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Mortality in patients with refractory temporal lobe epilepsy at a tertiary center in Cuba

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ABSTRACT

Objectives: We aimed to investigate the prevalence and risk of mortality in patients with refractory temporal lobe epilepsy.
Methods: Eligible patients included all adults referred to the National Institute of Neurology (NIN) in Havana, Cuba. All patients were followed up for 9 years. All analyses were made with the data available at the last follow-up. The frequency of death related to refractory TLE was analyzed taking into account the total number of patients included in the study. We analyzed the causes of death for each case. Multivariate analysis was made to determine the specific variables related to the death. All values were statistically significant if $p < 0.05$.
Results: Six out of 117 patients died during follow-up. Fifty percent of patients died because of suicide. Only the presence of aura, specifically experiential psychic auras, and prodromal depressive disorders were associated significantly with the deaths ($p < 0.05$). Patients who died had a higher concern about their seizures than patients who were still alive at last follow-up ($p < 0.01$); they also had a poor perception of the overall QOL ($p < 0.01$); and they were more concerned about the possible medication side effects than patients who did not die ($p < 0.05$). Logistic regression provided only one variable related to the deaths in our cohort in multivariate analysis: presence of prodromal depressive disorder.
Conclusion: The causes of death in patients with refractory temporal lobe epilepsy were similar to those documented in the general population of patients with epilepsy.

1. Introduction

Temporal lobe epilepsy (TLE) is the most frequently seen epileptic syndrome in a tertiary center. Multiple studies have encountered an increased rate of deaths in patients with this syndrome because of suicide, accident, and sudden death [1–5]. More than 30% of patients with TLE suffer from psychiatric disorders, many of their seizures have a marked autonomic component [6], and most of them have secondarily generalized tonic–clonic seizures. All of these variables have been associated with an increased risk of death through different pathogenic mechanisms [1,6–8]. Nevertheless, the possible causes of death in patients with TLE need to be clarified. To our knowledge, few studies have addressed this topic in Latin American countries, and in Cuba, none has been conducted. Knowing the epidemiological status concerning mortality in TLE could enhance general health strategies to prevent these deaths.

Thus, the object of this work was to investigate the prevalence and risk of mortality in a 9-year outpatient population of 119 individuals with TLE. To evaluate this, we compared patients with refractory TLE who died and patients with refractory TLE who were still alive during this 9-year follow-up.

2. Methods

Eligible patients included all adults referred to the National Institute of Neurology (NIN) in Havana, Cuba — a tertiary epilepsy center — from May 1st, 2004 to November 6th, 2013. The NIN tertiary center is one of three of its kind in Cuba, which has a population of nearly 12 million inhabitants.

Patients were included in the study if: 1) they were diagnosed with refractory TLE after the evaluation, and 2) they were between the ages of 18 and 65 years at the time of enrollment. The diagnosis of epilepsy and TLE were made according to the ILAE criteria.

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As seizures of all patients were refractory to antiepileptic drugs (AEDs), they were included in our epilepsy surgical program. At some point during the 9-year follow-up, all patients were admitted to the video-electroencephalogram (VEEG) department, and their evaluation included a complete presurgical assessment according to our hospital protocols (video-electroencephalography monitoring TV recording, volumetric brain MRI at 1.5 T, and neuropsychological evaluation). Neuropsychological evaluation always included an intellectual quotient (IQ) and evaluation using the Wechsler Adult Intelligence Scale (WAIS).

The epileptologists (RAM, AGA) characterized the type of epilepsy and epileptic foci based on past medical history, neurological exam, neuropsychological evaluation, VEEG data, and brain MRI.

They also established if the patient had refractory epilepsy, which was defined as uncontrolled epilepsy despite trials of two or more appropriate antiepileptic drugs at the highest tolerated dose. The seizure type was classified according to VEEG analysis and based on the ILAE classification of epilepsy.

A psychiatrist (AGE) trained in epilepsy evaluated the psychiatric comorbidities when patients were in the video-EEG unit or when any psychiatric symptom emerged during the follow-up. The diagnosis of an affective disorder or a psychotic disorder was clinically based. The Spanish version of the Mini-International Neuropsychiatric Interview scale (MINI) was applied in order to standardize the clinical interview, as the MINI is a well-recognized instrument to explore psychiatric symptoms in patients with epilepsy (PWE). Subsequently, the psychiatrist and the epileptologists classified the neuropsychiatric conditions as peri-ictal, interictal, ictal, or postictal according to the temporal relationship to seizure occurrence and the clinical symptomatology following the ILAE proposals [9]:

Interictal psychosis:

a) Psychosis characterized by strong affective components, but usually without affective flattening.
b) Personality and affection were preserved.
c) Psychotic features were usually independent of seizures.

