**Status epilepticus in adults: A 6-year retrospective study**

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**Abstract**

**Background:** Status epilepticus (SE) is one of the most common neurological emergencies with high mortality and morbidity. This study aims to determine the most common causes and outcomes of SE in adult patients from Fars Province in southern Iran. **Materials and Methods:** 134 patients with SE (either convulsive or non-convulsive), aged over 18 years, admitted to the Namazee Hospital, were enrolled from January 2006 to February 2012. A questionnaire was used to collect patients' demographics and disease characteristics and their outcomes according to Glasgow Outcome Scale (GOS). Statistical analyses were performed using SPSS version 15 software. P value less than 0.05 was considered statistically significant. **Results:** 70 patients were female and 64 were male with mean age of 42.97±19.66 years and 39.42±18.89 years, respectively. Sixty-two patients had a history of epilepsy, and 72 had no history of epilepsy. Antiepileptic drugs (ADEs) withdrawal and cerebral infarction were the most common causes of SE in epileptics and non-epileptics, respectively. 123 patients (91.8%) had generalized tonic-clonic SE. 30 patients (22.4%) could return to work and 33 (24.6%) died during hospitalization. There was a significant relationship between mortality and age over 60 years (P<0.001), and mortality and cerebral infarction or anoxia (P= 0.022). **Conclusion:** ADEs withdrawal in the epileptic patients was the main cause of SE (28.40% of the total population and 62% of the epileptic patients) which is preventable with patients and family education. This study showed that high mortality and morbidity was significantly related to the increasing age and etiology of SE.

**Keywords:** Status Epilepticus; Adult; Prognosis; Glasgow Outcome Scale

**Introduction**

Status epilepticus (SE) is one of the most common neurological emergencies with high mortality and morbidity [1,2]. It is defined as one seizure attack with sufficient prolonged time or at least two separate seizures with incomplete recovery of consciousness between them [3-5]. Although most studies have reported that the duration of seizure lasts 20-30 minutes, most physicians have advocated starting treatment after 5 minutes. SE is divided into two types: convulsive and non-convulsive. Each of these types has significant impact on mortality and morbidity [6]. Fever and infection is the most common cause of SE in children and stroke, hypoxia, alcohol intoxication, and metabolic disturbances are the major predisposing factors in adults [7-9].Mortality is about 16-25% that increases with age. The mortality rate is lower in children and higher in elderly patients and idiopathic and cryptogenic forms of SE [1,10].

The approach to SE should be conducted to terminate the attacks and to abort underling ongoing causes. Prognosis of SE largely depends on its etiology, for example, when SE occurs after stroke, it causes more disabilities or high mortality after anoxia [11]. However, some studies have reported that longer seizure duration or specific electroencephalogram (EEG) pattern are correlated with higher mortality [12]. Despite the high risk of mortality and neurologic disabilities with aggressive treatment and intensive cares, meaningful recovery is possible after prolonged SE [13].

In Iran, there are many studies which have been conducted on SE mostly in pediatrics [4,14-16], but there is paucity of data on adults. This cross-sectional retrospective study aims to determine the most common causes and outcomes of SE in adult patients in the last 6 years in order to make better preventive programs and more intensive cares during hospital admission.

