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Comorbidity between headache and epilepsy in a Chinese epileptic center

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Summary Here we investigated the characteristics and prevalence of headaches in patients with epilepsy in a Chinese epileptic center based on the International Classification of Headache Disorders, 2nd edition. We found that 60.14% (667/1109) of patients reported headaches. Headache was less prevalent in males (57.17%) than in females (63.75%). Interictal headaches were present in 34.62% of patients, and 139/1109 (12.53%) patients had interictal migraine, which was a higher percentage than reported in a large population-based study from the same area (9.3%) using the same screening question. In addition, 469 (70.31%) patients had postictal headache, migraine characteristics were present in 73.35% of these patients, and 15.35% also suffered from interictal migraine. Lastly, 8.85% patients had preictal headache. These results confirm that headache is very common in patients with epilepsy. Seizures often trigger postictal headaches with migraine features. The comorbidity of migraines and epilepsy should receive clinical attention, as it may influence antiepileptic drug choice, and the headache may require specific treatment.

Introduction

Epilepsy and headache are the two most common neurologic disorders affecting individuals of all ages worldwide. Approximately 50 million people suffer from epilepsy, and in the adult population, the prevalence of active headache is approximately 46% (Stovner et al., 2007). The relationship between headache and epilepsy is complicated, and the comorbidity of headache and epilepsy is still poorly understood. During the last 100 years, many authors have devoted a large amount of efforts to resolve the controversy concerning multiple aspects of this intriguing topic (Haut et al., 2006).

An association between migraine and epilepsy has been demonstrated in several studies (Ottman et al., 2011; Belcastro et al., 2011a), but the data are complicated, and

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studies have been limited by small sample sizes. The prevalence of migraine in patients with epilepsy ranges from 14 to 24%, and the prevalence of epilepsy in migraine subjects ranges from 1.1 to 17% (Tèllez-Zenteno et al., 2005; Leniger et al., 2003). This large variation is most likely due to differences in the classifications of both disorders, as well as in the selection of patient populations and diagnostic instruments (Tonini et al., 2012).

Headache may be temporally linked to seizures in different ways. It may occur prior to a seizure (preictal headache), during a seizure (ictal headache), after a seizure (postictal headache) or be unrelated to seizures (interictal headache) (Schon and Blau, 1987; Bernasconi et al., 2001; Yamane et al., 2004).

To date, no large-scale analysis has been conducted examining the association between headache and epilepsy in the Chinese population. The purpose of this study was to investigate the characteristics and prevalence of headaches in patients with epilepsy based on the International Classification of Headache Disorders, 2nd edition (ICHD-II). We also compared our findings with those of a population-based epidemiological study of headache in the same geographical area, a population-based door-to-door survey (PBDDS) (Yu et al., 2012).

Methods

Consecutive adult patients with epilepsy, referred to the outpatient clinic of the Epilepsy Center of PLA General Hospital between February 01, 2012, and May 10, 2013, were recruited for this study. All patients had a definite diagnosis of epilepsy as determined by at least two epileptologists. The patients included in this study were 18 years-old or older with the ability to autonomously answer the questionnaires. Patients with mental retardation, learning disabilities, behavioral disorders or other evident abnormalities that could compromise cooperation and the ability to respond the questionnaires were excluded. At the closing interview after one and a half years, 1109 patients, 607 men and 502 women, with a mean age of 28.20 (range 18—64) years, completed a questionnaire regarding headache. In those who confirmed headaches, a standardized semistructured telephone interview was performed, with questions about headache timing in relation to seizures, in addition to frequency, duration, intensity, localization, and associated features of the headaches.

The epilepsy was classified according to the criteria of The International League Against Epilepsy's Classification of Epileptic Seizures (1989). Further diagnostic questions were based on ICHD-II criteria and aimed at identifying migraine and tension-type headache (TTH). Respondents who might have more than one type of headache were instructed to focus on the subjectively most bothersome type. To arrive at diagnoses from responses to these questions, the ICHD-II criteria were applied first for migraine, then for TTH, probable migraine, and finally for probable TTH. The remaining cases were considered unclassifiable. In calculating the prevalence of migraine, we added cases of definite and probable migraine, as we did in the validation study (where the rationale is explained in detail) (Yu et al., 2011). Similarly for TTH, we added cases of definite and probable TTH.

The headaches were further categorized as preictal, migraine aura-triggered seizure, postictal or interictal. Preictal headache was defined as a headache starting not more than 24 h prior to the seizure and lasting until the onset of a seizure. Migraine aura-triggered seizure was defined as a seizure triggered by an attack of migraine with aura, where a seizure occurs during or immediately following a migraine aura, and postictal headache was defined as a headache starting within three hours after a seizure and ceasing within 72 h after the attack. Interictal headache was defined as headache starting not earlier than three hours after a seizure or a headache never proceeding directly into an epileptic fit.

The patients were asked to grade their usual headache intensity as mild (maintaining normal activities without problems), moderate (maintaining normal activities with difficulty), severe (must give up normal activities and lie down) or extremely severe (impossible to stay still).

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 14.0. Continuous variables were summarized as means and standard deviations, and categorical variables as numbers and percentages. Chi-square tests were used to compare the distributions of categorical variables between groups. Paired-sample *t*-tests were used to compare continuous variables. Statistical significance was set at $p < 0.05$.

Results

In total, 1109 consecutive adult epileptic patients were included in this study, of which 607 (54.73%) were males and 502 (45.27%) were females. Overall, 60.14% (667/1109) of patients reported headaches. Headache was less prevalent in males (57.17%) than in females (63.75%) ($p = 0.026$). Except for a lower mean age and age at onset of seizures in those with headaches ($p < 0.001$), there were no significant differences regarding type of epileptic syndrome between patients with and without headaches (Table 1).

Consent to further interviews was provided by 667 patients with headache (320 women and 347 men, mean age 28.20, range 18—64 years). Among the headache patients, the intensity of the pain was described as mild by 224 (33.58%) patients, moderate by 337 (50.52%) patients and severe by 106 (15.90%) patients. There was no significant difference in the frequency of seizures between patients with headaches and without headaches ($p = 0.27$) (Table 1).

Interictal headache was reported by 231 (34.63%) patients. In addition, 469 patients had postictal headache (70.31%), and 59 patients had preictal headache (8.85%), which including 82 patients who presented more than one type of headache (45 patients had postictal headache and interictal migraine; 17 patients had postictal headache and interictal tension-type headache; 9 patients had preictal and postictal headache; 9 patients had preictal, postictal headache and interictal migraine, and 2 patients had migralepsy and postictal headache). The clinical characteristics of the headaches are listed in Table 2.

Preictal headache

Fifty-nine patients had headaches that evolved into seizures, and for 38 of these patients, the headaches were