



Periictal and interictal headache including migraine in Dutch patients with epilepsy: A cross-sectional study



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ABSTRACT

As early as in 1898, it was noted that there was a need to find “a plausible explanation of the long recognized affinities of migraine and epilepsy”. However, results of recent studies are clearly conflicting on this matter. In this cross-sectional study, we aimed to define the prevalence and characteristics of both seizure-related and interictal headaches in patients with epilepsy (5–75 years) seeking help in the tertiary epilepsy clinic SEIN in Zwolle. Using a questionnaire, subjects were surveyed on the existence of headaches including characteristics, duration, severity, and accompanying symptoms. Furthermore, details on epilepsy were retrieved from medical records (e.g., syndrome, seizure frequency, and use of drugs). Diagnoses of migraine, tension-type headache, or unclassifiable headache were made based on criteria of the International Classification of Headache Disorders. Between March and December 2013, 29 children and 226 adults were evaluated, 73% of whom indicated having current headaches, which is significantly more often when compared with the general population ($p < 0.001$). Forty-nine percent indicated having solely interictal headache, while 29% had solely seizure-related headaches and 22% had both. Migraine occurs significantly more often in people with epilepsy in comparison with the general population ($p < 0.001$), and the occurrence of tension-type headaches conforms to results in the general population. These results show that current headaches are a significantly more frequent problem amongst people with epilepsy than in people without epilepsy. When comparing migraine prevalence, this is significantly higher in the population of patients with epilepsy.

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1. Introduction

The thought of migraine and epilepsy being associated has first been described in 1898, when in the editorial of the Journal of American Medical Association, it was noted that there was a need to find “a plausible explanation of the long recognized affinities of migraine and epilepsy” [1]. However, recent studies have taught us that this “long recognized affinity” between these two very common neurological disorders might not be as certain as has long been speculated. Several groups have studied seizure-related headache (i.e., preictal, interictal, and postictal headaches) and/or migraine in patients with epilepsy and furthermore, various studies have looked into the comorbidity of epilepsy in patients with migraine. Results, unfortunately, are clearly conflicting. In adult patients, preictal headaches are described in 1.2%–35.5% [2–6]. Ictal headaches are more scarce and described in less than 5% of patients

with epilepsy [4,7]. These ictal headaches represent a peculiar condition, probably underestimated in favor of the migralepsy concept, which, on the other hand, has recently been questioned [8]. Postictal headaches are far more frequent and described in 23.5%–64% [3,4,6,9–12]. Headaches in between seizures (interictal headaches) are known to occur in 20%–57.8% [2,13,14]. The prevalence of interictal headaches classifiable as migraine in patients with epilepsy is again subject to very conflicting results: various studies found no association between these two common neurological disorders, while others presented elevated numbers as high as 27% [2–4,10,12,14–16]. In children, studies into seizure-related headache or migraine in patients with epilepsy are even more scarce. Also, these numbers are somewhat different from that of the adult population: preictal headaches are described in 3.1%–30%, and postictal headaches are seen in 6.4%–62% [17,18]. There are no reports about ictal headaches in children, whereas interictal headaches are described in 5.9%–58% [17,18]. The prevalence of migraine in children with epilepsy is slightly better looked into and described in 5.1%–25% [17–22]. Reports are conflicting on whether the onset of these headaches occurs in the same year as the onset of the epilepsy.

The discrepancy in results is probably due to differences in study design (e.g., retrospective versus prospective), studied populations

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(general population versus patients with epilepsy from a tertiary center), and used diagnostic criteria, as previously stressed by P. Parisi et al. [23].

In this study, we aimed to define the prevalence and characteristics of seizure-related as well as interictal headaches in a heterogeneous population of both children and adults with epilepsy seeking help in a tertiary epilepsy clinic.

2. Participants and data collection

This is a cross-sectional study of children and adults who were evaluated between March and December 2013 in the tertiary epilepsy center SEIN in Zwolle, the Netherlands. Using an elaborate questionnaire (see Supplementary data), the subjects were surveyed on the existence of headaches and the frequency, characteristics, duration, severity, and accompanying symptoms of these headaches (such as nausea, vomiting, and photo- and phonophobia). Also, epilepsy characteristics were surveyed, including seizure frequency, onset of epilepsy, and whether there was a recent EEG (<5 years). Questionnaires were distributed by the neurologist and/or EEG technician to both new and return patients. Patients with a history of at least 2 unprovoked seizures were asked to complete the questionnaire. Patients aged 15–75 years old filled in the questionnaires themselves. Parents or caregivers of children aged 6 to 15 years filled in the questionnaires of the children and, if possible, together with their children. Patients who could not complete the questionnaire because of mental retardation or difficulty with the Dutch language were excluded. Children who could not indicate having headaches and were not able to describe this headache (e.g., because of mental retardation), were excluded as well.

