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Outcome of patients with psychogenic nonepileptic seizures with limited resources: A longitudinal study

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ABSTRACT

Purpose: The aim of the current study was to investigate the long-term outcome of patients with psychogenic nonepileptic seizures (PNES) and factors potentially associated with their outcome in Iran.
Methods: We investigated all patients with PNES admitted to the epilepsy monitoring unit at the Shiraz Comprehensive Epilepsy Center from 2008 through 2013. Patients included in this study had a confirmed diagnosis of PNES. In a phone call interview to the patients in December 2017, we obtained the following information: seizure outcome (seizure-free during the past 12 months or not), history of receiving any psychotherapy after confirming their diagnosis in the past, and number of psychotherapy sessions the patient had received.
Results: Eighty-six patients (54 females and 32 males) met the inclusion criteria. Seventy-four (86%) patients did not receive appropriate psychotherapy. Forty-seven (54.7%) patients were seizure-free during the past 12 months. Age at onset (P = 0.02), education (P = 0.01), and taking psychiatric drugs (P = 0.007) were associated with this outcome.
Conclusions: Resources to treat patients with PNES are limited in Iran; however, more than half of the patients became free of seizures. Lower education, comorbid psychiatric problems, and a later age at the onset of seizures may affect the seizure outcome in patients with PNES. Well-designed multi-center cross-cultural long-term studies should address factors associated with outcome in patients with PNES, considering that seizure frequency should not be the only outcome measure.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are common occurrences in epilepsy inpatient and outpatient centers [1]. Unfortunately, misdiagnosis and delay in diagnosis are common in patients with PNES [2]. In addition, long-term studies suggest that many patients with PNES will continue to experience seizures despite receiving neurological and psychotherapeutic care [3]. In a systematic review [4], the prognosis of PNES in adults was shown to be poor. From their reviewed data, fewer than 40% of newly diagnosed adults could be expected to become seizure-free within 5 years after making a diagnosis of PNES [4].

Data on PNES and their outcome is scarce from the developing countries, where the resources are limited. Predictors of outcome are not well-characterized, particularly in the developing world, either. In one previous study from Iran [5], we observed that there were no significant differences between Iranian patients and Western patients with respect to the clinical and semiological characteristics of PNES. However, access to resources are limited in Iran and many other developing countries compared to that in the Western countries. Current best practice in the management of patients with PNES includes combined psychotherapy (e.g., cognitive behavioral therapy) and treatment of any psychiatric comorbidities [6]. In spite of that, access to appropriate psychotherapy is limited in many places in Iran (see the methods). The aim of the current study was to investigate the long-term seizure outcome of patients with PNES and factors potentially associated with their seizure outcome in Iran (a developing country with limited resources).

2. Patients and methods

The original data, on which the current study is elaborated, was published previously [5]. We investigated all patients with PNES admitted to the epilepsy monitoring unit at the Shiraz Comprehensive Epilepsy Center from 2008 through 2013. Patients

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included in the current study had a confirmed diagnosis of PNES, determined by clinical assessment and video-EEG monitoring with ictal recording of their seizures. We routinely refer all the patients with PNES to our psychologist, who is the only psychologist with expertise in delivering an appropriate care to these patients in the region, for further assessment and treatment plans [typically, cognitive behavioral psychotherapy (CBT)]. However, since there is not such a service in other cities (other than Shiraz) in the region and also because psychotherapy is not covered by insurance companies and patients have to pay 100% out of the pocket, many patients would not receive such therapy. We excluded patients with comorbid epilepsy, abnormal EEG, or insufficient data. We excluded the patients with abnormal EEG to make sure that none of the patients included in the study had epilepsy, despite the fact that some patients with PNES may have abnormal EEG (e.g., as a genetic trait) without having epilepsy.

We extracted all of the relevant clinical and demographic data from our database. We studied the following variables at the time of the diagnosis: gender, age at onset, age at referral, disease duration before making the definite diagnosis, education (less than college and college education), employment, marital status, seizure characteristics and semiology, risk factors for PNES [i.e., sex abuse, physical abuse, childhood abuse (neglect, forced child labor, etc.), head injury, dysfunctional family (problematic relationships, divorce, etc.), and family history of seizures; these factors are often being asked in a one-to-one interview of the patients by the treating epileptologist], receiving any psychiatric drugs (as an indication of suffering from psychiatric illnesses, since we did not perform a standard psychiatric evaluation in our patients), and receiving antiepileptic drugs (AEDs). From 2014 until 2017, our epilepsy center was not active, as the primary investigator of the current study, who is the only epileptologist at this center, was out of the country. We re-established our epilepsy center in 2017. We decided to perform this investigation by calling all the patients and inquiring about their seizure outcome, if they were available and agreed to participate. In a phone call interview to the patients in December 2017, we tried to obtain the following information: seizure outcome (seizure-free during the past 12 months or not), history of receiving any psychotherapy after confirming their diagnosis in the past, and number of psychotherapy sessions the patient had received.

