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Gender differences in prevalence of psychiatric disorders, levels of alexithymia, and coping strategies in patients with refractory mesial temporal epilepsy and comorbid psychogenic nonepileptic seizures

Amanda Cristian Serafim de Barros, Ana Eliza Romano Furlan, Lucia Helena Neves Marques, Gerardo Maria de Araújo Filho *

Faculdade de Medicina de São José do Rio Preto (FAMERP), Brazil

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ABSTRACT

Objective: The objective of this study was to investigate the psychological aspects and psychiatric disorders (PDs) in patients dually diagnosed with refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) with psychogenic nonepileptic seizures (PNES) treated in a tertiary center in order to find any gender differences in psychiatric, clinical, and sociodemographic characteristics.
Method: Psychiatric assessment was performed through the Diagnostic and Statistical Manual for Psychiatric Disorders — 5th edition (DSM-5). The Brazilian versions of the Medical Outcomes Study 36 (SF-36), Toronto Alexithymia Scale (TAS-20), Hamilton Depression Scale (HAM-D), Hamilton Anxiety Scale (HAM-A), and Ways of Coping Checklist (WCC) were applied.
Results: Of the 47 patients enrolled (25 females; 53.2%), females were significantly more likely to have a history of previous psychiatric treatment ($P = 0.02$), family history of epilepsy ($P = 0.01$), and family history of PD ($P = 0.03$). They also presented earlier onset of PNES ($P = 0.01$) and higher PNES duration ($P = 0.02$) compared with males. Major depressive disorder (MDD) was the most frequent PD (24; 51.0%). Females presented more psychiatric diagnoses ($P < 0.001$), more diagnoses of MDD ($P < 0.001$), and posttraumatic stress disorder (PTSD) ($P < 0.001$). Several differences regarding quality of life, levels of alexithymia, anxiety/depressive symptoms, and coping strategies were observed between groups.
Conclusions: There are significant gender differences in psychiatric, clinical, and sociodemographic aspects in a group of patients with TLE-MTS and PNES, as well as in quality of life, levels of alexithymia, anxiety/depressive symptoms, and coping strategies. These gender differences suggest that specific approaches might be adopted depending on the patient's gender and, consequently, their distinct psychological/psychiatric profile.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are paroxysmal episodes superficially resembling epileptic seizures, but they are not associated with any electrical abnormalities [1–3]. Although PNES are a clinically heterogeneous group, most patients fulfill the diagnostic criteria of a functional neurological symptom (conversion) disorder (Diagnostic and Statistical Manual for Psychiatric Disorders — 5th edition (DSM-5)) or of dissociative convulsions (International Classification of Diseases — 10th revision (ICD-10)) [4,5]. Moreover, those patients frequently present other psychiatric disorders (PDs), such as mood and/or anxiety disorders. Patients with PNES represent an important subpopulation for epilepsy specialists because they require and can benefit from the differentiated diagnostic procedures these professionals provide. In addition, since most patients with PNES can be initially misdiagnosed as having epilepsy, specialists need their assistance and knowledge to diagnose PNES and manage the treatment [1,2,6]. It is believed that up to 20 or 30% of patients referred with apparently antiepileptic drug-refractory epilepsy receive a diagnosis of PNES after expert evaluation in tertiary epilepsy centers [1–3,6].

Temporal lobe epilepsy (TLE) is one of the most frequent epilepsy syndromes (ESs) and the most frequent ES found in patients with medically refractory epilepsy, especially among those followed up in tertiary epilepsy centers. Mesial temporal sclerosis (MTS) is the most frequent etiology of TLE observed among those patients. It compromises the primary structures of the limbic system, particularly the hippocampus and amygdala, and is associated with cognitive deficits, PDs, and a lower quality of life [7–10].

Although a number of studies have already found gender differences in sociodemographic, clinical, psychological, and behavioral aspects

* Corresponding author at: Av. Brigadeiro Faria Lima, 5416 – Nova Redentora, São José do Rio Preto, SP 15090-000, Brazil.
E-mail address: filho.gerardo@gmail.com (G.M. de Araújo Filho).

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among patients with PNES [7–10], there is a scarcity of data regarding possible gender differences in psychiatric diagnoses, especially in patients with dual diagnoses. The main objective of the present study was to investigate possible gender differences in sociodemographic, clinical, and psychiatric characteristics, as well as the presence and degree of alexithymia, anxiety/depression symptoms, and quality of life in a group of patients dually diagnosed with refractory TLE-MTS with comorbid PNES treated in a tertiary center.

2. Methods

2.1. Patients

At the time this study was conducted, 385 patients were being treated in a tertiary epilepsy center (outpatient epilepsy clinic of Faculdade de Medicina de São José do Rio Preto — FAMERP), 97 (25.1%) of whom had PNES. Of these, 47 patients (12.2%) fulfilled the clinical inclusion criteria, which were age 18 to 65 years, dual diagnoses of TLE-MTS and PNES confirmed through video-electroencephalography (VEEG), clear magnetic resonance imaging (MRI) findings consistent with MTS, presence of a psychiatric evaluation performed by one of the authors (GMAF), and having been treated for at least one year at the epilepsy clinic of FAMERP. Exclusion criteria were cognitive impairments preventing them from answering the questionnaires and the presence of epileptic syndromes other than TLE-MTS or only PNES at neurological evaluation. After the study was approved by the local ethics committee, all 47 patients were included.

