

Original Article

Etiology and short-term outcome of children with convulsive status epilepticus admitted to Tabriz Children's Hospital, Iran

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Abstract

Introduction: Status epilepticus (SE) are associated with high rates of morbidity and mortality, yet early diagnosis and treatment will improve patients' outcome. This study was carried out to determine etiology, and early-outcome of our overall management of pediatric SE in patients admitted to Tabriz Children's Hospital, Iran.

Methods: In this cross-sectional and analytical study from January 2013 to January 2014, 43 patients with SE under the age of 15 years were enrolled. Demographic characteristics, etiology and outcome of every patient were recorded. SPSS for Windows software was used for statistical analysis. P-value of less than 0.05 was considered to be statistically significant in all comparisons.

Results: The highest rate of SE was happened in age-subgroup of 1-5 years. The two most common causes of SE in our patients were remote symptomatic (55.8%) and prolonged febrile convulsions (20.9%). Refractory SE (RSE) was detected in 15 (34.8%) patients. Poor early-outcome was shown in 8 (18.6%) patients (4 mortalities and 4 morbidities) of whom 5 (33.3%) had RSE, and 3 (10.7%) from SE group (P = 0.010). Young age was a risk factor for mortality (P = 0.010). Recurrent SE was occurred in 3 (7.0%) of patients.

Conclusion: Early-outcome of SE in children is mainly determined by age and underlying disorder.

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Introduction

Status epilepticus (SE) is one of the most common neurologic emergencies of childhood. Convulsive SE was defined as 30 min or longer generalized seizure or repeated seizures over 30 min periods without restoration of consciousness between seizures. If the patient continues to experience states of seizure despite initial treatment with adequate doses of two or three anticonvulsant medications, or if the attacks last for 60 min or more, the condition is described as refractory SE (RSE). The overall incidence of convulsive SE in the pediatric population is estimated to reach

10-38 in 100000 children/year, of whom approximately 9-44% have RSE.¹⁻⁵

It has been known that SE is associated with high rates of morbidity and mortality, even though early diagnosis and treatment will improve patients' outcome. In a recent study, the mortality of 3% was reported in 91 children admitted for SE. All deaths in this study were in children whose SE had been diagnosed to be acute symptomatic or progressive forms.⁵⁻⁷ RSE is associated with higher rates of morbidity and mortality. A meta-analysis study of children with RSE has shown a total mortality of 16%; however, the mortality rate was 20% for those with acute

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symptomatic and 4% for idiopathic SE.⁸ SE episodes were divided to convulsive and non-convulsive subtypes, which defined as a generalized seizure and subtle seizure [mental changes or coma and ictal discharges on electroencephalography (EEG)], respectively.⁹

From an etiologic point of view, SE can be divided into; acute symptomatic status that is caused by acute brain insults, such as trauma, central nervous system (CNS) infection, or metabolic disturbances; and the remote symptomatic status that is used for status due to chronic encephalopathies including previous congenital or acquired epileptogenic brain damages. Idiopathic SE, which is sometimes called as cryptogenic, does not seem to be associated with any causal damage. The febrile SE includes epileptic seizures accompanied by fever lasting for 30 min or more, while cerebrospinal fluid analysis shows nothing in favor of CNS infection.^{10,11}

This study was designed to determine the demographic information, etiology, and immediate outcome of pediatric SE in patients admitted to Tabriz Children's Hospital, Iran.

Methods

In this cross-sectional and analytical study, 43 patients with SE under the age of 15 years were enrolled. All patients who met the criteria for diagnosis of SE (as defined in the literature) and were referred to the Tabriz Children's Hospital, from January 2013 to January 2014 have been included in this study.¹² Patients with more than one episode of SE were regarded as one case. The study design was approved by the Ethics Committee of the Tabriz University of Medical Sciences-Research Deputy.

All studied patients had been admitted to the pediatric intensive care unit (PICU), received an intravenous (IV) line (for IV fluid and drug therapies), and were monitored by continuous electrocardiography, pulse oximetry, and arterial blood pressure monitoring. Endotracheal intubation and mechanical ventilation were done for some patients whenever indicated according to the

rules of PICU care. They did not undergo EEG monitoring during their acute phase of PICU course; however, electroencephalographic study was accomplished as soon as possible after stabilization of patients' clinical conditions.