Alternative psychosis:

a) This diagnosis was considered when a patient alternated between periods of clinically manifest seizures and normal behavior, and other periods free of seizures but with behavioral disturbances.
b) If EEG confirmation was available, the diagnosis qualified further as "with or without forced normalization of the EEG".

Postictal psychosis:

a) This psychosis was diagnosed when postictal symptoms emerged following a cluster of seizures (rarely single seizures) usually after a 24- to 48-hour period of relative calm.
b) These episodes could last from a few days to several weeks.
c) Confusion and amnesia could be present, but this category was excluded in patients with postictal confusion and nonconvulsive status with psychiatric manifestations.

Affective-somatoform (dysphoric) disorders of epilepsy:

a) This diagnosis was made after reviewing the MINI and taking into account the clinical evaluation carried out by the psychiatrist.
b) The following symptoms should be present: irritability, depressive moods, anergia, insomnia, atypical pains, anxiety, phobic fears, and euphoric moods.
c) Three of these symptoms might occur at various intervals and tended to last from hours to 2 or 3 days, although they might last longer and cause significant disability.

Affective disorders were classified according to their temporal relation to seizure activity as follows: interictal dysphoric disorder and prodromal dysphoric disorder, postictal dysphoric disorder was not evaluated. Affective symptoms lasting 72 h before or after seizures were considered as peri-ictal affective disorder. Note that prodromal symptoms can be considered as peri-ictal symptoms.

Alternative affective disorder:

Depression or anxiety symptoms in a patient who alternates between periods of clinically manifest seizures and normal behavior, and other periods free of seizures accompanied by a behavioral disturbance.

The diagnosis of alternative affective disorder could be made without the EEG. If EEG confirmation was available, the diagnosis qualified further as "with or without forced normalization of the EEG".

As prodromal and postictal psychiatric symptoms subsided relatively earlier and most of them could not be observed by the authors of this paper, the diagnosis of these episodes was based on the clinical interviews obtained from a reliable witness or, in certain cases, were retrieved by reviewing the clinical records in the hospital where they were assisted.

Suicide risk was evaluated by using the MINI (Spanish version) suicidal module that specifies the current suicide risk based on scores. The scale scores from 1 to 33. Scores from 1 to 5 suggest low risk, scores in the range of 6–10 suggest moderate risk, and scores >10 suggest high risk. The psychiatrist applied this scale when the patient had a depressive disorder or discussed any suicidal thoughts with the epilepsy team.

The psychiatrist also administered the Hamilton Depression Rating Scale (HDRS), and results were analyzed in order to rate the severity of the affective disorder. According to the scoring, the depressive disorder was classified as: mild (8–15), moderate (16–23), or severe (>23). The HDRS was administered during enrollment, if the patient or the family reported depressive symptoms and when the patient was evaluated for epilepsy surgery.

Quality of life (QOL) was evaluated with the Spanish version of the Quality of Life in Epilepsy Inventory-31 survey (QOLIE-31), which has been previously validated in Cuba [10]. Evaluation with the QOLIE-31 was carried out in the video-EEG monitoring department by the epilepsy team. Patients were assessed in the video-monitoring TV recording unit. The survey evaluated seven dimensions: seizure worry, overall QOL, emotional well-being, energy/fatigue, cognitive function, medication effects, social function, and overall score. The scores vary from 1 to 100, with higher scores indicating a better QOL. The mean completion time was 22 min. A total score was also obtained for each patient. An adequate QOL was considered if the patient's overall result was higher than 60 points, and inadequate if otherwise. All dimensions were taken into account for the analysis.

After the abovementioned evaluation, the following information was obtained from all patients at some point during their follow-up: 1) sociodemographic data: age, gender, education level, occupational situation, marital status, and presence of children; 2) clinical data: age of onset, type and frequency of epileptic seizures (ES), duration of epilepsy, and use of AED; 3) data concerning the psychiatric diagnosis (reviewing complete structured interview using MINI and HDRS); and 4) QOLIE-31 results.

2.1. Information related to deaths

The follow-up and registration of the patients were strictly carried out through three pathways: 1) All of the patients with epilepsy had a follow-up every 3 months in the outpatient clinic, and each epileptologist had a list of all the cases that should be evaluated every week. Patients who did not attend the appointments were contacted by them learn the reason for their absence. 2) All patients with TLE assisted at the NIN are listed in a specific database in order to have a video monitoring recording as part of presurgical evaluation for epilepsy surgery. An appointment was made with all of them, and the clinical