



Abstract

Headache and epilepsy are two common neurological disorders and their relationship is still a matter of debate. Recent research suggests their shared pathophysiology and indicates similar genetic and environmental risk factors.

The objective of this study was to estimate the prevalence and clinical features of headaches in patients with epilepsy and evaluate a temporal relationship with epileptic seizures.

**Methods:** 200 patients with epilepsy aged  $\geq 16$  years treated in Epilepsy and Migraine Treatment Centre in Poland were consecutively recruited to the study. They underwent a semi-structured interview including the International Classification Headache Disorders (ICHD-III) criteria to diagnose the occurrence of headache during past year. The patients were also asked about temporal relationship between their headaches and seizures. Demographic data, epilepsy duration, seizure frequency, seizure type, epilepsy type and antiepileptic medications used were captured from the medical records. The results were compared to the headache prevalence in healthy control of 200 people.

**Results:** Headaches were more prevalent in people with epilepsy than in healthy control ( $p=0,015$ ) and the most prevalent type of headache was migraine (35% compared to 29%,  $p=0,007$ ). In both groups migraine was more prevalent among women irrespectively of age. Migraine was less prevalent among patients who were treated with valproic acid and/or topiramate and/or gabapentin in comparison to other antiepileptic drugs but that result was not statistically significant. Migraine was diagnosed more often in patients with focal epilepsy in comparison to patients with generalised epilepsy ( $p=0,031$ ). Occurrence of headaches during past year was not connected to the duration of epilepsy or seizure frequency. The most prevalent were inter-ictal headaches occurring in 87% of patients. Post-ictal headaches occurred in 48% and pre-ictal headaches in 16% of patients. Post-ictal headaches usually had clinical features of migraine ( $p=0,014$ ) and were more prevalent among patients who also suffered from inter-ictal headaches, but that tendency was not clinically significant.

**Conclusions:** In our study there was a clear connection between epilepsy and migraine regarding prevalence, temporal relationship with seizures and shared treatment.

Introduction

People with epilepsy often suffer from bothersome headaches, which can contribute to lowering their quality of life (1).

In the last two decades mechanisms underlying the pathophysiology of epilepsy and migraine were extensively explored. These two neurological diseases presumably have shared genetic background and pathophysiology in which essential part is played by alteration of conformation and function of ion channels and the imbalance between excitatory and suppressive neurotransmitters (2).

Comorbidity of epilepsy and headache, migraine in particular, has been investigated by several authors in recent years. The studies conducted to date brought conflicting results and the applied methodology does not enable to compare these results to the prevalence of headaches shown in general population studies.

Methods and Materials

In our study conducted in Epilepsy and Migraine Treatment Centre in Krakow, Poland, 200 consecutive patients with epilepsy and 200 people with no medical history of epilepsy were enrolled.

A questionnaire regarding frequency and type of headache during the last year was performed among all participants of the study.

Additionally, based on medical records, information on epilepsy duration, type of epilepsy, type of epileptic seizures, frequency of epileptic seizures in the last year, type of antiepileptic treatment and any temporal relationship between headaches and seizures was collected.

The diagnosis of the type of headache were made according to The International Classification of Headache Disorders, 3<sup>rd</sup> edition (ICHD-III)(3). Infrequent episodic tension-type headache was not regarded as bothersome headache and therefore was excluded from the results.

Results

In the last year 64% of patients with epilepsy suffered from headaches, that is more than in the control group (51%) – this result was statistically significant,  $p=0.015$ , figure 1.

The most prevalent type of headache in the epilepsy group was migraine, which was diagnosed in 35% patients, more often than in the control group (29%),  $p=0,007$ , figure 1.

Headaches in general and migraine among them were more prevalent in women in both epilepsy ( $p<0,001$ ) and control group ( $p=0,048$ ,  $p=0,003$ ).

Migraine was diagnosed more often in patients with focal epilepsy in comparison to patients with generalised epilepsy. (58% vs 37%,  $p=0,031$ ), figure 2.

A tendency to less prevalent migraine was seen in patients who were taking antiepileptic drugs used in migraine prevention (valproate, topiramate, gabapentin), but this result did not reach statistical significance, ( $p=0,069$ ).

Prevalence of headache and its type was not related to the duration of epilepsy or type of antiepileptic treatment: mono- or polytherapy.

In the group of 67 patients with both seizures and headaches present in the last year, inter-ictal headaches were experienced by 87% of patients. Post-ictal headaches were reported by 48% of patients and pre-ictal headaches by 16%.

