Original Article

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Convulsive Status Epilepticus- A Clinical Radiological and Outcome Study from Uttar Pradesh, India

Internal Medicine Section

MALINI KULSHRESTHA, MANMOHAN KRISHNA PANDEY, RAMESH KUMAR PATIAL

ABSTRACT

Context: Status Epilepticus (SE) is a neurological emergency which is associated with heterogeneous aetiopathologies, which vary with time and cultural and environmental factors.

Aim: To analyze the current trends of the clinical profile of SE in our region and to study the predictors of the response of Anti - Epileptic Drugs (AED).

Settings and Design: A prospective, cross sectional study was done on 50 patients who presented with SE with a duration of 5 minutes or more, at a medical college which is located in the state of Uttar Pradesh, India.

Materials and Methods: A detailed history was taken and neurological examinations and baseline investigations were done in all the patients. Cerebrospinal Fluid (CSF) analysis was done wherever it was indicated and CT scan / MRI of the brain was carried out in a majority of the patients. The response to the first line of drugs and the outcome were noted and they were correlated with the aetiology and the duration of SE.

Results: The mean age of the patients who presented with SE was 29.94±1.76 years and their ages ranged from 12 to 75 years. The duration between the onset of SE and the hospital treatment averaged at 23.56 ± 3.16 hours, ranging from 1hr to 90 hrs. Twenty six percent of the patients were presented within ≤ 6 hrs. The atiology was acute symptomatic in 52% of the cases and the commonest cause was Central Nervous System (CNS) infections. 22% cases of SE were established as epileptic cases with a poor drug compliance. CT/MRI was found to be normal in 44.1 % patients when it was done on 49 patients, wherein ring enhancing lesions were the commonest abnormality which was found. CSF analysis was done in seven patients who presented as meningo-encephalitis. 88% patients had responded to the first line drugs. Two deaths out of 3 corresponded to the acute symptomatic group.

Conclusions: SE had a variable prognosis depending on its duration and the aetiology of the seizure.

Key Words: Acute symptomatic SE, Duration of SE, Neurocysticercosis, Status epilepticus

INTRODUCTION

Status Epilepticus (SE) is a neurological emergency which may cause significant morbidity and mortality in the patients, if it is not treated effectively in time. The aetiology varies among the different age groups. Its incidence has a U-shaped curve, which is more common at the extremes of the ages [1]. The aetiopathologies may be heterogeneous, which may vary with time and cultural and environmental factors [1]. A periodic analysis is therefore necessary to know the current trends of the aetiology of SE. Due to the dearth of information on this aspect, 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 conducted at a medical college which is located in the state of Uttar Pradesh, India, after seeking the approval of the ethical committee of the college. All the patients of convulsive status epilepticus were included in the study after taking an informed consent from them. SE was defined as (a) a continuous seizure of more than 5 minutes duration or (b) two or more discrete seizures of five minutes duration between which there was an incomplete recovery of consciousness [2]. These patients were subjected to a detailed recording of their collateral history, neurological examinations and routine investigations which included a haemogram and a metabolic profile assessment which included that of serum calcium and magnesium. CT scan /MRI and lumbar puncture were done whenever they were indicated after controlling the seizures. All the patients were treated with intravenous diazepam and phenytoin according to the protocol- intravenous diazepam (0.15 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). 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) 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.

The aetiology of SE was classified as (1) acute symptomatic SE which occurred in patients with an acute medical or neurological illness; (2) remote symptomatic SE which owed to the conditions, resulting in a static encephalopathy or an antecedent insult such as stroke, head injury scars or calcifications (3) cryptogenic: SE which owed to the conditions which were presumed to be symptomatic,

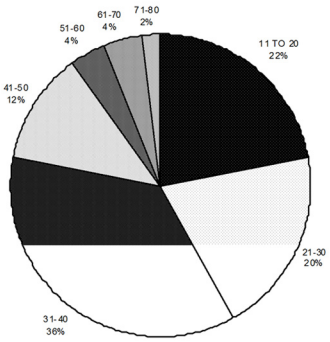
whose cause was unclear, and (4) established epilepsy (with or without non-compliance) [3]. The response to the Anti Epileptic Drug (AED) treatment was defined as the clinical cessation of the epileptic status for at least 12 hours after the completion of the drug administration. Those patients who failed to respond to the initial diazepam and the loading dose of phenytoin were defined as non responders. Variables like the duration of SE and the aetiologies were noted for the group of non responders also.

