Seizure: European Journal of Epilepsy 66 (2019) 22–25

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Natural history of patients with psychogenic nonepileptic seizures

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ARTICLE INFO

Keywords:
Prognosis
Nonepileptic seizures
Outcome
PNES

ABSTRACT

Purpose: The purpose of this study was to investigate the long-term outcome of patients with psychogenic nonepileptic seizures (PNES), who never visited a psychologist and never received a proper therapy for their condition (due to lack of resources). We also aimed to investigate factors potentially associated with the outcome in these patients.

Methods: We studied all patients with PNES, who were admitted to the epilepsy monitoring unit at the Shiraz Comprehensive Epilepsy Center, from 2008 until 2013. In a phone call interview to the patients in November and December 2018, we obtained the following information: seizure outcome, history of receiving any psychotherapy after confirming their diagnosis at referral, and finally, their current marital status, education, and employment status.

Results: 69 patients had the inclusion criteria. Thirty-six patients (52%) were seizure-free during the past 12 months, but 33 (48%) still suffer from seizures. The only variable (at diagnosis), which was significantly associated with their outcome, was duration of their condition before they received a definite diagnosis.

Conclusion: More than half of the patients with untreated PNES may become free of seizures after they receive a definite diagnosis and with the passage of time. Longer duration of PNES before the patients received a definite diagnosis may affect their long-term outcome.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are episodes of altered responsiveness, movements, sensation, or experience, similar to epileptic seizures; but, they are not caused by abnormal electrical brain discharges and are assumed to be caused by a psychological process [1]. They are common occurrences in epilepsy centers [2]. However, misdiagnosis and delay in making a definite diagnosis are common in these patients [3]. There are few long-term studies on outcome of PNES and they suggest that many patients with PNES will continue to experience seizures in spite of receiving standard psychotherapeutic care [1,4]. Most previous outcome studies had less than two years of follow-up, concentrated on the persistence of events (seizures) rather than social outcome of patients, and assessed no or few prognostic factors [1].

Information on outcome of PNES is particularly scarce from the developing countries, where the resources are often limited. In a previous study from a developing country [5], we perceived that there were no significant differences between patients from Iran and those from Western studies with regard to their clinical characteristics. Current best available practice in the management of patients with PNES constitutes psychotherapy [e.g., cognitive behavioral therapy (CBT)] and treatment of any psychiatric comorbidity [6]. Despite that, access to appropriate psychotherapy is limited for most patients in the developing world. In one previous study [7], we observed that most (86%) patients with PNES in Iran did not receive appropriate psychotherapy (53 out of 86 patients did not receive any and 21 patients received five or less sessions of CBT) [7].

The purpose of this study was to investigate the long-term outcome of patients with PNES, who never visited a psychologist and never received a proper therapy for their condition (due to lack of resources). Compared with our previous study [7], in the current study we tried to reach out to more patients and included a more uniform group of patients (i.e., those who never received any psychotherapy only). Besides, in a subanalysis, we even investigated patients who never visited a psychiatrist either and also did not have comorbid epilepsy (i.e., patients with PNES-only, who did not receive any psychiatric or psychological care). Finally, we also investigated long-term social achievements of the patients (i.e., education, employment, and marriage) in the current study. We also aimed to investigate factors potentially associated with the outcome in these patients. We hypothesized that some demographic (e.g., sex) or clinical (seizure semiology) factors may be associated with outcome in patients with PNES. This study may reveal

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https://doi.org/10.1016/j.seizure.2019.02.006
Received 15 January 2019; Received in revised form 8 February 2019; Accepted 10 February 2019
1059-1311/

valuable information on the natural long-term history of patients with PNES.

2. Materials and methods

We studied all patients with PNES, who were admitted to the epilepsy monitoring unit at the Shiraz Comprehensive Epilepsy Center, from 2008 until 2013. All these patients had a confirmed diagnosis of PNES, ascertained by a detailed clinical assessment and an ictal video-EEG monitoring. We routinely ask about the risk factors associated with PNES in a one-to-one interview of the patients by the treating epileptologist (accompanied by a female nurse in case of women). We consistently refer all patients with PNES to our psychologist, who is the only psychologist with expertise in delivering a proper care (i.e., CBT) to these patients in the area. But, since such a service is not available in other centers in the region and also because psychotherapy is not covered by most insurance companies and patients have to pay 100% of the cost out of their pocket, many patients would not receive such therapy. We studied patients who never visited a psychologist (even other psychologists from other centers) and never received an appropriate therapy for their condition. The only intervention that these patients had received was a conversation with the epileptologist in which they received information on their condition (a positive diagnosis of PNES was provided). The population of patients in this study has an overlap with our previously published paper [7]. However, we reached out to more patients in the current study (135 patients in the current vs. 86 in the previous study).

