ORIGINAL ARTICLE

GMJ.2014;3(3):153-59
www.gmj.ir

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), admitted to Namazi Hospital, were enrolled from January 2006 to February 2012. We designed a questionnaire to collect the 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<0.05 was considered statistically significant. **Results:** Seventy 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 (46.26%) had a history of epilepsy, and 72 patients (53.73%) 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. One hundred and twenty-three patients (91.8%) had generalized tonic-clonic SE. Thirty 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) that can be prevented by patient and family education. This study showed that high mortality and morbidity was significantly related to the increasing age and etiology of SE.
[GMJ.2014;3(3):153-59]

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 a single 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 a significant impact on mortality and morbidity [6]. Fever and infection are the most common

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causes of SE in children and stroke, hypoxia, alcohol intoxication, and metabolic disturbances are the major predisposing factors in adults [7-9]. Mortality rate is about 16-25%, which is lower in children and higher in the elderly patients as well as idiopathic and cryptogenic forms of SE [1, 10].

The approach to SE should finally terminate the attacks and abort the underlying 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 discussed SE, particularly in pediatric patients [4,14-16] , but there is a paucity of data in adults with SE [17]. This cross-sectional retrospective study aims to determine the most common causes and outcomes of SE in adult patients within a 6-years period.

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 between January 2006 to February 2012 to Namazi Hospital –a referral university hospital for neurological emergencies in Shiraz, Fars Province, Iran. 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 [18] with electrographic seizures in EEG for non-convulsive SE. All of the patients were evaluated by a neurologist at the time of admission, during the hospital course and immediately before discharging, and the patients' data were recorded daily. Patients were classified into 3 age groups: 19-39 years, 40-59 years, and ≥ 60 years. We designed a questionnaire to collect the 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) [18]. GOS scale consists of 5 scores of outcome: score 1 means death, score 2 means vegetative (unresponsive and speechless), score 3 identifies severe disability (dependent life), score 4 identifies moderate disability (independent 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 protocol (approval number: 55-4082).

Statistical Analysis

SPSS software version 15 (SPSS Inc, Chicago, IL) was used for the statistical analysis of the data. Frequency of sex and age of the patients were described by percent and mean ± standard deviation (SD), respectively. Chi-square and t-student tests were used to analyze the relationship between sex, age and etiology of SE with GOS scores of the patients and Spearman' correlation test was used to compare the outcomes and the hospital duration within each age and gender groups. P-value< 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 (46.26%) had a previous history of epilepsy (epileptic). Five patients (3.7%) had a family history of seizure, but the family history was unclear in 17 patients (12.6%). 39.35% of the patients 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. Etiologies of SE in this study are demonstrated in Figure-1.

One hundred and twenty-three (91.8%) patients had generalized tonic-clonic seizure. Four (3%) patients 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

In the present study, SE was terminated by intravenous diazepam followed by intravenous phenytoin in 94 patients (70%), but in the patients with continuous SE the effect of the second line drugs was minimal (response to phenobarbital and valproate sodium in 5 (3.7%) and 3 (2.2%) of the patients, respectively) so we had to use the third line agents in these refractory patients. Anesthetic drugs were effective agents in 28 patients (20.9%) for the termination of refractory SE (Figure-2).

Patients' GOS scores are demonstrated in Figure-3. Thirty-three 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 GOS scores of 4 and 5, e.g. living independently and full recovery (P=0.003), but the patients with acute brain insult secondary to cerebral anoxia and stroke had GOS scores of 2 and 3 (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]. While acute cerebral infarction was one of the main cause of SE in elderly patients [8, 17], acute cardiorespiratory decompensation and electrolyte imbalance were other common predisposing factors of SE in this group [17, 19]. CNS infection was 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