We studied factors potentially associated with the seizure outcome using Pearson Chi-square, Fisher's exact, Mann-Whitney, and Kolmogorov-Smirnov tests. Variables that were significant in univariate tests were assessed in a logistic regression model. Odds ratio and 95% confidence interval (CI) were calculated. Receiver operating characteristic curve (ROC curve) was run to identify the best cutoff point and the discriminatory ability of the age at onset to correctly pick up patients who were seizure-free in their follow-up. P values less than 0.05 were considered significant. The Shiraz University of Medical Sciences Institutional Review Board approved this study.

3. Results

Of the 249 patients with PNES in our database, 111 patients had available contact numbers and were contacted. One patient refused to participate. Eighty-six patients (54 females and 32 males) met the inclusion criteria and were studied. Age of the patients at the onset of seizures was 24 ± 10 years (minimum = 6 and maximum = 67 years). Seventy-four (86%) patients did not receive appropriate psychotherapy (53 patients did not receive any and 21 patients received five or less sessions of CBT). Therefore, we did not include receiving CBT in our statistical analyses (only 12 patients received six or more sessions of psychotherapy; an arbitrary grouping compared with 13 sessions in CODES trial [7]). Forty-seven (54.7%) patients were seizure-free during the past 12 months and 39 (45.3%) patients were still suffering from seizures. Demographic and clinical characteristics of these two groups of patients (seizure-free vs. not) are shown in Table 1. We put the variables with a $P < 0.05$ in the univariate analyses (marital status, education, age at onset, and taking psychiatric drugs) in a logistic regression model to investigate their independent significance. The model was significant ($P = 0.0001$) and could correctly classify 73.3% of the patients. Later age at onset ($P = 0.02$; Odds ratio: 1.067; 95% confidence interval: 1.010–1.128), lower educational level ($P = 0.01$; Odds ratio: 0.152; 95% confidence interval: 0.034–0.681), and taking psychiatric drugs ($P = 0.007$; Odds ratio: 6.257; 95% confidence interval: 1.640–23.866) remained significant in the model. In ROC curve, area under the curve was 0.652 ($P = 0.01$) and the best cutoff point and the discriminatory ability of the age at onset was at 22 years to correctly pick up patients who were seizure-free in their follow-up (classifying ability was poor: sensitivity = 59% and specificity = 60%).

In an additional analysis, we selected the patients who did not receive any CBTs (53 patients); 39 patients (74%) were seizure-free. However, no factor was significantly associated with seizure outcome in this group of patients when we compared patients who

Table 1
Demographic and clinical characteristics of patients with psychogenic nonepileptic seizures (seizure-free vs. not).

	Seizure-free patients 47 (54.7%)	Patients with seizures 39 (45.3%)	P value
Sex (Female: Male)	29: 18	25: 14	1
Age at onset (years)	21 ± 8	27 ± 10	0.01
Duration of the condition before making the diagnosis (years)	4.7 ± 8	2.7 ± 4.2	0.4
Employed	24 (51%)	17 (44%)	0.5
Married	18 (38%)	24 (62%)	0.03
College education	13 (28%)	3 (8%)	0.02
History of abuse (sexual, physical, or childhood)	11 (23%)	10 (26%)	1
Dysfunctional family	14 (30%)	13 (33%)	0.8
Family history of seizures	17 (36%)	9 (23%)	0.2
History of head injury	4 (9%)	3 (8%)	1
Seizure frequency per month	28 ± 41	58 ± 104	0.2
Bizarre movement during seizures	21 (45%)	16 (41%)	0.8
Incontinence with seizures	7 (15%)	3 (8%)	0.3
Nocturnal seizures	12 (26%)	15 (38%)	0.2
Prolonged seizures (>30 min)	12 (26%)	12 (31%)	0.6
Hospital admission due to seizures	22 (47%)	21 (54%)	0.6
Ictal injury	8 (17%)	12 (31%)	0.2
Taking psychiatric drugs	31 (66%)	35 (90%)	0.01
Taking antiepileptic drugs	21 (45%)	22 (56%)	0.3