries, a bi-modal peak has been described with a high incidence in infants and in the elderly.[6] The male to female ratio of 1.2:1 in the present study is similar to population based studies reported earlier.[7,8]

The most common etiology found was acute symptomatic (68%), which is comparable to studies from India[4,5] and most of the cases (38%) with SE caused by CNS infections is comparable with the earlier studies from developing countries[5,9], who have also reported similar etiological spectrum. Amongst the CNS infections, NCC was most common infection (10/19; 52.6%). This is also in concordance with the findings of Murthy *et al.* [4], in their study NCC accounted for 42.5% of the SE cases. Meningo-encephalitis accounted for the SE in five patients (26.3%) in our study, which was slightly lower than study from north India by Misra *et al.* [10] that reports one third of the SE cases caused due to meningo-encephalitis of which, nonspecific encephalitis was the commonest cause. We found out that the incidence of SE due to vascular etiology was 18% (9/50), out of which three patients had non haemorrhagic ischaemic stroke, five patients had haemorrhagic stroke and one patient suffered cerebral venous sinus thrombosis. A similar incidence (15%) of SE due to vascular etiology was also reported by Murthy *et al.* [4] A metabolic cause for SE was noted in 6 (12%) patients, which is quite similar to earlier studies.[4,5]

A total of 22% of the SE patients were established epileptics with poor treatment compliance, either due to forgetfulness or ignorance. The increased cost of the AED treatment and the intermittent drug supply were also the factors which were responsible for the noncompliance. A drug default was noted in 7.9% and 20% patients in studies by Kalita *et al.* [5] and Murthy *et al.* [4] respectively.

In the present study, 88% of the SE patients responded to the first-line drug treatment. The response rate was noted to be 50% and 88% in the studies by Kalita *et al*[5] and at Murthy *et al*[4] respectively. The non-responders were more in the acute symptomatic SE (15.4%) group as compared to those in other etiology groups (8.4%). CNS infection or haemorrhagic stroke was the common etiology amongst the non-responders, which was comparable to that in other studies. [5, 9-11] The duration of SE before the treatment in all the non-responders was more than 24 hours, which was similar to the observation made by Murthy *et al.* [4] In their study, duration and acute symptomatic etiologies were the independent predictors of no-response to first-line drugs. In our study only duration of SE was found to be statistically significant.

Table 3: Predictors of death following convulsive status epilepticus.

Variable	No. of cases	No. of deaths	X^2	*p*- value
Age				
11 – 30 years	17 (34)	01 (5.8)	2.98	> 0.05 (Not significant)
31 – 50 years	21 (42)	01 (4.76)		
51 – 80 years	12 (24)	03 (25)		
Gender				
Male	27 (54)	04 (14.8)	1.512	> 0.05 (Not significant)
Female	23 (46)	01 (4.34)		
Response to 1st line of treatment				
Responders	44 (88)	00	22.000	< 0.001 (Highly significant)
Non-responders	06 (12)	05 (83.34)		
Duration of SE				
< 24 hours	38 (76)	00	12.467	< 0.05
25 - 48 hours	08 (16)	03 (37.5)		
49 - 98 hours	04 (8)	02 (50)		
Etiology				
Acute symptomatic	34 (68)	04 (11.8)	0.368	> 0.05 (Not significant)
Other etiologies	16 (32)	01 (6.25)		

Note - Figures in parenthesis indicate percentages

In large hospital-based studies, the mortality varies from 3% -50 %, depending on the study design and the case inclusion criteria.[5,10,11] In our study, the mortality was lower (10%), probably due to the fact that the newer definition of SE was used for the case selection and management; unlike the other studies which were done with older definitions. Different clinical studies showed higher mortality amongst the elderly patients; [5,12,13] however, in our study three out of five deaths were between age 51-75 years, and four out of five deaths had occurred in the acute symptomatic group.

In the present study, five (83.3%) out of six non-responders to the AED treatment died had presented after 24 hours. It has been reported in earlier study that the longer the duration of SE, higher is the mortality and that a high degree of mortality is observed in the cases of refractory SE. [14] The statistically significant predictors of mortality in patients with SE were duration of status epilepticus and response to 1st line antiepileptic therapy. Age, gender and etiology of SE were found to be non-significant. Similar findings have also been noted by Murthy *et al*[4], where longer duration of SE, non-responsiveness to 1st line AEDs, acute symptomatic etiology and female sex were associated with poor outcome.

The access to specialist care is a major limiting factor in the developing countries because of the poor health infrastructure and the connectivity, and the delays in transportation. In the present study, those who presented after 24 hours were amongst the non-responder group and they had poor outcomes.

CONCLUSION:

The results of the present study indicate that status epilepticus can occur in epileptic as well as non-epileptic individuals. Intracranial infections are one of the major causes of status epilepticus in developing countries like India. Duration of status epilepticus and non-responsiveness to 1st line antiepileptic treatment are important predictors of a poor outcome.

It is concluded from the results of present study that early recognition of status epilepticus, good knowledge of various etiologies and prompt initiation of therapy and availability of ventilatory facility as well as ICU care is of paramount importance in the management of SE.

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