2.2. Procedures

All 47 patients underwent 2–6 days of continuous VEEG monitoring with 32-channel EEG recording. Mesial temporal sclerosis was defined as the presence of atrophy, an increased T2-weighted signal, a decreased T1-weighted signal, and disrupted internal structure of the hippocampus along with atrophy of the amygdala and/or temporal pole signal alteration on visual inspection of MRI pictures. Refractoriness to medical treatment was defined as seizures persisting after the utilization of at least two first-line medications for partial seizures at the highest tolerated doses for at least six months. Initial precipitant injury (IPI) was defined as the occurrence of severe cerebral events in the first year of life before the appearance of epilepsy that required medical intervention and/or hospitalization. Febrile seizures, meningoencephalitis, head trauma, or severe perinatal hypoxia were considered IPI. Data regarding previous psychiatric treatment, family history of epilepsy, family history of PD, age of PNES onset, and PNES duration were collected from patients' files and/or through patient/family information.

2.3. Instruments

The enrolled patients underwent standard psychiatric assessment according to DSM-5 criteria [4] and were assessed with the Brazilian versions of the following instruments:

a) Medical Outcomes Study 36 (SF-36) [11]: This is a 36-item multidimensional questionnaire grouped into 8 domains: functional capacity, physical aspects, pain, general health, vitality, social aspects, emotional aspects, and mental health. It carries a final score of 0 to 100 (obtained by summing the raw scores), where 0 corresponds to the worst general health condition and 100 corresponds to the best health status;
b) Toronto Alexithymia Scale (TAS-20) [12–14]: This is a scale designed to measure the degree of alexithymia, defined as the inability to express distress, and somatization. The instrument examines three main domains: ability to identify and to describe feelings and to distinguish feelings of bodily sensations, ability to daydream, and preference for focusing on external events rather than inner experiences. Each item of the TAS-20 consists of a sentence that can be answered through a five-point Likert self-assessment tool: 1: I strongly disagree, 2: I disagree in part, 3: I do not agree or disagree, 4: I agree in part, and 5: I totally agree. The score indicated by the instrument ranges from 26 to 130. Values lower than 62 do not indicate symptoms of alexithymia, and values higher than 74 indicate the presence of these symptoms. Values between 63 and 73 are inconclusive.
c) Hamilton Depression Scale (HAM-D) [15,16]: This quantitatively estimates the level of the patient's depressive symptoms and measures the results of treatments. The most used HAM-D version consists of 17 items. Scores above 25 points are characteristic of severely depressed patients; scores between 18 and 24 points, moderately depressed patients; and scores between 7 and 17 points, patients with mild depression.
d) Hamilton Anxiety Scale (HAM-A) [17,18]: This emphasizes the somatic aspects of anxiety and measures aspects such as mood and cognitive and somatic symptoms. The score ranges from 0 to 56. A score of 17 or less indicates mild anxiety severity. A score from 18 to 24 indicates mild to moderate anxiety severity. Scores higher than 25 and 30 indicate moderate and severe anxiety symptoms, respectively;
e) Ways of Coping Checklist (WCC) [19,20]: This instrument identifies which types of coping strategies have been used by the individual in relation to specific stressors. The Brazilian version consists of 45 items with eight subscales that express cognition and behaviors to address stressful events. The answers are given on a five-point Likert scale (1 = I never do this, 2 = I do it a little, 3 = I do it sometimes, 4 = I do it a lot, and 5 = I do it always), with a maximum score of 20.

2.4. Statistical analysis

The collected data were distributed in the form of mean and standard deviation (discrete variables) or according to their presence or absence (categorical variables). Since multiple comparisons between groups were done, the results obtained were statistically analyzed through analysis of variance (ANOVA) with Bonferroni's *post hoc* test when necessary. A P value of <0.05 was considered significant.

3. Results

Data from all 47 patients (25 females; 53.2%) were included. Mesial temporal sclerosis occurred more frequently on the left side (29 patients; 61.7%). Twelve patients (25.5%) had a history of IPI, with febrile seizures being the most frequent (seven cases; 14.9%). All patients had used two or more antiepileptic drugs (AEDs); carbamazepine (CBZ) was the most frequent AED, being prescribed to 31 patients (65.9%). Benzodiazepines (BZD), particularly clobazam (CLB), were the most common adjunctive drugs, being prescribed to 23 patients (48.9%). Female patients significantly more often had a history of previous psychiatric treatment ($P = 0.02$), family history of epilepsy ($P = 0.01$), and family history of PD ($P = 0.03$). They also presented earlier onset of PNES ($P = 0.01$) and higher PNES duration ($P = 0.02$) compared with males. Clinical and sociodemographic data of patients are shown in Table 1.

Since all patients (100%) presented diagnostic criteria for functional neurological symptoms disorder (FNSD) according to DSM-5, this diagnosis was not included in our statistical analysis. Other PDs were observed in all of the 47 patients (100.0%); major depressive disorder (MDD) was the most frequent PD (24 patients; 51.0%), followed by anxiety disorders (22 patients; 46.8%), posttraumatic stress disorder (PTSD) (19 patients; 40.4%), psychotic disorders (five patients; 10.6%), and excoriation disorder (two patients; 4.2%). Female patients presented significantly more psychiatric diagnoses than males ($P < 0.001$), as well as more diagnoses of MDD ($P < 0.001$) and PTSD ($P < 0.001$). Twenty-three