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De novo status epilepticus is associated with adverse outcome: An 11-year retrospective study in Hong Kong☆

Hoi Ki Kate Lui [a,*], Kwok Fai Hui [a], Wing Chi Fong [b], Chun Tak Ip [a], Hiu Tung Colin Lui [a,b]

[a] Department of Medicine, Tseung Kwan O Hospital, Hong Kong, China
[b] Department of Medicine, Queen Elizabeth Hospital, Hong Kong, China

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ABSTRACTS

Purpose: To identify predictors of poor clinical outcome in patients presenting to the intensive care units with status epilepticus (SE), in particular for patients presenting with de novo status epileptics.
Methods: A retrospective review was performed on patients admitted to the intensive care units with status epilepticus in two hospitals in Hong Kong over an 11-year period from 2003 to 2013.
Results: A total of 87 SE cases were analyzed. The mean age of patients was 49.3 years (SD 14.9 years). Eighteen subjects (20.7%) had breakthrough seizure, which was the most common etiology for the status epilepticus episodes. Seventy-eight subjects (89.7%) had convulsive status epilepticus (CSE) and 9 subjects (10.3%) had non-convulsive status epilepticus (NCSE) on presentation. The 30-day mortality rate of all subjects was 18.4%. Non-convulsive status epilepticus was more common in patients with de novo status epilepticus when compared to those with existing history of epilepsy (15.5% Vs. 0%, $p = 0.03$). Patients with de novo status epilepticus were older (52 Vs 43, $p = 0.009$). De novo status epilepticus was associated with longer status duration (median 2.5 days, IQR 5 days), longer ICU stay (median 7.5 days, IQR 9 days) and poorer outcome (OR 4.15, 95% CI 1.53–11.2).
Conclusions: For patients presenting to intensive care units with status epilepticus, those with de novo status epileptics were older and were more likely to develop non-convulsive status epilepticus. De novo status epilepticus was associated with poorer outcome. Continuous EEG monitoring would help identifying NCSE and potentially help improving clinical outcomes.

1. Purpose

Status epilepticus (SE) was the second most common neurological emergency presenting to the intensive care units. The incidence of status epilepticus in the United States was estimated to be 0.004% per year [1]. Status epilepticus was observed in up to one-tenth of patients with stroke and traumatic brain injury [2–5], and in up to 30% of patients with hypoxic ischemic encephalopathy [6]. Older age, cerebrovascular disease and central nervous system infection were associated with poor outcome [7–10], but other factors are controversial. Whether pre-existing history of epilepsy was associated with poor clinical outcomes showed conflicting results [11,12]. One observational study which included 128 status epilepticus episodes showed that de novo episodes were independent predictors of poor outcome [11]. One the other hand, a retrospective study which included 63 refractory status epilepticus episodes showed that de novo status epilepticus was not associated with poor clinical outcome [12]. The aim of the study was to identify predictors of poor clinical outcome in patients presenting to the intensive care units with status epilepticus, particularly in patients with de novo status epileptics.

2. Methods

This is a retrospective cohort study. The medical records of all patients with status epilepticus treated in the intensive care units in 2 hospitals over an 11-year period from June 2003 to June 2013 were retrieved. Adult patients older than or equal to 16 years old, with a clinical diagnosis of status epilepticus were included. Those who were younger than 16 years old were excluded from the study.

☆ This study was performed at Department of Medicine, Tseung Kwan O Hospital and Department of Medicine, Queen Elizabeth Hospital, Hong Kong Special Administrative Region.

* Corresponding author at: Department of Medicine, Tseung Kwan O Hospital, 2 Po Ning Lane, Hang Hau, Hong Kong. Tel.: +852 63859493.
E-mail address: katelui88@yahoo.com.hk (H.K.K. Lui).

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2.1. Data collection

Information including the baseline demographic data, history of epilepsy, clinical characteristics including the etiologies of status epilepticus, seizure semiology on presentation, electroencephalogram (EEG) patterns, durations of status epilepticus, pharmacological treatments and the outcomes including the length of intensive care unit (ICU) stay, length of hospital stay, 30-day mortality and functional outcome upon discharge were recorded. Status epilepticus was defined as a single epileptic seizure lasting longer than 30 min or a series of epileptic seizures during which consciousness was not regained between seizures for longer than 30 min.

Seizure semiology on presentation were classified as convulsive status epilepticus (CSE) and non-convulsive status epilepticus (NCSE). The duration of SE was defined as the time from the beginning of CSE seizures or EEG confirmation in patients with NCSE until the response to SE treatment. Response to treatment was defined by either the stopping of motor seizures in patients with CSE or EEG showing burst suppression in cases of NCSE. Etiologies were categorized as breakthrough seizure, encephalitis/meningitis, cerebrovascular accident (CVA), metabolic causes (including uremic and hepatic encephalopathy and hyponatremia), drug overdose/alcohol withdrawal, subarachnoid hemorrhage (SAH)/subdural hemorrhage (SDH), sepsis and hypoxic brain injury. If there was no clinical, biological or radiological evidence supporting a specific cause, the etiology was labeled as idiopathic. In cases SE was due to breakthrough seizure, the anti-epileptic drug (AED) level was recorded.