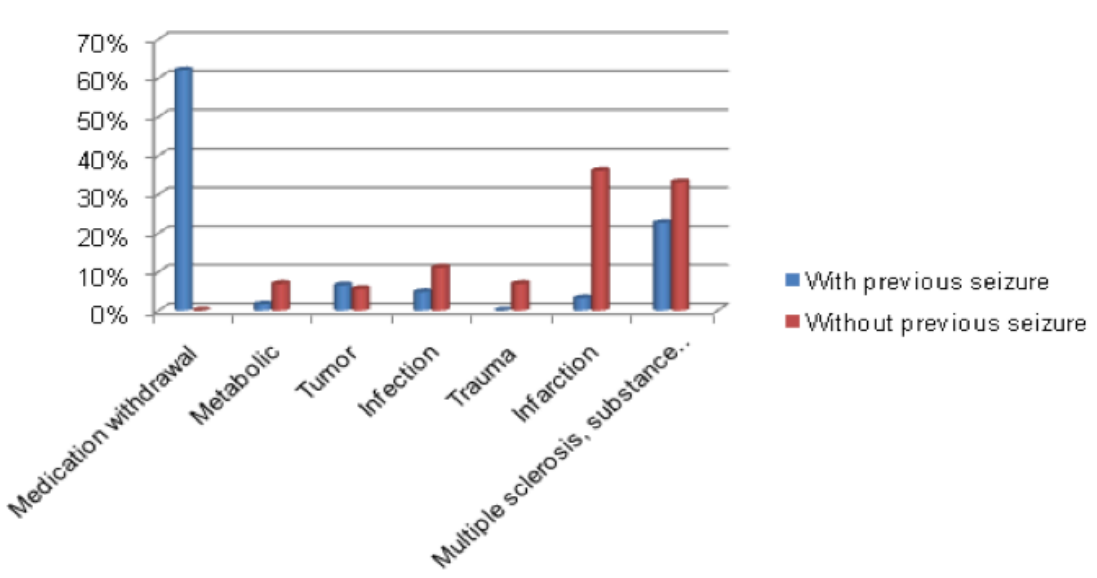

Figure 1. Major Cause of SE in 134 Patients with Status Epilepticus.

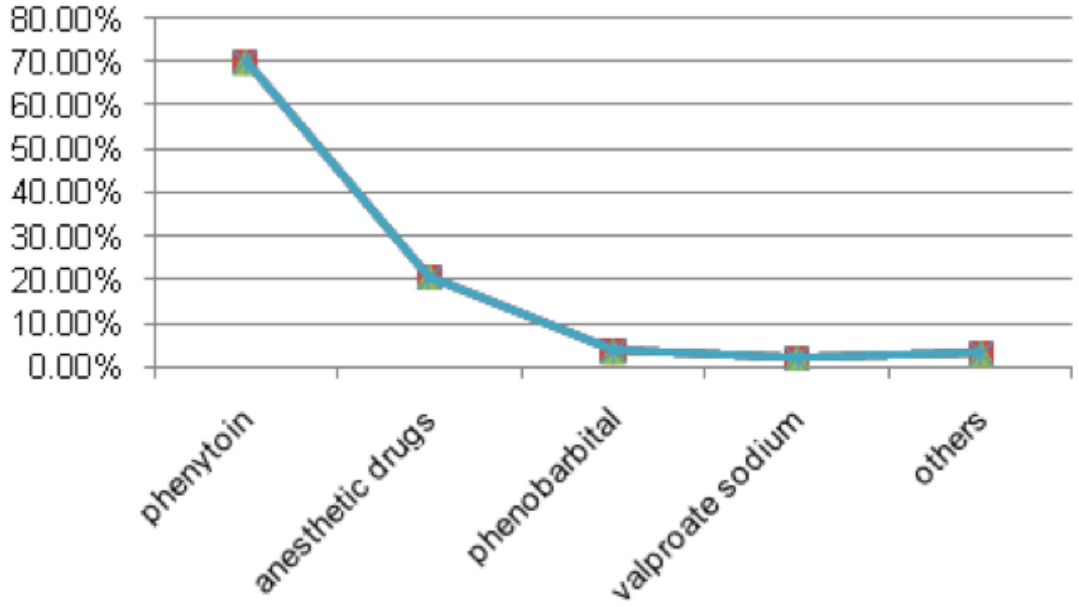

Figure 2. Frequency of drugs that terminated status epilepticus in 134 patients.

