Comparison of clinical profile and outcome of de novo convulsive status epilepticus with those with a past history of epilepsy in the elderly populace

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Abstract

Aim: To compare the clinical characteristics and etiological differences between de novo convulsive status epilepticus (CSE) with those with a past history of epilepsy in the elderly populace and the predictors of in-hospital mortality.

Methods: One hundred twenty-two elderly (≥60 years of age) hospitalized patients with CSE were evaluated for clinical profile, etiologies and predictors of in-hospital mortality.

Results: The mean age of the study population was 67.2±7.7 years. Among them, 77 (63.1%) cases were of de novo CSE and 45 (36.9%) cases had a past history of epilepsy. Most common etiologies in de novo CSE were acute symptomatic in 68.8%, followed by remote symptomatic in 24.7% of cases. In-hospital mortality in de novo CSE was 38.9 % and on multivariate analysis, it was found variables significantly related to mortality in CSE were the presence of comorbidities (odds ratio (OR) = 0.229, 95% confidence interval (CI) = 0.059- 0.897; p=0.03) low Glasgow Coma Scale (GCS) (OR =0.045 , 95% CI =0.013- 0.160 ; p= 0.01) and de novo CSE (OR= 0.093, 95% CI = 0.017- 0.503 ;p= 0.01).

Conclusions: De novo CSE in the elderly was associated with poorer outcomes in comparison to those with a past history of epilepsy. In-hospital mortality in CSE was related to the presence of comorbidities, low GCS and de novo CSE. Prompt and aggressive management of de novo CSE is the most effective way of preventing in-hospital mortality in the elderly.

Keywords: De novo CSE; CSE in elderly; in-hospital mortality; outcome.

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INTRODUCTION

Status epilepticus (SE) is a critical neurologic emergency characterized by high mortality and morbidity. The incidence rate of SE reveals an age-specific U-shaped curve or a bimodal distribution with peak rates among

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infants and the elderly. In patients who are 60 years or more, the annual incidence is 86/100,000, which is almost twice when compared with the general population [1]. SE was related to mortality at 38% in the elderly populace, approaching 50% in patients over 80 years of age [2].

The most frequent etiology of SE in the elderly consists of stroke, infection, degenerative disease, neoplasm and trauma [3]. Possible precipitating factors may be inadequate concentrations of antiepileptic drugs (AEDs), alcohol withdrawal, electrolyte imbalances and metabolic derangements [4].

Approximately 40 % of all cases of SE have been reported in the elderly [5]. Numerous studies showed that 40–60% of SE patients have no past history of epilepsy and often have worse outcomes [6-8]. There is a dearth of literature regarding predictors of risk factors for the poorer outcomes of de novo SE particularly in the elderly patients [9]. The outcome of de novo SE is poorer and this may be credited to the older age at onset and the potentially fatal etiologies.

The current study was aimed to (1) Compare the clinical characteristics and etiological differences between the de novo convulsive status epilepticus (CSE) with those with a past history of epilepsy in the elderly populace and (2) the predictors of in- hospital mortality.

METHODS

We conducted a hospital- based, cross-sectional study from July 2017 to September 2019 on the elderly (≥60 years of age) patients. The study was preapproved by the institutional ethical committee.

All subjects with CSE were prospectively evaluated after obtaining their informed consent. Patients having pseudoseizures, nonconvulsive status epilepticus(NCSE) , history of epilepsy or epileptic seizures before 60 years were excluded. We have excluded all the cases having possibility of ongoing NCSE on clinical ground like subtle or flickering movements with altered sensorium after CSE . Patients were divided into two groups de novo CSE and CSE with a past history of epilepsy.

A total of 1976 elderly patients with different neurological disorders were admitted during this period, out of which 122 patients with CSE met the inclusion criteria.

CSE is defined as continuous seizure activity or two or more distinct seizures between which there is incomplete recovery of consciousness lasting ≥30 minutes [10].

Clinical characteristics of patients were recorded including age, gender, seizure semiology, period of epilepsy, duration and etiology of CSE, neurological findings, treatment and duration of hospital stay and initial Glasgow Coma Scale(GCS). Relevant investigations (e.g., blood gas analysis, blood glucose, electrolyte levels, liver, renal function tests and CSF examination) were done. Patients also underwent evaluation with chest X-ray, ultrasound abdomen and echocardiography wherever considered necessary. Neuroimaging (CT and MRI) was done based on clinical indications. The 30 minutes electroencephalogram (EEG) recording was done using the 10–20 system of electrode placement within 12 hours of cessation of CSE.

All patients with CSE were treated with intravenous (IV) AEDs, lorazepam and phenytoin as per the standard protocol [IV lorazepam (0.1 mg/kg), followed by the IV loading of phenytoin (20 mg/kg) as the first-line drugs]. In unresponsive cases, the second-line drugs were given as an IV loading dose of valproate or levetiracetam and if CSE persisted patients received general anesthesia (coma induction). In addition, patients also received mechanical ventilatory support if required and suitable management of the underlying disease.

