Determinants of Outcome in Convulsive Status Epilepticus in Adults: An Ambispective Study

Authors
Dr I. D. Chaurasia¹, Dr Prateek Malpani², Dr Neeraj Mane³, Dr Vijay Nandmer⁴
Dr M. C. Songara⁵
¹Associate Professor, ²,³Resident, ⁴Associate Professor, ⁵Prof. & Head
¹,⁴Neurosurgery, Gandhi Medical College, Bhopal
²,³,⁵Dept. of Surgery, Gandhi Medical College, Bhopal
Corresponding Author
Dr Prateek Malpani

Abstract
Background: Ours is an ambispective observational study conducted in the Department of Neurosurgery attached to Gandhi Medical College, Bhopal.
The patients of convulsive SE (cSE), i.e., prolonged or intermittent seizures lasting beyond 5 minutes, without full recovery of sensorium, are admitted to our well equipped (NICU) and treated consecutively as per the departmental cSE treatment protocol adopted and modified from ILAE¹.
Study Designed: Ambispective Observational study
Result: Although the STESS score of >2 was found to be associated with higher odds of poor outcome (OR- 2.52, CI- 0.75-8.4, Table 1). With 55.8% of the patients with STESS>2 getting discharged and 23.9% of those with a score of ≤2 experiencing poor outcome, its ability to identify the unfavorable outcome correctly was poor (AUC 0.62, sensitivity of 75% and specificity of 45.7%).
Conclusion: In conclusion, our study identifies that low MAP, delay of >3.5h in treatment initiation or seizure control are the determinants of poor outcome in cSE. With incorporation of CSEOS, we believe that our findings can be helpful in the process of clinical decision making and prognostication of patients with cSE.
Keywords: Outcome, Convulsive, Epilepticus & Adults.

Introduction
Status epilepticus (SE), lasting beyond five minutes without regaining of consciousness,¹ is a neurological emergency associated with high short and long-term mortality and morbidity.²
The case fatality and incidence rates differ widely amongst the reports emerging from the different part of the globe. Sanchez et al.³ in a recent review, has reported the incidence of SE in the adult population of US to be 28.4/100,000/y, in Asian continent 42/100,000/y and Honduras 104/100,000/y.
The death rates associated with SE have declined from 50% to 20-39% in last few decades⁴. Recent investigators from India have found the mortality in SE in the range of 5% to 29.3%⁵,⁶,⁷.
Improved management strategies, availability of better antiepileptic medications might underlie the change in the outcome of SE.

**Material & Method**

Ours is an ambispective observational study conducted in the Department of Neurosurgery attached to Gandhi Medical College, Bhopal. The patients of convulsive SE (cSE), i.e., prolonged or intermittent seizures lasting beyond 5 minutes, without full recovery of sensorium, are admitted to our well equipped (NICU) and treated consecutively as per the departmental cSE treatment protocol adopted and modified from ILAE\cite{1}. Every patient with cSE is subjected to continuous electroencephalogram (EEG; 21 channel, RMS model- Maximus, version 4.2.54), noninvasive blood pressure (BP) and two hourly blood glucose monitoring. The mean arterial blood pressure (MAP) and blood sugar levels are actively maintained above 80 mmHg and below 140 mg% respectively.

Total 59 patients were admitted during the study period with ongoing convulsive seizures beyond 5 minutes, and altered consciousness\cite{1}. Patients with acute traumatic brain injury, myoclonic epilepsies and psychogenic seizures (n=4) were excluded. The medical records and study proforma (including raw EEG data) of remaining the 55 patients were reviewed between January-June 2017, and the following information was extracted- a. Age in years (y), b. Gender, c. History of epilepsy and treatment d. Type of seizure at the onset of SE, e. MAP and RBS at the time of admission, f. history of seizure/s with complete recovery of sensorium (premonitory seizure) in previous 24 hours (h), g. Time of onset and etiology of SE, h. Time of the first medical attention and treatment received, i. Time of the cessation of the clinical seizure, j. Treatment received after admission and k. The outcome, i.e., discharge with full recovery of sensorium; ability to wean-off from an induced medical coma at the time of discharge on request; the state of the brain function at the time of discharge on request /in-hospital death.

**Results**

**Demographic variables vs. outcome**

There were 36 (65.45%) men with mean age of the cohort being 39.09±15.34y (range 16-70). The odds of unfavorable outcome were significantly high for the women (OR 1.45, 95% CI 0.4-4.5) and those aged >40y (OR 3.05, 95%CI 0.9-9.6), furthermore the cutoff age associated with the unfavorable outcome was found to be >52y on ROC (sensitivity 50%, specificity 91.43, AUC 0.71).