We extracted all the pertinent clinical and demographic data from our database. We excluded patients with insufficient data. We studied the following variables at the time of the diagnosis: sex, age at onset, age at diagnosis, duration of the condition before making a definite diagnosis, education (college education vs. less than college education), employment status, marital status (married vs. not married), seizure characteristics and semiology, risk factors associated with PNES [i.e., sexual abuse, physical abuse, head injury, dysfunctional family (troublesome relationships, divorce, etc.), and family history of seizures], receiving any psychiatric drugs (as an evidence of suffering from psychiatric problems, since we did not execute a standard psychiatric evaluation in our patients), and receiving antiepileptic drugs (AEDs). We made a phone call to all patients and if they agreed to participate in our study we interviewed them; a prepared script was used for all phone interviews. In a phone call interview to the patients in November and December 2018 (i.e., at least, 5 years after they received a definite diagnosis of their condition), we obtained the following information: seizure outcome [their seizure status during the past 12 months (in order to minimize the risk of recall bias)], history of receiving any psychotherapy (by a psychologist) or psychiatry visit after confirming their diagnosis at referral, and finally, their current marital status, education, and employment status.

We studied factors potentially associated with their seizure outcome using Pearson Chi-square, Fisher's exact, Mann-Whitney, and Kolmogorov-Smirnov tests. P values less than 0.05 were considered significant. The Shiraz University of Medical Sciences Institutional Review Board (IRB) approved this study (1396-01-55-15766; NIMAD grant # 971,003).

3. Results

Of the 249 patients with PNES (from 2008 until 2013) in our database, 135 patients answered to our phone call; 69 patients had the inclusion criteria and were studied. A couple of patients did not have the required data and were excluded. Only one patient refused to be interviewed. Thirty-six patients (52%) were seizure-free during the past 12 months, but 33 (48%) patients still suffer from seizures. Characteristics of these two groups of patients (seizure-free vs. not, in their recent phone call follow-up), at the time of diagnosis, are shown in Table 1. Current status of these patients with PNES (seizure-free vs. not) are shown in Table 2. The only variable (at diagnosis), which was significantly associated with their outcome, was duration of their condition before they received a definite diagnosis.

Table 1

Characteristics of patients with psychogenic nonepileptic seizures at diagnosis (seizure-free vs. not).

	Seizure-free patients 36 (52%)	Patients with seizures 33 (48%)	P value
Sex (Female : Male)	23 : 13	21 : 12	1
Age at onset (years)	24 ± 12	22 ± 10	0.4
Age at diagnosis (years)	27 ± 12	30 ± 10	0.4
Duration of the condition before making the diagnosis (years)	3 ± 4.5	7.5 ± 10	0.02
Employed	9 (25%)	7 (21%)	0.7
Married	17 (47%)	20 (61%)	0.2
College education	7 (19%)	4 (12%)	0.4
History of physical abuse	3 (8%)	5 (15%)	0.4
History of sexual abuse	4 (11%)	0 (0%)	0.1
Dysfunctional family	14 (39%)	11 (33%)	0.6
Family history of seizures	12 (33%)	10 (30%)	0.8
History of head injury	5 (14%)	2 (6%)	0.4
Seizure frequency per month	45 ± 67	55 ± 105	0.6
Loss of responsiveness with seizures	31 (86%)	28 (85%)	1
Generalized motor seizures	33 (92%)	29 (88%)	0.7
Akinetic seizures	3 (8%)	3 (9%)	1
Incontinence with seizures	3 (8%)	2 (6%)	1
Nocturnal seizures	12 (33%)	8 (24%)	0.4
Ictal injury	7 (19%)	9 (27%)	0.5
Taking psychiatric drugs	6 (17%)	4 (12%)	0.7
Taking antiepileptic drugs	18 (50%)	23 (70%)	0.1
Medical comorbidities	13 (36%)	6 (18%)	0.1
Comorbid epilepsy	7 (19%)	10 (30%)	0.4

Table 2

Current status of patients with psychogenic nonepileptic seizures (seizure-free vs. not).

	Seizure-free patients 36 (52%)	Patients with seizures 33 (48%)	P value
Employed	12 (33%)*	7 (21%)	0.2
Married	23 (64%)**	22 (67%)	0.9
College education	13 (36%)***	4 (12%)	0.02
Taking psychiatric drugs	3 (8%)	8 (24%)	0.07
Taking antiepileptic drugs	6 (17%)	15 (45%)	0.01

* improvement (3 people) compared with the pre-diagnosis status is not significant (p = 0.4).

** improvement (6 people) compared with the pre-diagnosis status is not significant (p = 0.1).

*** improvement (6 people) compared with the pre-diagnosis status is not significant (p = 0.1).

In an additional subanalysis, we selected the patients who did not visit even a psychiatrist after they received their diagnosis and also did not have comorbid epilepsy (42 patients); 25 patients (60%) were seizure-free. The results were the same as the above; the only variable (at diagnosis), which was significantly associated with their outcome, was the duration of their condition before they received a definite diagnosis (2 ± 2.5 years in seizure-free patients and 10 ± 12 years in others; p = 0.002). At the follow-up, none of the patients with PNES-only, who were seizure-free and 4 (24%) patients, who still had seizures, were taking AEDs.