RESULTS

This study was conducted during October 2011 to March 2012. 50 patients with convulsive SE were admitted to the emergency ward of the medicine department, whose mean age was 29.94 ± 1.76 years and whose ages ranged from 12 to75 years. 11 patients were in the younger age group i.e. 11-20 years, whereas a majority of the patients (28) fell into the young adult group i.e., 21-40 years [Table/Fig-1]. The male to female ratio was found to be equal i.e., 1:1.1. The SE was of the generalized tonic–clonic type from the onset in thirty four patients and and it had a focal onset with secondary generalization in 16 patients.

The mean duration of SE was 23.56 ± 3.16 hours, which ranged from 1 to 90 hours. Out of 13 patients who presented within ≤ 6 hours, only 3 patients were presented within the first hour of the onset of the epileptic status. All the patients with an SE duration of ≤ 6 hours (n=13) were residents of the city where the institute was located. [Table/Fig-1]. The aetiology was acute symptomatic in 52 % patients, it was remote symptomatic in 2 % patients and it was cryptogenic in 24 % patients. 11 of the SE patients were identified as established epileptics with a poor drug compliance. Amongst these, [5] patients missed the AED treatment due to forgetfulness, [4] had financial limitations in continuing the drugs and 2 stopped the medicines due to ignorance. In the acute symptomatic SE patients, CNS infections were the commonest aetiology (n=19 patients). Neurocysticercosis (NCC) was found to be the most frequent infection, followed by meningo-encephalitis [Table/Fig-2].

In the vascular aetiology of symptomatic SE, non haemorrhagic-ischaemic stroke was found to be the commonest cause (n=5). One of the patients in this subgroup had associated rheumatic



[Table/Fig-1A]: Distribution of age in SE patients.

Sl. No.	Duration of SE	No. of patients	Remarks
1.	< 6 hours	13	3 patients in this subgroup came in first hour
2.	7-24 hours	25	
3.	25-48 hours	8	
4.	49-98 hours	4	Delay in transportation

[Table/Fig-1B]: Duration of SE at the time of presentation

Aetiology-major group	No. of patients	Sub group	Disease
1)Acute symptomatic	26	a) CNS Infection (19)	i) Neurocysticercosis (10)
			ii) Meningo-encephalitis (5)
			iii) Tuberculoma/TBM (3)
			iv) Pyogenic meningitis (1)
		b) Vascular (5)	i) Non hemorrhagic Infarct (4)
			ii) Hemorrhagic (1)
		c) Metabolic (2)	i) Hyperglycemia (1)
			ii) Hyponatremia (1)
2) Remote symptomatic	1	Small calcific lesion (1)	
3) Cryptogenic	12		
4) Established Epilepsy	11		

[Table/Fig-2]: Aetiologies of Status Epilepticus.

Sl. No.	CT/MRI findings	Total no . of patients	Patient diagnosed with CT scan brain	Patients diagnosed with MRI brain
1.	Normal	23	18	5
2.	Ring Enhancing Lesion	10	6	4
3.	Tuberculoma/TBM	3	2	1
4.	Meningo-encephalitis	5	0	5
5.	Focal edema	2	1	1
6.	Hemorrhagic CVA	1	1	0
7.	Non-hemorrhagic infarct	4	2	2
8.	Calcific lesion	1	1	0
	Total patients	**49**	**31**	**18**

[Table/Fig-3]: CT/MRI profile of SE patients.

Aetiology	Responders to first line AED		Non-responders to first line AED	
	No. of patients	Percentage	No. of patients	Percentage
Acute symptomatic	22	84.6	4	15.6
Other etiologies	22	91.6	2	8.4
Total	44	88	6	12