**Clinical variables vs. outcome**

The premonitory seizures were seen in 27.2% (15 of 55) patients, the mean time lapse between them and the SE was 6.48±5.6h (range 0.5-19h). The absence of a previous history of epilepsy (de novo SE) was associated with higher odds of unfavorable outcome (OR 3.36, 95% CI 0.9-12.1).

Acute symptomatic cSE, when compared with cSE because of other etiologies (remote symptomatic, unknown cause), showed that 53.4% patients of the later group had poor outcome as compared to 30% in the former. The difference was not statistically significant.

**Severity scales vs. outcome**

Although the STESS score of >2 was found to be associated with higher odds of poor outcome (OR-2.52, CI- 0.75-8.4, Table 1). With 55.8% of the patients with STESS>2 getting discharged and 23.9% of those with a score of ≤2 experiencing poor outcome, its ability to identify the unfavorable outcome correctly was poor (AUC 0.62, sensitivity of 75% and specificity of 45.7%).
### Table No. 1 Clinical characteristic of cohort (n=55) vs. outcome

| Variable                     | Division       | Favorable outcome (35) n(%) | Unfavorable outcome (20) n(%) | Statistical significance OR* (95% CI) |
|------------------------------|----------------|-----------------------------|------------------------------|-------------------------------------|
| Age(years)                   | ≤ 40, n=34     | 25 (73.5)                   | 9 (26.5)                     | 3.05 (0.9-9.6)                      |
|                              | >40, n=21      | 10 (47.7)                   | 11 (52.3)                    |                                     |
| Gender                       | Male, n=36     | 24 (66.7)                   | 12 (33.3)                    | 1.45 (0.4-4.5)                      |
|                              | Female, n=19   | 11 (57.9)                   | 8 (42.10)                    |                                     |
| Premonitory seizures         | Yes, n=15      | 11 (73.3)                   | 4 (26.7)                     | 0.82 (0.25-2.6)                     |
|                              | No, n=40       | 24 (60)                     | 16 (40)                      |                                     |
| Breakthrough seizures        | Yes, n=20      | 16 (80)                     | 4 (20)                       | 3.36 (0.9-12.1)                     |
|                              | No, n=35       | 19 (54.3)                   | 16 (45.7)                    |                                     |
| Etiology of SE               | Acute symptomatic n=40 | 28 (70)           | 12 (30)                      | 0.37 (0.11-1.26)                    |
|                              | Others, n=15   | 7 (46.6)                    | 8 (53.4)                     |                                     |
| Type of SE as per onset      | GTCS, n=45     | 27 (60)                     | 18 (40)                      | 2.66 (0.5-14.02)                    |
|                              | Partial with secondary gen, n=10 | 8 (80)           | 2 (20)                       |                                     |
| MAP at admission (mmHg)      | ≤ 80, n= 11    | 5 (45.4)                    | 6 (54.6)                     | 2.57 (0.66-9.8)                     |
|                              | > 80, n= 44    | 30 (75)                     | 14 (25)                      |                                     |
| RBS at admission (mg/dl)     | ≤ 140, n=28    | 18 (64.2)                   | 10 (35.8)                    | 1.05 (0.35-3.17)                    |
|                              | > 140, n=27    | 17 (62.9)                   | 10 (37.1)                    |                                     |
| t2MA (hrs.)                  | ≤ 5, n=42      | 35 (83.3)                   | 7 (16.7)                     | 127.8 (6.8-2394)                    |
|                              | >5, n=13       | 0                           | 13 (100)                     |                                     |
| t2CS (hrs.)                  | ≤ 3.5, n=33    | 27 (81.2)                   | 6 (18.18)                    | 7.87 (2.2-27.2)                     |
|                              | > 3.5, n=22    | 8 (36.4)                    | 14 (63.6)                    |                                     |
| EEG patterns (n=42)          | Type A, n=26   | 16(61.5)                    | 10(38.5)                     | 1.87 (0.47-7.45)                    |
|                              | Type B, n=16   | 12 (75)                     | 4 (25)                       |                                     |
| STESS                        | ≤ 2, n=21      | 16 (76.1)                   | 5 (23.9)                     | 2.52 (0.75-8.4)                     |
|                              | >2, n= 34      | 19 (55.8)                   | 15 (44.2)                    |                                     |
| CSEOS                        | ≤ 1, n=26      | 23 (88.4)                   | 3 (11.6)                     | 10.86 (2.6-44.6)                    |
|                              | >1, n=29       | 12 (41.3)                   | 17 (58.7)                    |                                     |