**Materials and Methods**

We performed a cross-sectional retrospective chart review study in which all patients with SE (either convulsive or non-convulsive), aged over 18 years, who were admitted to Namazee Hospital –a major center for neurological emergencies in Shiraz, Fars Province, Iran– were eligible to participate and were enrolled from January 2006 to February 2012. All patients were evaluated by a neurologist at the time of admission, during the hospital course and immediately before discharging from the hospital, and the patients' data were recorded daily. The inclusion criteria were (1) seizure lasting at least 30 minutes, (2) at least two attacks of seizure without returning to normal level of consciousness between them for convulsive SE, and (3) clinically unrecognized seizure[17] with electrographic seizures in EEG for non-convulsive SE. Patients were classified into 3 age groups: 19-39 years, 40-59 years, and ≥ 60 years. A questionnaire was used to collect patients' demographic data, history of epilepsy in the patients or their family, antiepileptic medications, previous CNS insult or disease, duration of hospital course, imaging data, EEG findings and outcomes of the patients according to Glasgow Outcome Scale (GOS) [17]. GOS scale consists of 5 scores of outcome: score 1 means death, score 2 means vegetative (unresponsive and speechless), score 3 identifies severe disability (independent life), score 4 identifies moderate disability (dependent life but unable to return to work), and score 5 refers back to good recovery (able to work). The medical research ethics committee of Shiraz University of Medical Science approved the study (approval number: 55-4082).

SPSS software version 15 (SPSS Inc, Chicago, IL) was used for the statistical analysis of the data. Chi-square test, Mann-Whitney U test and Fishers' exact test were used to analyze data and Spearman’ correlation test was used to compare the outcomes and the hospital duration in each sex and age groups. P value less than 0.05 was considered statistically significant.

**Results**

Out of a total of 134 patients with SE during a 6-year period, 70 patients (52.2%) were female with a mean age of 42.97±19.66 years and 64 (47.8%) were male with a mean age of 39.42±18.89 years. The youngest patient was 20 years old and the oldest patient was 92 years. Frequency of SE was 72 (53.7%), 32 (24.9%), and 30 (22.4%) patients in the age groups of 19-39 years, 40-59 years, and ≥ 60 years, respectively. Mean duration of hospital admission was 12.98±14.37 days with a minimum of 2 days and a maximum of 100 days.

Sixty-two patients (46.3%) had previous history of epilepsy (epileptic) and 72 (53.7%) had no history of epilepsy (non-epileptic). One hundred and twelve patients (83.6%) had no family history of seizure and 5 patients (3.7%) had a family history of seizure, but the family history was unobtainable in the remaining patients. A majority of epileptic patients (39.35%) took one antiepileptic medication (monotherapy) and the frequencies of patients, who were treated with two, three and four AEDs, were 31.15%, 22.95%, and 6.55 %, respectively. Etiology of SE in this study is demonstrated in Figure-1.

One hundred and twenty-three patients (91.8%) had generalized tonic-clonic seizure. Four patients (3%) presented with non-convulsive SE and 3 patients (2.2%) presented with myoclonic SE. There were also 4 patients (3%) who had both generalized tonic-clonic and myoclonic SE. SE was terminated by intravenous diazepam followed by intravenous phenytoin in 70% of the patients and in the other patients, anesthetic drugs (20.9%) were the most effective agents for the termination of SE (Figure-2).

Patients' GOS scores are demonstrated in Figure-3. In the present study, 33 patients (24.6%) died (GOS score 1) and GOS score was significantly higher in the patients older than 65 years (P<0.001). In addition, the findings showed that GOS scores were correlated with the etiology of SE. Patients who presented with SE due to the withdrawal of AEDs had higher scores e.g. minor deficit and full recovery (P=0.003), but the patients with acute brain insult secondary to cerebral anoxia and stroke had lower scores (P= 0.022). However, There was no correlation between the hospital duration, age and GOS of the patients (P=0.848 and P=0.24, respectively).

**Discussion**

In this study, our findings showed that the withdrawal of AEDs was the most common cause of SE in all of the patients (28.40%) and in the epileptic patients (62%). These findings also replicate the findings of other studies [2,6,8,9]. However, in some of these studies, which evaluated SE in children, fever has been reported as the most responsible cause of SE [4,5]. Cerebral infarction is the known cause of SE in elderly patients [8] and CNS infection is the most prevalent cause of SE, especially in the developing countries [8]. Although cerebral infarction was the leading cause of SE in the non-epileptic patients of our study (35%), arterial/venous infarction (21.9%) and central nervous system infection (8.2%) were the second and third common etiologies of SE in all the patients, respectively (Figure-1). Substance abuse (1.5%) and ischemic-hypoxic brain damage (2.2%) were the least common cause of SE in the present study.