[Table/Fig-4]: Response to drugs in SE

heart disease with mitral stenosis and mitral atrial fibrillation and a thrombo embolic infarct. 2 patients had SE due to metabolic disorders like hyperglycaemia and hyponatraemia. Depending upon the affordability, MRI and CT of the brain could be done in 18 and 31 patients respectively. One patient attendant did not allow any of these radiological investigations due to the fact that this patient had established epilepsy and as he/she had presented with an abrupt AED withdrawal. CT / MRI was unremarkable in 23 (44.1 %) patients. A ring enhancing lesion was seen in 10 patients, among which 6 had solitary cysticercus granuloma, while 4 had multiple cysticercus granuloma on radiological examination. 2 SE patients with meningo-encephalitis were suspected to be cases of Japanese encephalitis on the basis that they had myokimic SE and

bilateral thalamic hyper intensities on MRI. 2 were found to have generalized white matter oedema on MRI. They were grouped as nonspecific meningo-encephalitis on the basis of this CSF abnormality. One SE patient was suspected to be a case of herpetic encephalitis due to a temporal lobe hyper intensity on MRI and a CSF abnormality [Table/Fig-3].

CSF analysis was done in those who had the clinical signs of meningial irritation (n=7). One patient had findings which were suggestive of pyogenic meningitis, whereas the other had TB meningitis. 5 patients had mild lymphocytic pleocytosis with a mild increase in proteins, which as suggestive of aviral aetiology. Of the 50 patients with SE, 44 (88%) responded to the first-line drugs and 6 (12%) patients required second-line drugs. The variables which were studied to predict the response to the first-line-drugs, included the duration of SE and its aetiology [Table/Fig- 4]. The non-responders in acute symptomatic SE were 15.4 % as compared to 8.4 % in other aetiologies [Table/Fig-4]. The duration of SE and the delay in starting the treatment in all of the non-responders were more than 24 hours. 2 out of 3 deaths (6 %), were seen in the acute symptomatic group, one of them being a case of massive intra-cerebral bleeding and the other had Japanese encephalitis with refractory SE. The third death fell into the established epilepsy group whose SE was of 36 hours duration and he had primary epilepsy with intractable seizures, which caused acute renal failure and metabolic acidosis as terminal events.

DISCUSSION

SE has been defined as a condition in which "a seizure either persists for a sufficient length of time or is repeated frequently enough, to produce a fixed and enduring epileptic condition" in the first international classification of epileptic seizures [4]. Slight modifications were made in the subsequent definitions; however, the uncertainty about the duration of the seizures remained [5]. Te recommendation of the Epilepsy Foundation of America's Working Group on Status Epilepticus, in 1993, defined SE as (a), continuous seizure activity of more than 30 minutes, (b) two or more sequential seizures without the full recovery of consciousness [6]. Experimental studies have shown that a neurological injury can occur much earlier than 30 minutes [7]. Theodore et. al., (1994) reported that the mean seizure duration was 62 seconds. No seizure lasted for more than 2 minutes. The more prolonged seizures encourage the development of SE and a need for intravenous therapy [8]. Based on the above study, it was proposed by Lowenstein et al., (1999) that the definition of SE should be: (a), a continuous seizure of more than 5 minutes duration or (b), 2 or more discrete seizures of 5 minutes duration between which there is an incomplete recovery of consciousness [2].

The duration of SE and its aetiology are important predictors of its outcome [1,8,9]. In the developed countries, pre-hospital treatment protocols were available for the paramedics to reduce the duration of SE and to improve its outcome [5]. SE is a common medical emergency which accounts for 1% – 8% of all the hospital admissions for epilepsy [10]. In the present study, SE was observed in 50 patients (1.43 %) out of 3500 patients, who visited the emergency department during October 2011 to March 2012. The mean age of the patients with SE was 29.94 ± 1.76 years (12–75 years), 22 % were in the younger age group (11-20 years) and 56 % fell into the young adult group (21-40 years). These findings were in agreement with those from another hospital based series from the developing countries, wherein a higher proportion of the patients with SE were either children or young adults (20–40 years) [9,11]. However, in the developed countries, a bi-modal peak has been described with a high incidence in infants and in the elderly [12]. This difference could either be due to various aetiological factors viz. post-anoxic or congenital lesions which are common in childhood or due to stroke or neurodegenerative disorders that are common in elderly patients. In the developed countries, socio-cultural factors viz. health insurance and the care of the elderly could be the important factors which account for this difference.

In our study, the mean duration of SE before admission was 23.56 ± 3.16 hours, which ranged from 90 hours, which was comparable to that of a similar study which was done in south India [9]. The most common aetiology which was found was acute symptomatic (52%), which was again comparable to that in another studies from India [9,11]. Of the acute symptomatic aetiology, cerebro-vascular disease was the predominant (40%-50 %) cause of SE in the developed countries [13,14,15,16], whereas CNS infections accounted for 28–67 % of the aetiological spectrum in the developing countries [11,17,18]. In the present study, 38% of the cases with SE were caused by infections, NCC being the commonest one (10/19; 52.6%).