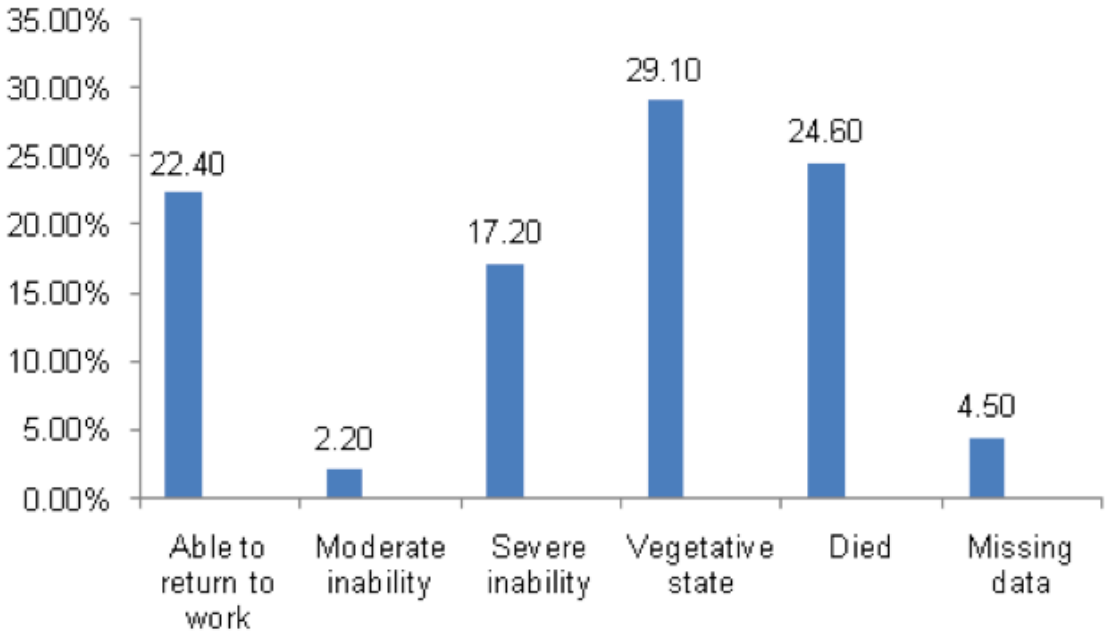

Figure 3. Glasgow Outcome Scale (GOS) at the time of discharge in 134 patients with status epilepticus.

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 [20] and usually occurs in critically ill patients who manifested with very subtle or without motor component [21]. Unexpected 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 the confirmation of SE, as it was not available in our emergency ward and led to easily missing the patient with non-convulsive SE.

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. However, our results demonstrated that the effect of phenobarbital and valporate in about 6% of refractory cases of SE to first line therapy and anesthetic drugs with control the SE in 20.9% of the patients have shown higher effect. 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 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 [25,26].

High mortality in our patients (24.6%) was consistent with the results of other studies which have shown that about 10-30% of mortality rate depends on age, etiology and the duration of seizures [27-29]. Studies on elderly cases of SE in our country have still shown a high mortality rate of 60% [17]. A study conducted by Murthy has reported that only one-third of patients could return to their previous functional status [30]. Retrospective nature of our study coupled with inadequate hospital chart data made us unable to evaluate the relationship between the duration of seizure and mortality. However, our results showed a significantly higher mortality rate 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 better outcome in the patients with the withdrawal of AEDs ($P=.003$) and poorer outcome in the elderly patients as well as 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 due to the severity of the underlying causes (e.g. stroke) in these groups of patients [17, 31-33]. In contrast, SE that is related to alcohol and withdrawal of AEDs accompanies a lower mortality rate [34].

Limitations

This was a retrospective chart review study and incomplete chart data was one of the limitations of this study. Another 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 serious etiologies, such as stroke and cerebral anoxia, were poor prognostic factors in our study. Over half of 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.

Acknowledgements

The authors would like to thank Ms. Hosseini and Ms. Gholami of Shiraz Neurosciences Research Center for their help.

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