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Comparison of pediatric patients with status epilepticus lasting 5–29 min versus ≥30 min

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ABSTRACT

The most common thresholds for considering prolonged seizures as status epilepticus (SE) are 5 and 30 min. It is unknown whether these different thresholds (5 or 30 min) identify patient populations with different electroclinical characteristics. We compared the characteristics of patients with SE lasting 5–29 min (SE_{5-29}) with those with SE lasting ≥30 min ($SE_{\geq 30}$). Inclusion criteria were the following: 1) 1 month to 21 years of age at the time of SE, 2) convulsive seizures, and 3) seizure duration ≥5 min. Exclusion criteria were the following: 1) exclusively neonatal seizures, 2) psychogenic nonepileptic seizures, or 3) incomplete information about seizure duration. Four hundred forty-five patients (50.1% male) with a median (p_{25}–p_{75}) age at SE of 5.5 (2.8–10.5) years were enrolled. Status epilepticus lasted for 5–29 min in 296 (66.5%) of subjects and for ≥30 min in 149 (33.5%). Patients with $SE_{\geq 30}$ were younger than the patients with SE_{5-29} at the time of seizure onset (median: 1 versus 2.1 years, $p = 0.0007$). Status epilepticus as the first seizure presentation was more frequent in patients with $SE_{\geq 30}$ (24.2% versus 12.2%, $p = 0.002$). There was a tendency towards a higher rate of abnormalities in the magnetic resonance imaging at baseline in patients with $SE_{\geq 30}$ (70.5% versus 57.1%, $p = 0.061$). Differences were not detected in seizure frequency, seizure types, presence of developmental delay, and electroencephalogram abnormalities at baseline. In the pediatric population, SE thresholds of either 5 or 30 min identify groups of patients with very similar electroclinical characteristics, which may influence future definitions of pediatric SE.

1. Introduction

The classical definition of status epilepticus (SE) or "established" SE requires that seizures last for a minimum of 30 min [1]. This definition has been widely used in the literature. However, when seizures last longer than 5 min, they are unlikely to stop spontaneously both in adults and in children [2,3] and meet the definition of "impending" SE [4]. At present, both definitions of SE (with a threshold seizure duration of 5 and 30 min) coexist in the literature, but there is a striking lack of data comparing the characteristics of "impending" SE versus "established" SE [5]. A series of 226 patients (135 adults and 91 children) with prolonged seizures compared the characteristics of "impending" and "established" SE [5]. However, in this study, the characteristics of the 91 pediatric patients were analyzed together with those of the 135 adult patients [5]. Therefore, there is the need to evaluate whether the different thresholds for SE duration (5 or 30 min) identify patient populations with different electroclinical characteristics.

This study aimed to address this gap in knowledge by describing and comparing the electroclinical characteristics of pediatric patients with a SE duration of 5–29 min (SE_{5-29}) to those with a SE duration of ≥30 min ($SE_{\geq 30}$).

2. Patients and methods

2.1. Study characteristics, design, and setting

This study was approved by the Institutional Review Board of Boston Children's Hospital, and, therefore, has been performed in accordance

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with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This was a retrospective descriptive cohort study of pediatric patients presenting with seizures of at least 5 min in duration at a tertiary referral pediatric hospital.

2.2. Participants

Charts of patients admitted to the hospital for seizures from January 1st, 2005 to December 31st, 2010 were screened. Patients were identified through two different word search mechanisms of our electronic medical records. The search terms "seizure", "status epilepticus", "convulsions", and "epilepsy" were used in the reason for admission, discharge diagnoses, and body of the clinical documents. Inclusion criteria were the following: 1) 1 month to 21 years of age at the time of a SE episode, 2) convulsive seizures at onset of SE, and 3) seizure duration of at least 5 min. Exclusion criteria were the following: 1) exclusively neonatal seizures, 2) psychogenic nonepileptic seizures or seizures of unclear epileptic nature, and 3) SE with incomplete or unclear information about seizure duration.

If a patient presented with an episode of ≥30 min during the study period, that patient was considered to belong to the $SE_{\geq 30}$ group regardless of whether this patient had a seizure of 5 to 29 min at any other time during the study period. Both single continuous prolonged seizures and repetitive seizures without return to baseline were considered as SE as long as they met the threshold duration. Both focal and generalized seizures were considered SE as long as they met the threshold duration.

2.3. Clinical variables

Demographic and clinical variables included age at seizure onset, age at SE, seizure frequency, number of antiepileptic drugs, seizure semiology at baseline, and EEG and magnetic resonance imaging (MRI) results.

