

# Frequency of attacks in patients with psychogenic non-epileptic seizures

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**ABSTRACT** – *Aims.* The aim of this study was to investigate the frequency of attacks (psychogenic seizures) in patients with psychogenic non-epileptic seizures (PNES) and to characterize factors potentially associated with attack frequency.

*Methods.* In this retrospective study, all patients with PNES, who were studied at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, Iran, from 2008 until 2018, were reviewed. We categorized the attack frequency in the patients as (1) daily; (2) weekly; and (3) frequency of less than one per week.

*Results.* Three hundred and ten patients were studied. Attack frequency in patients was  $34 \pm 67$  per month. One hundred and eleven patients (36%) had daily attacks, 93 (30%) had weekly attacks, and 106 (34%) had less than weekly attacks. Sixty-five patients (21%) reported having more than one attack per day. Demographic variables, attack-related variables, PNES associated factors, and use of AEDs were not significantly associated with attack frequency in the patients.

*Conclusion.* We observed that two thirds of the patients with PNES had frequent daily or weekly attacks. The findings of our study could be helpful in designing future clinical trials. First, attack frequency is an unbiased outcome measure in the design of such studies. Second, it is easily measurable using attack calendars; we suggest that attack frequency be assessed daily using daily attack calendars. Finally, it is very easy to recruit patients with PNES for clinical trials (with regards to their attack frequency) since many of them have frequent attacks.

**Key words:** frequency, psychogenic, PNES, seizure

Psychogenic non-epileptic seizures (PNES) are commonly diagnosed at epilepsy centres. They consist of paroxysmal changes in responsiveness, movements, or behaviour that superficially resemble epileptic seizures, but lack a neurobiological origin similar to epileptic seizures

and are not associated with electrophysiological epileptic changes; they are associated with psychological problems (Asadi-Pooya, 2017). In this article, we have investigated the frequency of psychogenic seizures in patients with PNES and we have used the term “attack” for

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psychogenic seizures. Patients with PNES often have frequent attacks. Additionally, recurrent attacks are important factors in PNES; they are disabling and may cause severe injuries (Asadi-Pooya *et al.*, 2014). Attack frequency is often the primary outcome measure in studies involving patients with PNES; psychosocial and functioning measures are often secondary outcomes (LaFrance *et al.*, 2010, 2014).

To the best of our knowledge, no study has ever investigated the attack frequency and the associated factors in patients with PNES. The aim of this study was to investigate the frequency of attacks in patients with PNES and to characterize factors potentially associated with attack frequency. We hypothesized that some demographic variables (e.g. sex) or risk factors (e.g. a history of sexual abuse) may affect the attack frequency in patients with PNES.

## Materials and methods

In this retrospective study, all patients with PNES, who were studied at Shiraz Comprehensive Epilepsy Center at Shiraz University of Medical Sciences, Iran, from 2008 until 2018, were reviewed. The diagnosis was made based on a careful clinical assessment, and documented by ictal recording during video-EEG monitoring by the epileptologist. A diagnosis of PNES was routinely based on: compatibility with a detailed clinical history; attacks witnessed by the epileptologist showing semiology typical of PNES during video-EEG monitoring; and finally, no epileptiform activity detected immediately before, during or after the attack, based on ictal video-EEG recording. Patients were excluded if their data were not available.

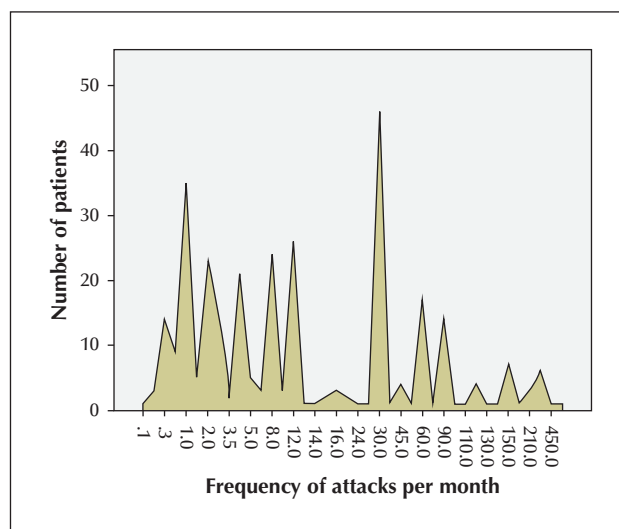
The data were obtained through a face to face interview between the epileptologist and patients/their caregivers. Age, gender, age at attack onset, attack semiology, attack frequency (based on the patients' report on admission to the epilepsy monitoring unit [their attack frequency in the preceding couple of months in order to minimize the risk of recall bias]), ictal injury and factors potentially predisposing to PNES (history of physical abuse [*i.e.* corporal punishment or any physical injury resulting from aggressive behaviour towards the patient]), sexual abuse, child abuse (*i.e.* neglect, emotional/verbal abuse), a dysfunctional family (*i.e.* divorce, single parent, significant family disputes, *etc.*), academic failure (school dropout or repeated grades), any medical comorbidities, family history of seizures, and driving, employment, and marriage status were registered routinely. We arbitrarily categorized the attack frequency in the patients as:

- daily (one or more attacks per day);
- weekly (1-6 attacks per week);
- and frequency of less than one per week.

Demographic variables and relevant clinical variables were summarized descriptively to characterize the study population. The Pearson Chi-square (two-tailed), Mann-Whitney, Kolmogorov-Smirnov, and t-test were used for statistical analyses. *P* value less than 0.05 was considered as significant. This study was conducted with the approval by Shiraz University of Medical Sciences Review Board.

