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Original Article

A Study of Clinical Profile of Headache in Epilepsy Patients

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Abstract

Background: Headache is the most common symptom encountered in neurology outpatient department (OPD). One-fifth of patients in neurology clinics present with headache. Headache was long been found to be associated with epilepsy, especially migraine both chronic neurologic disorders share possible clinical interrelationships. Studying their association is necessary as identification of clinical subgroups vulnerable to develop to both disorders can be made possible in the future.

Aims and Objectives: The objective of the study was to analyze the characteristic features of various types of headaches in epilepsy patients and their causal association.

Materials and Methods: A total of 100 epilepsy patients with headache were recruited from the OPD of the neurology department in a tertiary care center and interviewed regarding the characteristic features of headache through a questionnaire.

Results: Out of our study population, female outweighs the male (53, 47). Out of all, interictal was more prevalent (57%), followed by post-ictal (48%), pre-ictal (22%), and intra-ictal (0%) among epilepsy patients. Migraine was found to be the most common type of headache in all subgroups of headaches in epilepsy patients (pre-ictal – 77% of migraine, postictal – 81% of migraine, and interictal – 61% of migraine). Associated characters of headaches such as photophobia (42%) and their prevalence are also studied.

Conclusions: Stronger association between migraine and headache is validated, and the strongest associated with migraine in postictal headache is highlighted (81%). This can strengthen the theories proposed so far such as the frequent triggering of headache by a seizure. Further research on common etiologic or pathophysiological processes to these associations can lead to a common therapeutic strategy and prevention of morbidity in patients.

Key words: Epilepsy, Headache, Interictal headache, Migraine, Post-ictal, Pre-ictal headache, Tension-type headache

INTRODUCTION

Headache is the most common neurologic symptom prevalent among the general population. Epilepsy is the most common neurologic disorder affecting all age groups.[1] The existence of primary headaches in epilepsy patients is still a topic of debate.

Headache occurring in epilepsy patients can be classified broadly as interictal headache (inter –IH) and peri-ictal headache (peri – IH). Peri-ictal headache is again classified as pre-ictal, intraictal, and postictal headache according to its relationship with seizures.[2]

According to the International Classification of Headache Disorders (ICHD),[3] pre-ictal headache is defined as an episode that developed within 24 h before the seizure and lasting until the start of the seizure. Intraictal headache is defined as an episode of headache occurring simultaneously with the onset of seizure ipsilateral to the epileptic discharges. This occurs more commonly with partial seizures. Hemicrania epileptica is a terminology used interchangeably with intraictal headache in the ICHD.[3,4] Post-ictal headache is defined as an episode that has developed within 3 h after a seizure but resolved within 72 h after the epileptic seizure is terminated.

Interictal headache is defined as an episode which not started within 3 h after an epileptic seizure or never

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proceeding directly into an epileptic fit. Migraine is found to be the most common interictal headache among epilepsy patients according to various studies.[5] Studying the prevalence of interictal and peri-ictal headache, and it's characteristic features help us to find out the casual association between headache and epilepsy.

Aim

The aim of the study was to analyze the characteristic features of various types of headaches in epilepsy patients and their causal association.

MATERIALS AND METHODS

This study was done in a tertiary care hospital in the Southern Tamil Nadu state of India. All patients attending the neurology outpatient department in our tertiary care hospital with the diagnosis of epilepsy between November 1, 2019, and December 31, 2019, were recruited in this study.

All patients who are included in this study are more than 18 years and satisfy the inclusion criteria, already a known case of seizure disorder on treatment with a history of headache. Patients <18 years, who are unwilling to participate in the study, never suffered a headache, with mental retardation, other behavioral or learning disorders, and patients presented with the first episode of seizures are excluded from this study.

A questionnaire was prepared, and all patients included in this study were interviewed after getting informed written consent. The questions about the nature of the headache in the questionnaire were based on the ICHD-II criteria.[3,6] The patients were asked about the type of headache, its temporal relationship with seizures, duration of headache, the intensity of pain, frequency, lateralization, quality of pain, aggravating factors, relieving factors, and use of analgesics by the patient during the episode. All these modalities were described for all types of headaches experienced by the patients (pre-ictal, post-ictal, and interictal). The presence of accompanying features such as photophobia, phonophobia, vomiting, nausea, and other aura symptoms is asked and recorded. According to the ICHD-II criteria,[3] the patient's headache was typed as migraine, tension-type headache (TTH), and unclassifiable. Details of seizures such as semiology (generalized tonic-clonic seizures [GTCS], complex partial seizures [CPS], myoclonic, and atonic), duration of illness, frequency, and type of treatment were also collected from the patient. All patients underwent electroencephalogram after the interview and reports were collected.