2.4. Assessments

The main exposure was duration of seizures stratifying by 5 or 30 min. Based on the two subgroups defined by these two seizure duration thresholds, the outcome measures, electroclinical characteristics, were compared in subjects with SE_{5-29} versus those with $SE_{\geq 30}$.

2.5. Statistical analysis

On univariate analysis, categorical variables were compared with Fisher's exact tests, and continuous variables were compared with Wilcoxon rank-sum tests. On multivariate analysis, the influence of seizure duration on death was evaluated controlling for potential confounders. All tests were performed at a "two-sided" significance level of 0.05. For all statistical analyses, STATA 12.0 (Stata Corp., College Station, TX, USA) was used.

3. Results

3.1. Demographic and clinical characteristics

Four hundred forty-five patients with a median age at SE of 5.5 years were included. Status epilepticus lasted for 5–29 min in 296 (66.5%) patients and for ≥30 min in 149 (33.5%). The specific duration of SE is presented in Fig. 1. Patients with $SE_{\geq 30}$ were younger at the time of seizure onset and at the time of the SE episode. After stratification by SE type (febrile versus nonfebrile SE), the differences in age at the first seizure persisted for the group with nonfebrile SE. In contrast, stratification by SE type showed that the differences at the age of the SE episode were reflecting the different distributions of febrile SE in the comparison groups. Additionally, patients with $SE_{\geq 30}$ more frequently presented SE as the first seizure presentation compared to patients with SE_{5-29}. After stratification by febrile versus nonfebrile SE, the predominance of SE as the first seizure presentation for the $SE_{\geq 30}$ group remained marginally significant for the nonfebrile SE group. Etiologies were different between the two groups. Three hundred thirty-three patients had a prior diagnosis of epilepsy, 246 of whom were on treatment without a difference in duration 5–29 or ≥30 min between those treated and those not treated at baseline. Details are presented in Table 1.

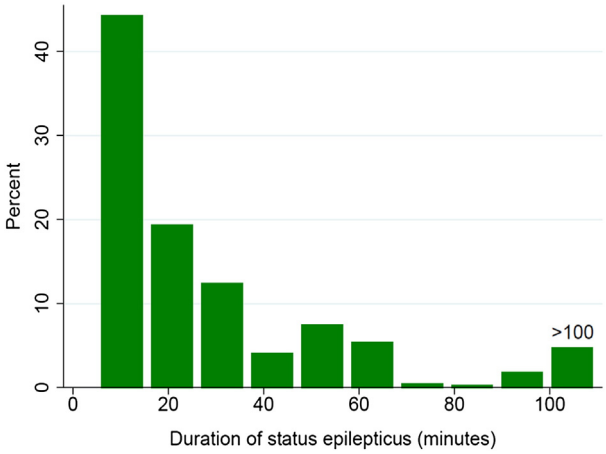

Fig. 1. Bar graph representing the percentage of cases within each seizure duration category. The last column includes all cases with seizure duration of more than 100 minutes.

3.2. Electroencephalographic findings

An EEG was performed prior to SE in 252 patients, with the baseline being abnormal in 218 (86.5%). The most frequent EEG abnormalities were generalized, and the most frequent types of abnormalities were spikes and nonepileptiform abnormalities such as slowing or asymmetries. There was no difference between patients with SE_{5-29} and patients with $SE_{\geq 30}$. Details are presented in Table 2.

3.3. MRI findings

An MRI was performed in 227 patients prior to the SE episode, being abnormal in 140 (61.7%). Among the abnormalities found in the MRI, most were bilateral, the most frequent localization was in the temporal lobe, and this site was observed to be more common in patients with SE_{5-29} than in patients with $SE_{\geq 30}$. The most frequent type of MRI abnormality was volume loss. Details are presented in Table 3.

3.4. Outcomes

Patients were followed up for a median of 3.7 years after SE. Twenty-one patients (4.7%) died, with a median time of 3.1 years from SE until death, and most of these deaths were unrelated to epilepsy (Table 4). Using logistic regression considering death as the primary outcome and duration of SE as the predictor and controlling for duration of follow-up, every additional minute of SE duration increased the odds ratio of dying by 0.005 (Online Table 1). When controlling for both duration of follow-up and age, this association persisted and also showed an increase of 0.005 in the odds of dying per minute of SE duration (Online Table 2). When controlling for duration of follow-up, age, and etiology, this association persisted and showed an increase of 0.004 in the odds of dying per minute of SE duration (Online Table 3). The increase in mortality with increasing duration of SE does not appear to be secondary to an outlier effect as shown by the progressive increase in the proportion of mortality across all SE durations (Fig. 2 and Table 5).