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Factors influencing the duration of generalized tonic–clonic seizure

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ABSTRACT

Purpose: This study investigated the duration of generalized tonic–clonic seizure (GTCS) and the factors that prolong GTCS duration.
Method: We retrospectively analyzed clinical data collected from a consecutive group of patients who underwent video-electroencephalography (EEG) and experienced at least one GTCS during monitoring. Each seizure was divided into seven phases. The duration of GTCS was defined as the comprehensive duration of each GTCS phase, particularly those of Phase 3 to Phase 7.
Results: The mean GTCS duration per patient was 74.6 s. The results indicated that patients with an age of seizure onset <2 years exhibited a significantly longer duration than those with an age of seizure onset >2 years ($p = 0.033$). A significant difference was also observed in the duration of GTCS between wakefulness and sleep (wakefulness 76.2 ± 38.5, sleep 66.3 ± 27.8, $p = 0.017$). Our data suggest no significant differences between primary and secondary GTCS. The correlations between the duration of GTCS and many risk factors were also analyzed, including gender, age, neurological examination, cognitive status, family history of epilepsy, location of MRI brain abnormalities, reported seizure frequency at time of admission, number of current AEDs, history of SE, and duration of epilepsy.
Conclusions: The mean duration of GTCS was < 2 min. The age of seizure onset and the circadian pattern of seizure are the major factors influencing the duration of GTCS.
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1. Introduction

For patients suffering from epilepsy, ictal hypoxemia, prolonged partial complex seizures, and tapered antiepileptic drugs (AEDs), generalized tonic–clonic seizure (GTCS) is a critical risk factor for sudden death [1]. The longer a seizure lasts, the greater the damage to a patient will be.

Several studies have been conducted to determine the seizure duration and its pathological significance. Jenssen et al. compared the electroclinical duration of seizures in patients undergoing scalp video-electroencephalography (EEG) recordings. The median durations of the tonic–clonic phase in secondary and primary GTCS were 74 s and 66 s, respectively, but the difference was not significant [2]. Two other studies have shown different mean durations of GTCS (64 s and 52.9 s, respectively) [3,4]. Furthermore, major differences have been observed between adult and pediatric seizures: the total seizure duration, the tonic phase, and the recovery phase are significantly shorter in child patients than in adults [5]. Despite these findings, the potential factors affecting the duration of GTCS have not been thoroughly elucidated. Therefore, this study aimed to reveal factors that would prolong the duration of GTCS.

2. Methods

2.1. Patient selection

We studied a consecutive group of patients who underwent video-EEG and experienced at least one GTCS during monitoring from January 2009 to December 2009. Patients were excluded due to missing data (no recorded seizures) or because the patient's GTCS was evolving into status epilepticus (SE). A total of 153 patients were enrolled in our study and analyzed.

Clinical data from patients who satisfied the preceding criteria were reviewed. The following data were collected and processed: age at administration, gender, cognitive status (normal/borderline vs. mentally retarded), family history of epilepsy, age at seizure onset, duration of epilepsy, history of SE, neurologic examination, circadian onset of seizure (wakefulness/sleep), location of brain abnormalities [temporal lobe, frontal lobe, parietal and occipital

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lobe, multiple lobes, and normal, as determined by high-resolution magnetic resonance imaging (MRI)], quantity of prescribed AEDs at the time of admission, and baseline seizure frequency (categorized as daily, less than daily to monthly, or less than monthly) in the preceding 12 months.

2.2. Seizure selection

A total of 310 cases of GTCS were analyzed. Considering that closely spaced seizures could influence the duration of their subsequent seizures, we excluded those seizures occurring within 60 min after the previous seizure. Cases in which AEDs were administered intravenously were excluded to eliminate interference from the drug administration method on seizure duration. We also excluded seizures which developed into status epilepticus. Ultimately, a total of 275 GTCS were included in the research.

2.3. Video-EEG monitoring

A 10–20 electrode placement system with additional sphenoidal electrodes or anterior temporal electrodes (if necessary) was used in a 64-channel acquisition system. Video recordings were continuously performed by digital cameras throughout the day. Photic stimulation and hyperventilation were applied to all of the patients. AEDs were tapered in patients with pre-surgical evaluation. Specific patterns, such as history of SE, seizure frequency, and seizure severity, were considered.