4. Discussion

In this study, we noticed that many patients with PNES in Iran (a developing nation) did not receive a proper treatment for their condition. In an international survey by the ILAE PNES Task Force [8], PNES were acknowledged as a diagnostic and therapeutic challenge in all nations. That study showed a clear relationship between income and access to resources; limited access to resources was most frequently reported from the developing nations [8]. In many developing countries (including Iran), the available resources are usually concentrated in larger cities, while people in most places in those nations are deprived and have limited access to resources. In addition, in Iran, most patients have to pay some of the medical costs (e.g., psychology visits) out of their pocket and most insurance companies do not cover these expenses (the authors' observations).

In spite of the above observation, most of our patients became free of their psychogenic seizures with the passage of time and after they received a definite diagnosis of their condition. In a similar study of 27 patients from Italy, 63% of their patients became seizure-free with communication of the diagnosis as the only intervention [9]; this is very similar to our observation. However, there are other studies with contradictory results [10,11]. For example, in a study of 148 patients [who were probably treated appropriately (this was not mentioned in that paper)], outcome was classified as "poor" in 44%, "intermediate" in 40%, and "good" in 16%; more than 11 years after the manifestation and more than four years after the diagnosis, 71% of their patients continued to have seizures [1]. Resolving this apparent contradiction by designing future studies has paramount significance in advancing our knowledge of the best management strategy in these patients and their long-term outcome. In designing such studies, one should consider that using event (seizure) frequency as the only outcome measure in patients with PNES is not enough [12]. In a previous study, 43% of patients with PNES, who achieved seizure remission, were still unproductive due to other psychiatric problems [12]. In our study, only one-third of seizure-free patients were employed; none of the patients, who still suffer from PNES, has become employed, but three (8%) of those, who became seizure-free, are currently employed (Tables 1 and 2). We had a similar observation with respect to their educational achievements and marital status (those who were seizure-free had some non-significant improvements). This is consistent with that previous study [12].

Getting to know the long-term outcome of patients suffering from PNES across borders and cultures has significant clinical implications. In a recent clinical trial on 38 patients with a short follow-up period of 16 weeks [13], the investigators observed that combined CBT with sertraline (considered as the best practice) resulted in 59% event (seizure) reduction which was significantly better compared with that in the treatment as usual group. On the other hand, a recent meta-analysis that synthesized data from 13 previous studies on 228 patients with PNES [14], demonstrated that 47% of patients with PNES achieved seizure freedom upon completion of a psychological intervention. These outcome figures on patients, who were treated properly (according to the current guidelines) [14], are not much different from what we found in our untreated patients in long-term. Therefore, we suggest designing cross-cultural clinical trials with longer follow up periods, in contemplation of evaluating different treatment strategies in patients with PNES.

The only factor that affected the long-term outcome in patients with untreated PNES in our study was duration of their condition before they received a definite diagnosis; this is consistent with previous studies [15,16]. In a previous study [15], early and definitive diagnosis of PNES showed prognostic significance with regard to short-term outcome. Our observation shows that this (i.e., early diagnosis) is also important in long-term with regard to the outcome. In contradiction, a previous review concluded that communicating the diagnosis to the patient may stop PNES in short-term, but without dedicated further treatments, PNES are likely to restart in the majority of patients [17]. In addition, other outcome measures (e.g., quality of life, health care utilization, and levels of functioning) may not improve without appropriate psychological interventions in these patients [18]. This should be investigated by designing future international long-term studies.

In conclusion, more than half of the patients with untreated PNES may become free of seizures with the passage of time and after they receive a definite diagnosis of their condition. Longer duration of PNES before the patients received a definite diagnosis may affect their long-term outcome. Well-designed international cross-cultural long-term clinical trials should investigate the best treatment strategies, the outcome, and factors potentially associated with long-term outcome in patients with PNES.

5. Limitations of the study

This was a retrospective study and recall bias is a possible limitation. Recall bias could have been augmented by the absence of seizure logs and family/witness confirmation of the seizures. In addition, current status of the patients was investigated by a phone call interview with all the limitations which may be associated with such a method (e.g., time restriction).

Contributions

Ali A. Asadi-Pooya, M.D.: Database development, study design, data collection, statistical analysis, manuscript preparation.

Zahra Bahrami, M.D. and Maryam Homayoun, M.D.: Data collection, statistical analysis, manuscript preparation.

Disclosures

Dr. Ali A. Asadi-Pooya, M.D., consultant: UCB Pharma; Honorarium: Hospital Physician Board Review Manual and Cobel Darou; Royalty: Oxford University Press (Book publication). Others, report no disclosures.

Acknowledgments

This study was supported by the National Institute for Medical Research Development Grant (No. 971003). We also thank the Neuroscience Research Center, Shiraz University of Medical Sciences for supporting this study.

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