Post-ictal headaches occurred most frequently after focal seizures with impaired consciousness and after tonic-clonic seizures. Migraine was the most frequent type of post-ictal headache ( $p=0.014$ ).

People with post-ictal headache often also suffered from inter-ictal headache, but that tendency was not statistically significant, ( $p=0,109$ ).

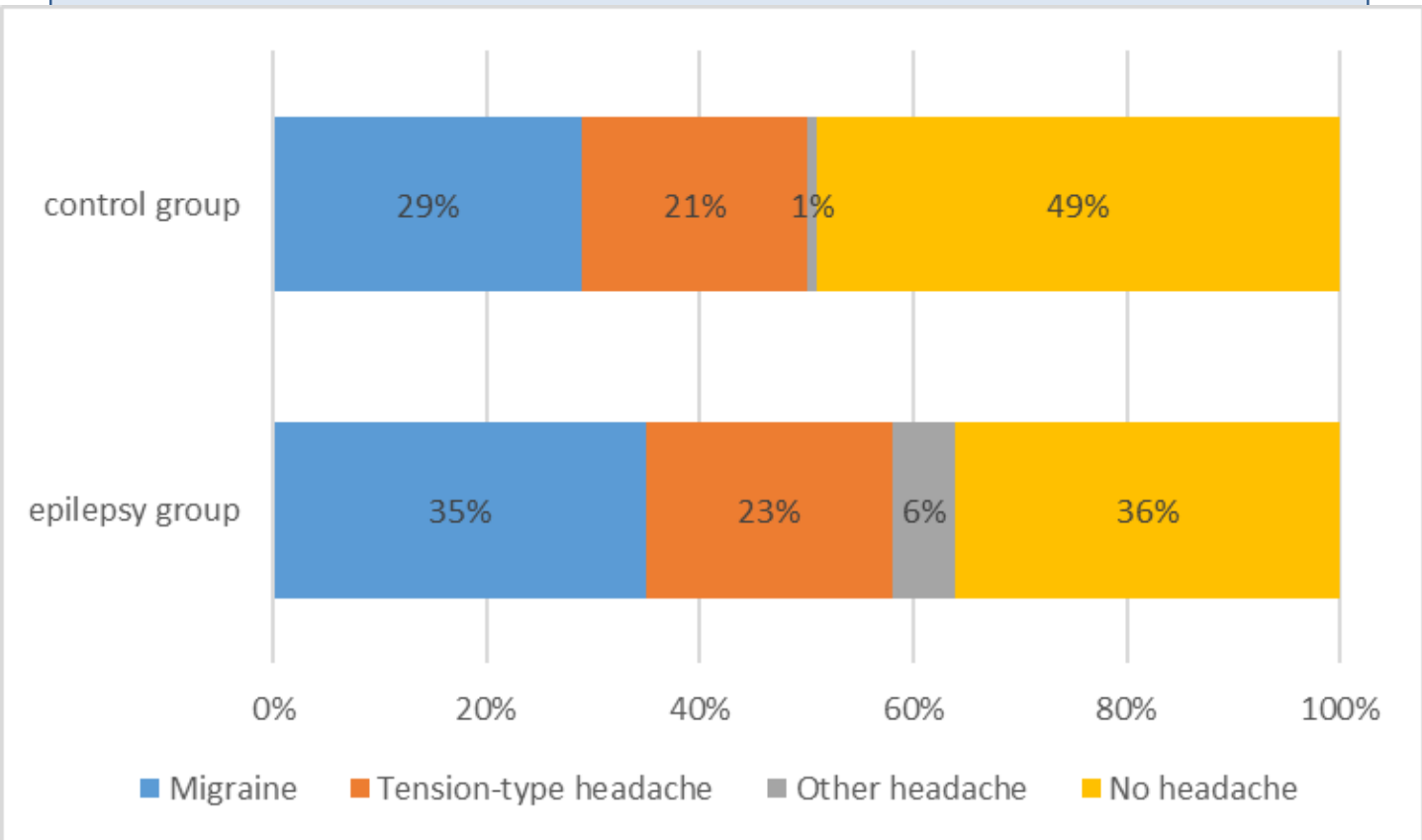


Figure 1. Prevalence and type of headache in epilepsy and control group.