The treatment objective was full control of patients' clinical epileptic seizures and their electroencephalographic seizure activities. If patients experienced SE for more than one episode, only the first attack was included in this study.

All patients were treated based on the same protocol; first, they received IV diazepam 0.3 mg/kg (3 doses, every 15 min) along with IV phenytoin 20 mg/kg (at a rate of 1 mg/kg/min); if the seizures were continuing, they received IV phenobarbital at the dose of 20 mg/kg every 10-30 min. If SE were abiding despite the above-mentioned treatments, the patient would receive IV midazolam (with a loading dose of 0.2 mg/kg and maintained by 1-5 µg/kg/min IV infusion). If the seizures still persisted, general anesthesia was implemented by sodium-thiopental IV injection. Midazolam was gradually tapered off if the patient was seizure-free for 24 h at a decreasing infusion rate of 1 µg/kg/min every 2 h until complete discontinuation. Close observation of the patient was conducted by repeated physical and neurological examinations during and after cessation of seizures.

A blood sample from each patient was collected for the complete blood count, and electrolytes, including calcium, phosphorus, magnesium, glucose, creatinine, and lactate. According to the patients' history, clinical examinations, and the initial test results, certain metabolic and toxicology tests were performed on blood and urine samples of some patients. If meningitis or encephalitis were suspected (as was the case in all febrile patients), the cerebrospinal fluid was tapped for cellular and biochemical analysis, bacterial cultures and polymerase chain reaction for herpes simplex virus.

Brain computed tomography, or magnetic resonance imaging was performed if needed. Information regarding patients' age, gender, history of neurological and medical

examinations, type of seizure, etiology, duration of SE, different types of used treatments and side effects of the administered medications were recorded. At discharge from the hospital, the patients were divided into three distinct groups based on their short-term outcome: death, new neurological defect, and recovery. Poor outcome was defined as death or development of new neurological deficit. Type of seizure was determined based on the international classification of epileptic seizures.

SPSS for Windows (version 17; SPSS Inc., Chicago, IL, USA) statistical software was used for statistical analysis. Findings were presented as mean \pm standard deviation, frequency, and percentage values. Quantitative variables were compared using the Student's independent t-test and one-way ANOVA tests. The qualitative variables were compared using the Chi-square test or Fisher's exact test. P-value of less than 0.05 was considered as statistically significant in all instances.

Results

During 1 year of the study, 43 children at the age of 1 month to 15 years were admitted to the

Tabriz Children's Hospital. The mean age of the study population was 46.1 ± 37.4 months (age range: 3-136 months); 9 (20.9%) patients were younger than 1 year and 21 (46.5%) were 1-5 years and 14 (32.6%) were older than 5 years of age. The age subgroup of 1-5 years showed the highest rate of SE in our study. About 13 (30.2%) patients were male and 30 (69.8%) were female.

SE occurred more frequently in spring and summer (27 patients, 62.8% of cases) than in autumn and winter (16 patients, 37.2%), but all deaths happened in autumn and winter. There was no significant difference between seasons in comparison of RSE and SE subgroups ($P > 0.050$). The two most common etiologic types of SE among our patients were remote symptomatic (24 patients, 55.8%) and prolonged febrile convulsion (8 patients, 18.6%). Six patients (14.0%) were admitted following an acute symptomatic SE (Figure 1).