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel and Statistical Package for Social Sciences software Version 24.0 (SPSS) was used for analysis. Quantitative variables were assessed by unpaired t-test while categorical variables were assessed using the Chi-Square test and Fisher Exact test. The risk factor for mortality was set up by univariate and multivariate logistic regression, using the odds ratio (OR) and 95% confidence interval (CI). The p-value of less than .05 was considered statistically significant.

RESULTS

A total of one hundred twenty-two elderly patients with CSE were recruited. Out of which 97 (79.5 %) cases

were men and the mean age of the study population were 67.2±7.7 years (range: 60–90 years). Among them, 77 (63.1%) cases were of de novo CSE and 45 (36.9%) cases had a past history of epilepsy. CSE was well controlled with the first-line drugs in 89.3% of cases. The main seizure type was focal with bilateral convulsive seizure in 63.1 % of cases. The median duration of de novo CSE was 5.52±2.56 hours roughly the same as compared with CSE with a past history of epilepsy in the elderly that is, 4.98±2.88 hours. The clinical characteristics of the patients are shown in Table 1.

Most common etiologies in de novo CSE were acute symptomatic in 68.8%, followed by remote symptomatic in 24.7%, and unknown in 6.5 % of cases. In CSE with a past history of epilepsy remote symptomatic etiology were present in 66.7 % followed by non-compliance in 15.5 % of cases (Table 2).

In-hospital mortality in the CSE in the elderly was 32 (26.2 %) in our series. Immediate cause of death in 20(16.4 %) cases were underlying diseases and in 12 (9.8%) cases the cause of death was CSE.Amongst them, stroke was the most common cause of mortality (acute

Table 1: The clinical characteristics of the patients with CSE

Type of epilepsy	New onset epilepsy (n=77)	With past history of epilepsy (n=45)	p- value	Chi square
Age, year (mean ± S.D.)	67.14 (7.655)	66.36 (5.519)	0.516	0.650#
Gender				
Male	61 (79.2)	36 (80.0)	0.918	0.011
Female	16 (20.8)	9 (20.0)		
Co morbidities				
Hypertension	20 (26.0)	17 (37.8)	0.689	0.160
Diabetes	12 (15.6)	6 (13.3)		
Dyslipidemia	1 (1.3)	2 (4.4)		
CAD	2 (2.6)	2 (4.4)		
Type of seizure*				
Tonic clonic	31 (40.3)	14 (28.9)	0.195	2.976
Focal onset with bilateral convulsive seizure	46 (59.7)	31 (68.9)		
Duration of seizures in hours				
≤12	71 (92.2)	41 (91.1)	0.831	0.045
>12	6 (7.8)	4 (8.9)		
Duration of stay in hospital in days (mean ± S.D.)	5.52 (2.563)	4.98 (2.888)	0.302	1.038#
Response to 1st line of treatment*				
Responder	66 (85.7)	43 (95.6)	0.089	2.889
Non responder	11 (14.3)	2 (4.4)		
GCS				
0-7	31 (40.3)	7 (15.6)	0.001	8.082
8-15	46 (59.7)	38 (84.4)		
Outcome				
Improved	47 (61.0)	43 (95.6)	0.001	17.487
Death	30 (39.0)	2 (4.4)		
EEG findings within 12 hours of cessation of CSE				
Attenuation of background	54(70.1)	38(69.1)	0.898	0.01
Return to baseline background	23(29.9	17(30.9)		

#The means of two groups was compared used t- test and the value is t score

*The p value indicated is calculated using Fisher's Exact test

Table 2: Etiology of convulsive status epilepticus in elderly

Type of epilepsy	New onset epilepsy (n=77)	With past history of epilepsy (n=45)	Total (n=122)	P value
Established epilepsy			7 (5.8)	0.001
Non compliance	0 (0.0)	7 (100.0)		
Acute symptomatic	53 (100.0)	0 (0.0)	53 (43.4)	0.001
CNS infections	9 (17.0)	0 (0.0)		
Neurocysticercosis	5 (9.4)	0 (0.0)		
Meningoencephalitis	1 (1.9)	0 (0.0)		
Tuberculoma/TBM	3 (5.7)	0 (0.0)		
Vascular	35 (66.0)	0 (0.0)		
Infarct	22 (41.5)	0 (0.0)		
Hemorrhage	12 (22.6)	0 (0.0)		
Thrombosis	1 (1.9)	0 (0.0)		
Metabolic	9 (17.0)	0 (0.0)		
Hypoglycemia	1 (1.9)	0 (0.0)		
Hyperglycemia	2 (3.8)	0 (0.0)		
Hyponatremia	1 (1.9)	0 (0.0)		
Alcohol	5 (9.4)	0 (0.0)		
Remote symptomatic	19 (38.8)	30 (61.2)	49 (40.1)	0.001
Post traumatic	6 (12.2)	4 (8.2)		
Old Infarct	11 (22.4)	18 (36.8)		
Old Hemorrhage	0 (0.0)	3 (6.1)		
Tumors	2 (4.1)	0 (0.0)		
Focal cerebral calcifications	0 (0.0)	5 (10.2)		
Cryptogenic	5 (38.4)	8 (61.6)	13 (10.7)	0.069