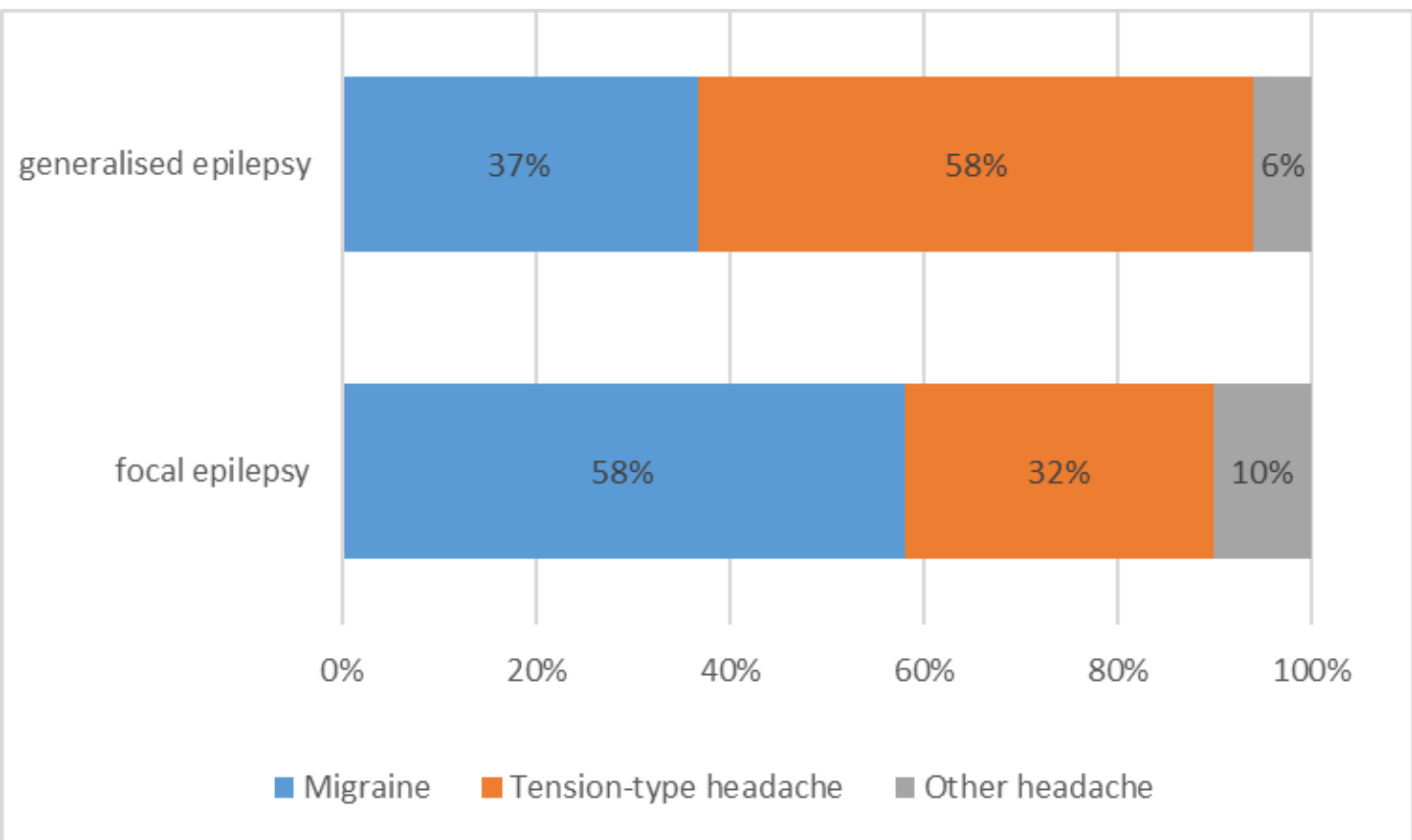


Figure 2. Type of headache in generalized and focal epilepsy.

Conclusions

- Headaches were more prevalent among people with epilepsy than in the control group. The most prevalent type of headache in the study group was migraine.
- Headaches and migraine among them were more prevalent in women with epilepsy.
- Migraine was more prevalent in patients with focal epilepsy then in patients with generalised epilepsy.
- Headaches were the most frequent during the interictal period.
- Among postictal headaches migraine was the most frequent type of headache.

References

(1) Mameniškienė R, Karmonaitė I, Zagorskis R. The burden of headache in people with epilepsy. Seizure. 2016;41:120–126.

(2) Rogawski MA. Migraine and Epilepsy—Shared Mechanisms within the Family of Episodic Disorders. In: Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV, editors. Jasper’s Basic Mechanisms of the Epilepsies 4th ed. Bethesda (MD): National Center for Biotechnology Information (US); 2012

(3) Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38:1–211.