Among 43 patients with SE, 15 (34.8%) had RSE. Most of cases (60.5%) treated with first-line medications (Table 1). There was no meaningful difference between two genders in RSE and SE groups ($P > 0.050$). There was

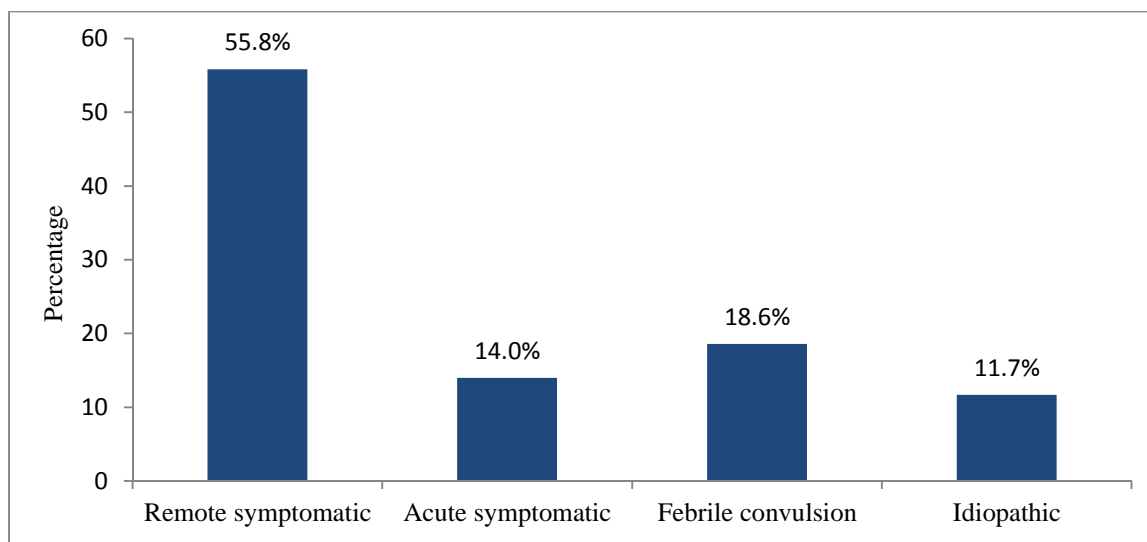


Figure 1. The cause of status epilepticus in children with convulsive status epilepticus admitted to Tabriz Children's Hospital in 2013

Table 1. Anticonvulsant medication used for control of seizures in status epilepticus patients admitted to Tabriz Children's Hospital

Drugs	Number (%)	Number (%) control of SE
Diazepam + phenobarbital + phenytoin	43 (100)	65.12
Diazepam + phenobarbital + phenytoin + midazolam	13 (30.23)	69.23
Diazepam + phenobarbital + phenytoin + midazolam + thiopental	4 (9.30)	100

SE: Status epilepticus

no correlation between patients' age and duration of SE in this study ($P > 0.050$). The mean hospital stay was 9.50 days (2-41 days, median 6 days). Mean duration of PICU course was 8.54 ± 8.10 days (1-31 days). The mean hospital stay for RSE (14.20 ± 11.50 days) was significantly higher than SE (7.10 ± 7.60 days) group ($t = -2.1, P = 0.045$).

In 20 patients (46.5%), the seizure controlled in less than 30 min and in 8 (18.6%) patients it took 31-60 min. Rate of refractory seizure was 34.8%. The most common etiologic type of RSE was remote symptomatic etiology (45.8%). Adverse effect such as respiratory suppression and hypotension occurred during treatment in 17 patients (39.5%). After discharge from hospital three patients (7.0%) experienced another episode of SE (recurrent SE). All of them were in a remote symptomatic category.

Regarding the patients' short-term outcome, there were four deaths (9.3%), 1 (6.7%) of them from RSE, and 3 (10.7%) from SE groups ($P > 0.050$); however, deaths in SE group had been caused by underlying disorders rather than SE. The mean age of deceased patients (18.75 ± 14.20) was lower than the others (49.35 ± 37.96) ($P = 0.010$). There was no meaning relation between age and morbidity in this study ($P > 0.050$). No significant difference was found between two genders in short-term outcome, mortality and morbidity rates ($P > 0.050$).

Morbidity rate was 9.3%. Morbidity following SE was seen in acute and remote symptomatic categories. The most common morbidity occurred after remote symptomatic SE (3 out of 24 patients got sequela, 12.5%). There was no new sequela or death after idiopathic or febrile SE. None of patients with febrile or idiopathic epilepsy had morbidity or mortality after SE. In this study, the morbidity rate was significantly higher in RSE group. Four cases of the RSE group (26.7%) got new sequela after seizure, this rate was zero for SE group ($P = 0.011$).