OR * - Odds Ratio  S* - Significant  
CI* - 95% Confidence Interval  
NS* - Not significant  
t2MA - Time to medical attention  
t2CS - Time to control clinical seizures  
RBS - Random blood sugar  
MAP - Mean arterial blood pressure  
STESS - Status epilepticus severity score  
SEOS - (proposed) status epilepticus outcome score
Demographic variables vs. outcome

There were 36 (65.45%) men with mean age of the cohort being 39.09±15.34y (range 16-70). The odds of unfavorable outcome were significantly high for the women (OR 1.45, 95% CI 0.4-4.5) and those aged >40y (OR 3.05, 95%CI 0.9-9.6), furthermore the cutoff age associated with the unfavorable outcome was found to be >52y on ROC (sensitivity 50%, specificity 91.43, AUC 0.71).

Discussion

Our ambispective study shows that age >40y, female gender, de novo SE and type of SE (GTCS) are the chief clinical determinants associated with the unfavorable outcome of cSE. Association of older age and female gender, de novo SE and GTCS, with poor outcome has been reported previously. The mortality of patients with our cohort was 14.5%. The mortality in SE has been reported to vary between 5 to 29.2%. The variability in the reported mortality rates could be due to the differences in the cohort characteristics. While our cohort consists solely of cSE while those reporting higher mortality than us have included non-convulsive SE, which is known to have poorer outcome. In contrast, the low fatality rates of 5% as reported by Bhalla et al. could be explained by inclusion of higher percentage of patients of SE related to alcohol and drug default known to have better outcome. Our patients with cSE related to drug default and alcohol had lowest incidences of unfavorable outcomes a finding in line with Towne AR et al.

Conclusion

In conclusion, our study identifies that low MAP, delay of >3.5h in treatment initiation or seizure control are the determinants of poor outcome in cSE. With incorporation of CSEOS, we believe that our findings can be helpful in the process of clinical decision making and prognostication of patients with cSE.

References

1. Trinka E, Kalviainen R. 25 Years of Advances in Definition, Classification and Treatment of Status Epilepticus. SEIZURE: European journal of epilepsy
2. Nair PP, Kalita J, Misra UK. Why, what, and how. J Postgrad Med.2011;57:242-52.
3. Sanchez S, Rincon F. Status Epilepticus: Epidemiology and Public Health Needs. J ClinMed.2016;5(8):71.
4. Kalita J, Nair PP, Misra UK. A clinical, radiological and outcome study of status epilepticus from India. J Neurol 2010;257:224-229.
5. Murthy JMK, Jayalaxmi SS, Kanikannan MA. Convulsive status epilepticus: Clinical profile in a developing country. Epilepsia.2007;48(12):2217-2223.
6. Bhalla A, Das B, Som R, Prabhakar S, Kharbanda PS. Status epilepticus: Our experience in a tertiary care center in Northwestern India. Journal of Emergencies, Trauma, and Shock. 2014;17(1).
7. Kalita J, Misra UK, Patel R. Initial EEG in status epilepticus is helpful in predicting seizure recurrence. Electromyogr. clin. neurophysiol.2006;46.
8. Rossetti AO, Hurwitz S, Logroscino G, Bromfield EB. Prognosis of status epilepticus: role of etiology, age and consciousness impairment at presentation. J Neurol Neurosurg Psychiatry 2006;77:611-615.
9. Rossetti AO, Logroscino G, Milligan TA, Michaelides C, Ruffieux C, Bromfield EB. Status Epilepticus Severity Score (STESS). J Neurol.2008;255:1561-1566.
10. Delorenzo RJ, Hauser WA, Towne AR, Boggis JG, Pellock JM, Penberthy L, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. Neurology 1996Apr;46 (4):1029-35.
11. Novy J, Logroscino G, Rossetti AO. Refractory status epilepticus: a prospective observational study. Epilepsia. 2010 Feb;51(2):251-6.

12. Drislane FW, Blum AS, Lopez MR, Gautam S, Schomer DL. Duration of refractory status epilepticus and outcome: Loss of prognostic utility after several hours. Epilepsia. 2009;50(6):1566-1571.

13. Hassan H, Rajiv KR, Menon R, Menon D, Nair M, Radhakrishnan A. An audit of the predictors of outcome in status epilepticus from a resource-poor country: a comparison with developed countries. Epileptic Disorder. 2016;18(2): 163-172.

14. Towne AR, Pellock JM, Ko D, Delorenzo RJ. Determinants of mortality in status epilepticus. Epilepsia. 1994 Jan-Feb.