Association of headache with epilepsy and it's various characteristic features are compared with the clinical profile of epilepsy patients through statistical analysis.

RESULTS

Out of 100 patients included in our study, 47 were males and 53 were females Figure 1. The study population falls in the age group of 19 years–71 years. The mean age among males was 38.9 years and females were 35.6 years. The duration of illness among our study population ranges from 1 year–45 years. Among our study group, ten patients had CPS; the rest of the 90 patients had GTCS Figure 2. Among our study group, 31 patients are taking mono drug therapy (antiepileptic medications), 53 patients are found to take dual drug therapy, and 16 patients are taking multidrug therapy Figure 3.

Pre-ictal Headache

Among our study group, 22 patients were found to have pre-ictal headaches Figure 4. Out of 22 patients,

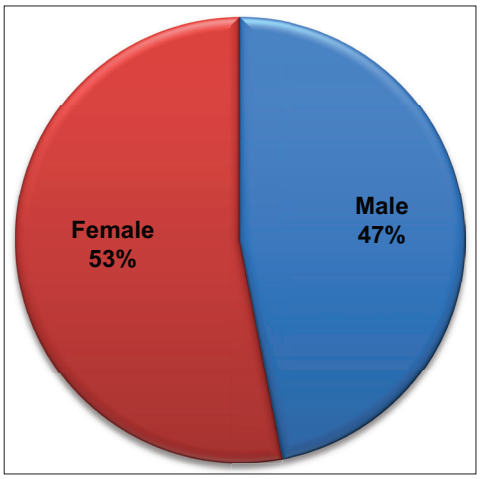

Figure 1: Sex distribution among our study population

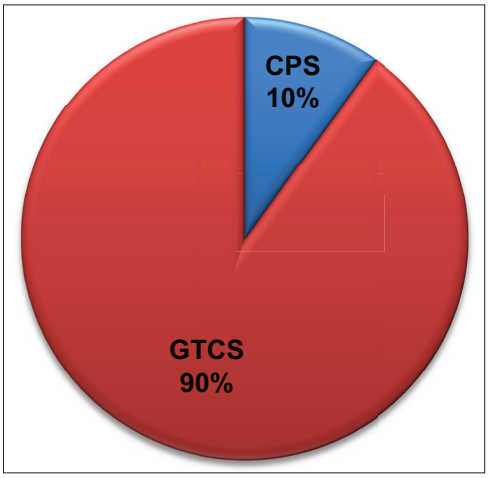

Figure 2: Distribution of semiology of seizures

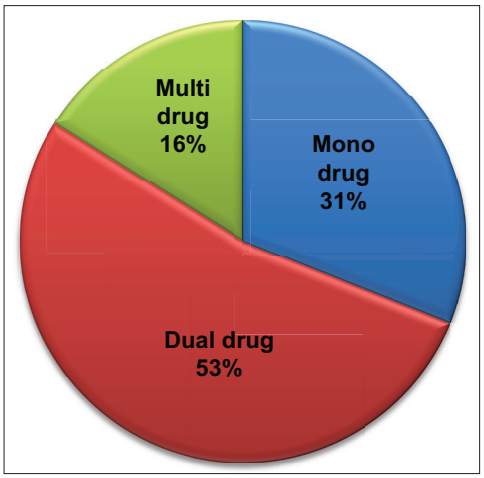

Figure 3: Distribution of patterns of therapy among our study group

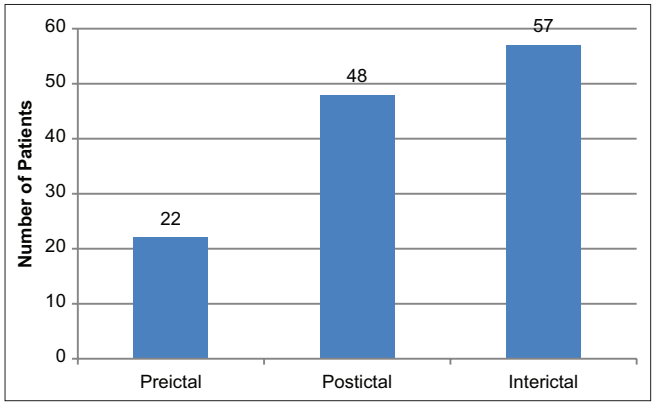

Figure 4: Distribution of various headaches among epilepsy patients in our study group