Subsequently, the patient's record was reviewed for seizure type, age at epilepsy onset, and drug therapy. Seizure syndrome was assigned if the patient's neurologist had documented a specific diagnosis in the medical record. Preictal headache was defined as a headache starting before the seizure until the onset of the seizure. Ictal headache was defined as a headache only occurring during the seizure. Postictal headache was defined as a headache starting directly after the seizure. Individuals were diagnosed with migraine with aura, migraine without aura, tension-type headache, possible medication overuse headache, or unclassifiable headache based on the criteria of the International Classification of Headache Disorders (ICHD-2, 2004 & 2005) [24,25].

As the questions asked were considered part of an elaborate history taking, the Institutional Medical Ethics Committee had no objections.

Statistical analysis was performed using the χ^2 -test, Fisher's exact test, t-test or Welch test (in samples with normal distribution), and Mann-Whitney U test (in samples that were not normally distributed). Statistical Package for the Social Sciences v.17.0 was used for analysis.

3. Results

A total of 29 children (mean age: 10.9 years, range: 6 to 15 years) and 226 adults (mean age: 40.7 years, range: 16 to 75 years), 129 male and 126 female patients, were included in the study (see Table 1). Of our population, 73% indicated having current headaches (which is significantly more than in the general population, $p < 0.001$). Of those, 11% indicates having daily headaches, 25% more than once a week, 17% once a week, 17% a few times per month, 12% once a month, 11% a few times per year, and 7% less than that. Forty-nine percent of headaches were solely interictal, 29% were solely seizure-related (preictal, ictal or postictal), and 22% of patients suffered from both interictal as well as seizure-related headaches (see Fig. 1). Of all people with epilepsy, 36% experienced solely interictal headaches, 1.2% experienced preictal headaches, no patients indicated to have ictal headaches, 11% had postictal headaches, 9.4% had periictal headaches, and 16.1% had both periictal as well as interictal headaches. For headache characteristics, see Table 2.

When defining the headaches using the criteria of the ICHD-2, 25.5% of patients with epilepsy have migraines ($p < 0.001$ in comparison with people without epilepsy), and 38% suffer from tension-type headaches (conforming to results in the general population). Six percent of headaches could not be classified, and 6 and 7 patients, respectively, had headaches in which other causes could not be excluded (e.g., patients with brain tumors) or headache due to medication overuse was possible. Younger and female patients were more likely to have headaches ($p = 0.018$ and $p = 0.001$, respectively). There is no relation between epilepsy focus (temporal versus extratemporal) or side of epilepsy focus and headaches, but there is a trend that people with idiopathic generalized epilepsy more frequently have headaches than patients with localized epilepsy ($p = 0.103$). The type of seizures (i.e., simple or complex partial seizure, tonic-clonic, absence, myoclonic, atonic, clonic, or tonic seizure) or seizure frequency does not influence headache prevalence. The same holds true for the type of used antiepileptic drug or the number of used antiepileptic drugs.

When looking into epilepsy onset versus headache onset, both were known for 112 patients. Of those, epilepsy onset lay before the start of

Table 1
Population characteristics when split into groups with and without current headaches.

	No headache (<i>n</i> = 68)	Headache (<i>n</i> = 187)	Total number	<i>p</i> -Values
Mean age (min–max, in yrs)	42.1 (7–75)	35.5 (6–71)	255	*
Sex	48 M; 20 F	81 M; 107 F	255	***
Mean epilepsy onset (min–max)	16.8 (0–63)	16.4 (0–59)	255	ns
Mean epilepsy duration (min–max)	25.3 (0–73)	19 (1–71)	255	*
Epilepsy type				ns, although trend ($p = 0.103$)
Idiopathic generalized	6	33	39	
Focal	56	145	201	
Unknown	6	9	15	
Number of AEDs	1.8 (0–5)	1.8 (0–6)	255	ns
Headache in first grade relatives				ns
No	47	110		
Yes	21	77		
Side of epilepsy focus	19 R; 14 L	45 R; 30 L		ns
Epilepsy focus				ns
Temporal	19	44		
Extratemporal	14	28		
Seizure type				ns

min: minimum, max: maximum, yrs: years, M: male, F: female, ns: not significant, R: right, L: left.

* $p < 0.05$.

*** $p \leq 0.001$.

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