stroke in 24 cases ,old infarct 1 case and old hemorrhage in 1 case) followed by posttraumatic (n=4), CNS infection (n=2). Factors like the presence of comorbidities, low GCS and de novo CSE were found to be significantly associated with the poor outcome. On multivariate analysis, it was found that people with comorbidities were at a higher risk of facing mortality with an AOR of 0.229, 95% CI: 0.059-0.897, who had GCS less than 8 had a poorer prognosis with an AOR of 0.045, 95% CI:0.013-0.160 and de novo CSE with an AOR of 0.093,95% CI: 0.017- 0.503 (Table 3).

DISCUSSION

The prognosis of de novo CSE is associated with worse outcomes nevertheless; there are constrained published data on predictors of outcome among the elderly especially from the rural populace in a resource-poor country like India.

We observed in-hospital mortality in the de novo CSE in the elderly was 38.9 % (30/77) and 4.4 % (2/45) in CSE with a past history of epilepsy. This is in accordance with a retrospective study on factors predictive of outcome in patients with de novo SE reported in-hospital mortality was 36% (30/83) and 29% (24/83) developed post-SE symptomatic epilepsy and 8.43% (7/83) had recurrent SE [(11)].

Amongst CSE cases in the elderly in our series 63.1 % of cases presented as de novo CSE and were also significantly associated with mortality. The poor outcome in de novo SE may be attributed to the older age at onset and lethal etiology such as infection and metabolic derangement [(11)]. Malter et al. also reported de novo SE occurred in 56% of all patients with SE without age-related preponderance; yet, 67% of the patients with de novo SE were aged 60 years [(12)]. De novo SE was allied

Table 3: Risk factors for mortality: Multiple logistic regressions

Factors	Died (n=32)	Unadjusted OR	(95% CI)	P value	Adjusted OR	(95% CI)	P value
Gender			(0.896- 5.764)	0.08		0.963- 20.468	0.05
Male	22 (22.7)	2.273			4.439		
Female	10 (40.0)	1			1		
Comorbidities			(0.194- 1.003)	0.05		0.059- 0.897	0.03
Present	17 (36.2)	0.441			0.229		
Absent	15 (20.0)	1			1		
GCS			(0.012- 0.104)	0.01		0.013- 0.160	0.01
0-7	26 (68.4)	0.036			0.045		
8-15	6 (7.1)	1			1		
CSE			(0.016- 0.323)	0.01	0.093	0.017- 0.503	0.01
De novo	30 (39.0)	0.73			1		
With past history of epilepsy	2 (4.4)	1					
Etiology							
Stroke	26(38.8)	0.889	0.972-3.34	0.346	2.212	0.078-0.854	0.02
Posttraumatic	4(40)	16.611	0.763-3.89	0.728	30.812	0.460-5.742	0.03
Infection	2(22.2)	1			1		
Duration of seizures in hours							
≤12	28(25)	2.723	(.432-2.802)	.02	6.522	.051-0.846	.010
>12	4(40)	1			1		

with a greater risk of developing new-onset refractory status epilepticus (in up to 50% of the cases), non-convulsive status epilepticus, having a longer duration of status, longer ICU stay and poorer clinical outcome [13-14].

The degree of consciousness impairment at presentation is a notable prognostic factor for outcome after SE [15], which is additionally a critical prognostic factor in our study also.

In our study mortality in CSE in the elderly was related to the presence of comorbidities. In another study on prognostic variables of SE in the elderly reported factors independently connected with mortality were younger age, a higher number of comorbidities, and de novo SE [16]. One probably justification for high mortality in de novo SE may be its association with acute symptomatic etiology and serious comorbidities compared to SE with a history of epilepsy.

Limitations of the study: Only CSE cases were included due to the non-availability of complementary tests like continuous video- EEG monitoring; being a single centre, hospital-based study; it does not reflect the general population.

De novo CSE in the elderly was associated with poorer outcomes in comparison to those with a past history of epilepsy. In the present series, the predictors of in-hospital mortality in CSE in the elderly were related to the extent of consciousness impairment, de novo CSE and presence of comorbidities. The present study signifies that prompt and aggressive treatment of de novo CSE in the elderly is the most effective means of preventing in-hospital mortality.

Conflict of Interest: None of the authors has any conflict of interest to disclose.

Ethical approval: The study is in accordance with the ethical standards of the institution. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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