Discussion

SE is one of neurologic emergencies that can occur as a result of various etiologies.

Different studies show a different variety of etiologies for SE. Komur et al. reported different etiologies for SE in different studies.⁶ In one study, it was reported that infections of the CNS was the most common cause of SE. Raspall-Chaure et al. reported that the most frequent cause of SE was prolonged febrile seizure.⁷ Nishiyama et al. reported that the two most common causes of SE were febrile status and acute symptomatic etiologies.¹³ Similar to the study of Komur et al.⁶ in Turkey, the most common cause of SE was remote symptomatic etiology in our study. The incidence of this etiology in our study was similar to that of Komur et al. too (55.8% vs. 52.8%).⁶

Lin et al. reported that two-third of their patients with SE in Taiwan were under 5 years of age and highest incidence was in 1-5 years old group (51.8%).⁴ Furthermore, Hussain et al. reported 1-5 years of age as the largest subgroup (55.0%).⁵ Similarly, 46.5% of patients were in the same age category in our study.

Raspall-Chaure et al. reported a risk of recurrence of SE ranging from 3.0% to 56% in their review of 17 studies; which shows that recurrence rate might be higher in population-based studies.⁷ Recurrence is determined by the underlying etiology, that is, it is low in febrile and idiopathic SE (< 4%) and high in the acute, remote, and progressive, symptomatic groups (11, 44, and 67.0% respectively).⁷ We did not follow our patients as long, as they may not come back to our hospital in the case of relapsing seizures; the rate of recurrent SE may seem to be lower in this study (7.0%) compared with those of the others who have followed their patients for more than 1 year. Children with pre-existing neurological abnormalities are 23.7 times more likely to develop a recurrence than those without.⁷ All of recurrences in our study were in a remote symptomatic category.

In our study, the rate of preexisting seizure before status attack was 72.1%. It looks like Komur et al. reported but was higher than other studies because both similar studies have performed in tertiary care and referral hospitals.⁶ More similarly, the most common

previous seizure history was in a remote symptomatic category (87.5%).

Refractory seizure is a seizure longer than 60 min. The rate of refractory seizure in this study was 34.9%. Refractory seizure rate ranges from 24.8% to 33.0%. Komur et al. reported a rate of 34.8% for refractory seizures⁶ and Saz et al. identified RSE in 33.0% of children with convulsive SE.¹⁴ In another study by Barzegar and Jafari Roohi on 121 patients with SE in our hospital in 2002-2005 the rate of RSE was 38.0%.¹⁵

The observed differences between different studies can be attributed to social, economic, and geographical diversity of the study populations and the referral bias existing in their selection and also the lack of a standard definition for RSE. Since the Tabriz Children's Hospital is a third level referral center, more seriously ill patients whose conditions are more critical are referred to this center for hospitalization.

The mortality and morbidity rate in our study was 9.3% and 9.3%, respectively. Various morbidity and mortality rates have been reported in other studies on pediatric SE: ranging from 3.0% to 30.0%.¹⁶ Kang et al. reported mortality rate of 3.0% and morbidity of 33.0% in 189 Korean children.¹⁷ Maegaki et

al. examined 234 patients in Japan and reported 13.6% poor outcome and 4.0% mortality.¹⁸ Gulati et al. evaluated 30 patients with SE in India whose mortality rate in this study was 30% during hospital course.¹⁹ They reported seizure duration of more than 45 min and "septic shock" as the underlying cause of their high mortality.¹⁹ Asadi-Pooya and Poordast reported mortality and morbidity rate of 12.6% and 27.3%, respectively in Iran.²⁰ They claimed that patient's outcome meaningfully correlates with the etiology of SE.²⁰ Outcome of SE in children is mainly determined by underlying disorders.

Conclusion

It can be concluded that outcome of SE in childhood is mainly dependent on underlying disorders.

Conflict of Interests

Authors have no conflict of interest.

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