This was also in concordance with the finding of another study from Hyderabad, where NCC accounted for 42.5% of the SE cases [9]. Meningo-encephalitis accounted for the SE in 5 patients (26.3%) in our study, which was slightly lower than that which was reported in a study from north India, where one third of the SE cases was caused due to meningo-encephalitis of which, nonspecific encephalitis was the commonest cause [19]. However, the lowest incidence of meningo-encephalitis has been reported to be 15% [9]. We found out that the incidence of SE due to stoke was 10% (5/50), out of which four patients had non haemorrhagic ischaemic stroke. A thrombo embolic infarct was seen in one patient with rheumatic heart disease (MS and MR) with atrial fibrillation. A similar incidence (12.8%) of SE due to stroke was also reported by Kalita et al., [11].

It was also noted that 24% patients pertained to cryptogenic SE, which was comparable (19%) to the findings of a study from Hyderabad [9]. 22% of the SE patients were established epileptics with a 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 which were done at Lucknow and Hyderabad respectively [9,11].

A metabolic cause for SE was noted in 2 (4%) patients, which was lesser than that which was reported by Murthy et al., (11%) and Kalita et. al., (14.5%). This difference may be due to the small sample size of the present study. In the present study, one patient (2%) had remote symptomatic SE due to calcified lesions. Murthy et al., noted around 7% patients in this group; small calcified lesions being the most common finding [9]. The CT/MRI scan was normal in 46% patients with SE, which was comparable to that in another Indian study [11]. CT /MRI was abnormal in 23 out of 26 acute symptomatic SE patients (88.46%). In our 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 from

Lucknow and Hyderabad respectively [9, 11]. The non-responders were more in the acute symptomatic SE (15.4%) group as compared to those in other aetiology groups (8.4%). CNS infection or haemorrhagic stroke was the common aetiology amongst the non-responders, which was comparable to that in other studies [11,18,19,20]. The duration of SE before the treatment in all the non-responders was more than 24 hours, which was similar to the observation which was made by Murthy et. al., [9].

In large hospital-based studies, the mortality varies from 3%-50 %, depending on the study design and the case inclusion criteria [11,19,20]. In our study, the mortality was lower (6%), 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. 2 out of 3 deaths had occurred in the acute symptomatic group. One of these patients with refractory SE had suspected Japanese encephalitis. In a study which was done by Kalita et. al., on SE and CNS infections, it was observed that those with encephalitis had refractory seizures and poor outcomes [19]. One of the patients in the established epilepsy group had refractory SE, who died due to acute renal failure and metabolic acidosis. Studies have shown that the terminal events could be hyperpyrexia, circulatory collapse, ATN and epileptic encephalopathy [21].

In the present study, three out of 6 non-responders to the AED treatment, expired (50%). All of them had presented after 24 hours. Cherian et. al., commented that the longer the duration of SE, higher was the mortality and that a high degree of mortality was observed in the cases of refractory SE [12]. 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 [8]. In the present study, those who presented after 24 hours were amongst the non responder group and they had poor outcomes.

It can be concluded that the duration of SE and acute symptomatic seizure are important predictors of a poor outcome. However, the present study had limitations due to its small sample size, the follow up of the patients and the non-availability of various serological tests to diagnose the type of meningo-encephalitis and the ring enhancing lesion. Further studies with large sample sizes and follow up of the patients are needed for the validation of these predictors and to look for long term outcomes.

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AUTHOR(S):

1. Dr. Malini Kulshrestha
2. Dr. Manmohan Krishna Pandey
3. Dr. Ramesh Kumar Patial

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Medicine,
2. Assistant Professor, Department of Medicine,
3. Professor and Head of Department of Medicine,

Rohilkhand Medical College & Hospital,
Bareilly (U.P.)-243006 , India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Malini Kulshrestha,
Assistant Professor, Department of, Medicine
Rohilkhand Medical College & Hospital,
Bareilly (U.P.)-243006, India.
Phone : 09897112341
E-mail: malinik@gmail.com

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