## Results

During the study period, 325 patients were registered in our database. For 310 patients, data on attack frequency was available and these patients were studied further. Sex ratio of the patients was 1.9 (203:107 [female: male]). Age of the patients was  $29 \pm 10$  years and age at the onset of attacks was  $24 \pm 10$  years. One hundred and ninety-seven patients (64%) were taking antiepileptic drugs (AEDs). Attack frequency in patients was  $34 \pm 67$  per month (minimum: one/year; maximum: 600/month; median: eight per month). One hundred and eleven patients (36%) had daily attacks, 93 (30%) had weekly attacks, and 106 (34%) had less than weekly attacks. Sixty-five patients (21%) reported having more than one attack per day; up to 20 attacks per day in one patient. Twenty-seven patients (9%) reported having less than one attack per month. *Figure 1* shows the distribution of attack frequency in patients with PNES. Demographic variables (*i.e.* gender, age, age at onset, duration of the condition, family history, employment, marital status, and driving), attack-related variables (*i.e.* aura, loss of responsiveness, attack semiology, incontinence, attack-related injury), PNES associated factors (*i.e.* a



**Figure 1.** Attack frequency in patients with psychogenic non-epileptic seizures.

history of head trauma, a history of physical or sexual abuse, a history of family dysfunction, academic failure, and medical comorbidities), and use of AEDs were not significantly associated with attack frequency in the patients (all *p* values were > 0.05) (table 1) .

## Discussion

In this study, we observed that two thirds of the patients with PNES had frequent daily or weekly attacks. In a recent small study of 23 patients from

Argentina (Korman *et al.*, 2019), 40% of the patients had daily attacks, 42.5% of the patients had weekly attacks, and 8.5% had monthly attacks; this is very similar to our observation. Attack frequency as the primary outcome measure has been used in previous clinical trials in patients with PNES; psychosocial and functioning measures, including psychiatric symptoms, social interactions, quality of life, and global functioning, were often secondary outcome measures (LaFrance *et al.*, 2010, 2014). We also observed that attack frequency in patients with PNES was not associated with any demographic (including sex) or clinical variables

**Table 1.** Demographic and clinical characteristics of patients with psychogenic non-epileptic seizures (PNES) with different seizure frequencies.

	Daily seizures (111 patients) (n)	Weekly seizures (93 patients) (n)	<Weekly seizures (106 patients) (n)	<i>p</i> value
Sex ratio (F:M)	75:36	65:28	63:43	0.2
Age (years)	28 ± 10	30 ± 10	28 ± 10	0.3
Age at onset (years)	24 ± 11	24 ± 10	24 ± 11	0.9
Duration of PNES (years)	4.3 ± 7	6.5 ± 8.5	5.5 ± 7	0.09
Aura	71	62	63	0.6
Loss of responsiveness	94	75	94	0.2
Generalized motor seizures	102	81	88	0.1
Akinetic seizures	6	9	15	0.09
Urine incontinence	9	13	11	0.4
Ictal injury	31	33	30	0.5
Family history of seizures	38	29	28	0.5
History of head injury	6	6	3	0.4
History of physical abuse	18	12	10	0.3
History of sexual abuse	9	9	7	0.7
History of child abuse	8	8	14	0.2
History of dysfunctional family	40	29	39	0.6
History of academic failure	11	3	9	0.1
Driving	22	11	21	0.2
Employment	20	15	24	0.4
Married	52	54	48	0.3
Medical comorbidities	33	28	22	0.2
Comorbid epilepsy	25	22	19	0.5
Taking antiepileptic drugs	69	62	66	0.7

(including a history of sexual abuse). One explanation for this observation might be the high frequency of attacks in most patients with PNES; other possible reasons should be explored in prospective studies in the future. However, this observation negated our hypothesis and showed that attack frequency could be considered as an independent and unbiased outcome measure in studies of patients with PNES. The findings of our study could be helpful in designing future clinical trials in patients with PNES. First, attack frequency is an unbiased outcome measure in the design of such studies. Second, attacks are frequent in these patients and therefore, they are easily measurable by using attack calendars; we suggest that attack frequency be assessed daily using daily attack calendars since more than a fifth of the patients may report having more than one attack per day. Finally, it is very easy to recruit patients with PNES for clinical trials (with regards to their attack frequency) since many of them have frequent attacks.

Unfortunately, long-term studies suggest that many patients with PNES will continue to experience attacks despite receiving neurological and psychotherapeutic care (Reuber *et al.*, 2003). Based on a systematic review, the authors concluded that the prognosis of PNES in adults was poor. In their study, fewer than 40% of newly diagnosed adults with PNES could be expected to become attack-free within five years after diagnosis (Durrant *et al.*, 2011). Therefore, considering the high prevalence and incidence of PNES (Asadi-Pooya and Sperling, 2015) and the significant impacts of this condition on the lives of the patients (Jones *et al.*, 2016), it is necessary to design studies in order to establish robust and more effective ways of treating these patients (Asadi-Pooya, 2016).

This study has some limitations including its retrospective design that may have caused recall bias. The time period considered for the calculation of the frequency of PNES (two months) may have been too short; some patients may present periods of improvement followed by worsening of their psychogenic attacks. However, this period was chosen in order to minimize the risk of recall bias. Since patients did

not routinely keep an attack journal (diary) and the frequency was based on their recall and estimate, a prospective evaluation with more rigorous data collection could potentially reveal different results. □

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