Functional status on discharge was defined by the Glasgow Outcome Score (GOS) which consists of five degrees of handicap [13]

(1) Death within the first month.
(2) Vegetative state.
(3) Severe disability—conscious but requiring constant supervision.
(4) Moderate disability—neurological impairment, but independent.
(5) Good recovery—leading an independent life, with or without minimal neurological impairment.

Poor outcome was defined as death or functional deterioration of one or more points on the GOS among survivors at discharge when compared with pre-admission states.

2.2. Statistical analysis

The data were analyzed by Statistical Package for Social Sciences (SPSS) Version 20. Categorical variables were compared by Chi-square test or Fisher's exact test where appropriate Continuous variables were analyzed with independent-sample *t*-test and Mann-Whitney-*U* test, respectively for parametric and non-parametric data. A p value of <0.05 was considered to be statistically significant. All p-values were 2-sided.

Table 1
Clinical characteristics of study subjects ($n = 87$).

Age, mean (SD)	49.3 (14.9)
Male, *n* (%)	48 (56.3%)
Previous history of epilepsy, *n* (%)	29 (33.3%)
Clinical manifestations of status epilepticus, *n* (%)	
Convulsive status epilepticus (CSE)	78 (90.0%)
Non-convulsive status epilepticus (NCSE)	9 (10.0%)
Presumed etiologies of status epilepticus, *n* (%)	
Breakthrough seizure	18 (21.0%)
Encephalitis/meningitis	16 (18.3%)
Cerebrovascular accident	10 (11.5%)
Metabolic causes	9 (10.3%)
Drug overdose/alcohol withdrawal	7 (8.0%)
Hypoxic brain damage	6 (6.9%)
Sepsis	4 (4.6%)
Traumatic subarachnoid hemorrhage/subdural hemorrhage	4 (4.6%)
Idiopathic	13 (14.9%)

SD, standard deviation.

3. Results

3.1. Clinical characteristics

The clinical characteristic of subjects is presented in Table 1. Eighty-seven cases were identified over the study period. The mean age of subjects was 49.3 years (SD 14.9 years). Forty-eight subjects (56.3%) were male. Forty-eight (56.3%) subjects had history of epilepsy. Seventy-eight subjects (89.7%) had convulsive status epilepticus while 9 subjects (10.3%) had non-convulsive status epilepticus on presentation. Eighteen subjects (20.7%) had breakthrough seizure, which was the most common etiology for status epilepticus in the study cohort. Anti-epileptic drug level was checked in 86% of cases, in which low AED level was confirmed in 59.1% of cases. Among the nine cases with confirmed low AED level, two of them were secondary to recent medication titration and the remaining cases were due to poor drug compliance. The other causes of SE included central nervous system infection ($n = 16$, 18.4%), cerebrovascular accident, either acute symptomatic and chronic ($n = 10$, 11.5%), metabolic causes ($n = 9$, 10.3%), drug overdose/alcohol withdrawal ($n = 7$, 8.0%), hypoxic brain damage ($n = 6$, 6.9%), traumatic subarachnoid hemorrhage/subdural hemorrhage and sepsis ($n = 4$, 4.6%). No identifiable cause was found in 13 subjects (14.8%) (Table 2).

3.2. Treatment profiles

Thirty-seven subjects (42.5%) received a single anti-convulsant for seizure control while 28 subjects (32.2%) received two

Table 2
Mortality and outcomes of patients with various etiologies of status epilepticus.

	Total SE cases, *n* (%)	30-day mortality, *n* (%)	Poor outcome on discharge, *n* (%)
All etiologies	87 (100%)	16 (18.4%)	40 (46%)
Breakthrough seizure	18 (21.0%)	0 (0%)	2 (11.1%)
Encephalitis/meningitis	16 (18.3%)	3 (18.8%)	7 (43.8%)
Cerebrovascular accident	10 (11.5%)	2 (20.0%)	6 (60.0%)
Metabolic cause	9 (10.3%)	3 (33.3%)	5 (55.6%)
Drug overdose/alcohol withdrawal	7 (8.0%)	1 (14.3%)	4 (57.1%)
Hypoxic brain damage	6 (6.9%)	2 (33.3%)	6 (100%)
Traumatic SAH/SDH	4 (4.6%)	2 (50.0%)	3 (75.0%)
Sepsis	4 (4.6%)	2 (50.0%)	3 (75.0%)
Idiopathic	13 (14.8%)	–	–

SE, status epilepticus; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage.
(–) Data not available.