Generalized tonic-clonic SE (91.8%) was the most common form of SE in our study and the frequency of non-convulsive SE was 3%. Frequency of non-convulsive SE is about 25–50% of all patients of SE [18] and usually occurs in critically ill patients who manifested with very subtle or without motor component [19]. Unexpectedly low frequency of non-convulsive SE in our study was mainly because we had difficulty in picking up the patients to take the long term continuous EEG monitoring, which was required for confirmation of SE, as it was not available in our emergency ward and led to easily missing the patient with non-convulsive SE.

After bolus administration of benzodiazepine (lorazepam or diazepam) for emergent management of SE, phenytoin (or phosphenytoin) is the second step for urgent termination of SE [20,21]. In our center, intravenous diazepam followed by intravenous phenytoin is the first line treatment for the patients with SE, and the second choice for treatment is the injection of phenobarbital and/or valproate sodium. In the present study, most of our patients responded well to phenytoin (70%), but in the patients with continuous SE the second line had a little effect (phenobarbital 3.7% and valproate sodium 2.2%) that we had to use the third line of treatment for these refractory patients. Some studies have reported the same results and showed that in patients in whom using lorazepam and phenytoin did not stop SE, only 2.1% of patients had a response to phenobarbital [22,23]. Moreover, another study has been reported that only 5% of SE was controlled with phenobarbital when lorazepam and phenytoin failed to control it [24]. It may be concluded that aggressive treatment (e.g. anesthetic agents) should be considered earlier in refractory SE [20,25].

High mortality in our patients (24.6%) was consistent with the results of other studies in which they have shown that about 10-30%of mortality rate depends on the age, etiology and duration of seizures [26-28]. A study conducted by Murthy has reported that only one-third of patients could return to their previous functional status [29]. Retrospective nature of our study coupled with inadequate hospital chart data that made us unable to evaluate the relationship between the duration of seizure and mortality. However, our results showed significantly higher mortality in the elderly patients (P<0.001) and in the patients in whom SE was secondary to acute brain insults, such as stroke and cerebral anoxia (P=0.022). GOS scores and the etiology of SE showed lower scores (better outcome) in the patients with the withdrawal of AEDs (P=.003) and higher scores (poorer outcome) in the elderly patients and those with acute brain insults (P<0.001). Many studies emphasize that SE is usually associated with high mortality and morbidity in the elderly patients and better outcomes in the young patients that may be because of severe underlying causes of SE (e.g. stroke) in these groups of patients [30-32]. In contrast, SE that is related to alcohol and withdrawal of AEDs causes low mortality rate [33].

This was a retrospective chart review study and incomplete chart data was one of the limitations of this study. The other limitation was unavailable long term continuous EEG monitoring that led to easily missing the patients with non-convulsive SE.

**Conclusion**

SE is one of the most common neurological emergencies with high mortality and morbidity. Ages older than 60 years and etiologies, such as stroke and cerebral anoxia, were poor prognostic factors in our study. Over half of all the patients in the present study were young adults (20 to 39 years of age) and the withdrawal of AEDs was the main cause of SE. Designing a practical education on taking antiepileptic drugs will prevent SE in most of these patients.

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**Figure Legends**

**Figure 1.** Major cause of SE in 134 patients with status epilepticus.

**Figure 2.** Frequency of drugs that terminated status epilepticus in 134 patients.

**Figure 3.** Glasgow Outcome Scale (GOS) at the time of discharge in 134 patients with status epilepticus.

**Figure 1.** Major cause of SE in 134 patients with status epilepticus.



**Figure 2.** Frequency of drugs that terminated status epilepticus in 134 patients.



**Figure 3.** Glasgow Outcome Scale (GOS) at the time of discharge in 134 patients with status epilepticus.