2.4. Durations and phases of GTCS

Seizures were divided into seven phases, depending upon presentence of antecedent seizure (usually complex or simple partial) and the integrity of rGTCS. The first two phases were classified as antecedent seizure and the next five phases were classified as complete or fragmentary GTCS. Among them, Phase 1 was classified as simple partial seizure. Phase 2 consisted of one of the four seizure types, namely, complex partial, clonic, tonic, or absence seizures. (Complex partial seizure was characterized by localized signs or symptoms with altered consciousness. Clonic seizure was characterized by rapid onset of bilateral clonic jerk, which may be asymmetric. Tonic seizure was characterized by sudden onset of increased tone, usually symmetric and involving the trunk. The absence of seizure was characterized by an alteration in consciousness and a range of associated clinical phenomena.) Phase 3 was the onset of generalization and was characterized by versive head/body movement and vocalization. Phase 4 was the pre-tonic/clonic stage between the end of the versive head movement and the onset of the bilateral, symmetrical tonic extension. Phases 5–7 were characterized as the tonic, tremulous and clonic stages of one seizure, respectively [3]. Therefore, the total duration of GTCS was a comprehensive sum of each GTCS stage's time span, which was counted from Phases 3 to Phase 7 during one seizure.

2.5. Semiology analysis

Video records were analyzed by two independent observers who were blinded to patients' clinical history, diagnosis, and other relevant data. The duration of each phase was measured according to the criteria we set up above.

2.6. Statistical analysis

Statistical analysis was performed with binomial testing using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Correlations with duration of GTCS were examined using one-way ANOVA for categorical data; two-tailed $p < 0.05$ was considered statistically significant. Post hoc analysis was performed to compare significant correlations. Variables with significant correlation were subsequently subjected to linear regression analysis.

3. Result

A total of 275 seizures satisfied our inclusion criteria. The mean ± SD of GTCS duration per patient was 74.6 ± 37.6 s. Every GTCS had either a tonic or a clonic phase. The proportion of seizures including Phase 1 (simple partial) was 21%. The ratio was 60.7% for Phase 2 (complex partial or clonic or tonic or absence), 51.3% for Phase 3 (onset of generalization), 23.6% for Phase 4 (pre-tonic clonic), 75% for Phase 5 (tonic), and 100% for Phase 6 or 7 (clonic). Only 12% had all five GTCS phases (3 through 7) (Fig. 1).

Based upon the phase when a seizure was triggered, seizures were classified into a primary GTCS group (seizures beginning in Phases 1 and 2) and a secondary GTCS group (seizures beginning in Phases 3–7). No significant differences were observed between the durations of the two groups (primary GTCS 67.2 ± 26.8, secondary GTCS 73.4 ± 36.4, $p = 0.365$).

A total of 153 patients who satisfied our inclusion criteria were identified. Table 1 shows the following patient characteristics: age at administration, gender, cognitive status, family history of epilepsy, age at seizure onset, duration of epilepsy, history of SE, MRI brain abnormalities, and other characteristics.

The duration of GTCS did not correlate with gender ($p = 0.6$), age ($p = 0.55$), neurologic examination ($p = 0.73$), cognitive status ($p = 0.50$), family history of epilepsy ($p = 0.34$), location of MRI brain abnormalities ($p = 0.71$), reported seizure frequency at time of admission ($p = 0.54$), number of current AEDs ($p = 0.29$), GTCS recorded per patient during monitoring ($p = 0.46$), history of SE ($p = 0.24$), or duration of epilepsy ($p = 0.80$).

In contrast, age at seizure onset correlated with the duration of GTCS ($p = 0.033$). Age at seizure onset was classified as 0–2, 3–7, 8–13, or >14 years. The statistics of each classified group are shown in Table 2. Among the groups, Groups 0–2 showed the longest duration (mean = 88.3 s), which significantly differed from Groups 3–7 ($p = 0.015$), 8–13 ($p = 0.033$) and >14 ($p = 0.015$). On the other hand, no significant difference was noted among the other groups (Groups 3–7 vs. Groups 8–13, $p = 0.774$; Groups 3–7 vs. Group >14, $p = 0.890$; Group >14 vs. Groups 8–13, $p = 0.682$). As we divided the seizures into different phases, the durations of different phases in different age at seizure onset groups are shown in Table 3. In Phases 6 and 7, Groups 0–2 showed the longest duration and also significantly differed from Groups 3–7 ($p = 0.030$), Groups 8–13 ($p = 0.156$) and Group >14 ($p = 0.023$). However, in other phases, there were no such significant differences noted among the groups.

A circadian pattern of seizure was observed. A total of 153 (56%) seizures occurred in wakefulness and 122 (44%) occurred during sleep. The duration of GTCS significantly differed between wakefulness and sleep groups (wakefulness 76.2 ± 38.5, sleep 66.3 ± 27.8, $p = 0.017$).

4. Discussion

The present study examined the duration of GTCS and the factors that prolong GTCS duration seizure in 153 patients. Our findings indicated that the mean GTCS duration per patient was 74.6 s and the duration of seizures with onset age of <2 years were significantly longer than those with onset age of >2 years. A significant difference was also observed in the GTCS duration between the wakefulness and sleep status of patients. However, no correlation between GTCS duration and other clinical parameters (e.g., gender and gender) was observed. Similarly, no significant difference was noted between primary GTCS and secondary GTCS.

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