19 patients had a headache for <1 h before seizure onset, and three patients suffered from headache for 1–3 h before seizures. Seventeen patients had headache of migrainous type and other unclassifiable types in five patients. Out of 22 patients, 11 patients also had a headache during the interictal period also. Among these, 11 patients who have both pre-ictal and interictal attacks of headache, nine patients (9/11) had resembled the same quality of pre-ictal and interictal headache with the migrainous feature, whereas other two patients (2/11) headache were unclassifiable. Among patients with pre-ictal headache, 18 patients (18/22) were known to have GTCS and four patients were known to suffer from CPS (4/22).

Postictal Headache

Of our study population, 48 patients were found to have post-ictal headache. Out of 48 patients, 26 patients (26/48) had headache for <24 h duration from seizure termination and 22 patients had headache for more than 24 h duration (22/48). Among patients having post-ictal headache, 39 (39/48) had features of migrainous type and 9 (9/48) patients had features of TTH, out of these 48 patients, 16 patients also headache during the interictal period (16/48). Among the 16 who are found to have both post-ictal and interictal headache, eight patients had migrainous type (8/16), seven had TTH type (7/16), and one patient had the unclassifiable type of interictal headache (1/16). Nausea (15/48) was found to be the common accompanying feature in postictal headache, followed by vomiting (13/48), photophobia (10/48), and myalgia (5/48), respectively. Among 48 patients, 44 patients had GTCS and four patients had CPS as seizure semiology.

Interictal Headache

Among our study population, 57 patients had interictal headache. Among them, 35 patients had a migrainous type, 12 patients had TTH type, and ten had the unclassifiable type of headache. Females are more common among the migraine subgroup (28/35). Among our entire study population, two patients were found to have pre-ictal, post-ictal, and interictal headache episodes, with one being having migrainous type, and the other having TTH type of headache. Regarding characteristic features of interictal headache, 14 had unilateral headache and 27 had a bilateral headache. Unilateral headache was more commonly associated with migrainous type. Forty-eight patients use analgesics in addition to anti-epileptic medications during an episode of interictal headache for resolution of symptoms. Common associated features accompanying interictal headache are photophobia (24/57), followed by nausea (23/57), vomiting (17/57), phonophobia (8/57), and aura (8/57). Out of 57 patients, 52 of them were found to suffer from GTCS and five patients had CPS. Seventeen patients were taking monotherapy, 29 taking dual drug therapy, and 11 patients on multidrug therapy among these 57 patients with interictal headache. Among these patients with interictal headache, 24 patients were suffering from seizures for <5 years duration, nine patients for 6–10 years duration, and 24 patients had seizures for more than 10 years duration.

DISCUSSION

Study on association between headache and epilepsy is a topic of controversy due to differences in classification criteria, race, age, and sex differences among targeted population, the methodology of data collection among existing studies.[6]

Among our study population, the peri-ictal headache was present (pre-ictal 22%, and post-ictal 48%) in 35% of patients in accordance with other studies in the literature (28–50%).[7] The prevalence of pre-ictal headache was 22% in our study which was slightly higher when compared to other study designs Mainieri *et al.*[8]

Table 1: Correlation between postictal headache and migraine among our study population

Post-ictal	Post migraine		Total	*P*-value
	No	Yes		
No	52	0	52	<0.0001
Yes	9	39	48	
Total	61	39	100	

Table 2: Correlation between presence of pre-ictal headache and duration of epilepsy

Duration in years	Pre-ictal		Total	*P*-value
	No	Yes		
<5	36	10	46	0.667
6–10	15	6	21	
>11	27	6	33	
Total	78	22	100	

Table 3: Correlation between presence of post-ictal headache and duration of epilepsy

Duration in years	Post-ictal		Total	*P*-value
	No	Yes		
<5	22	24	46	0.73
6–10	12	9	21	
>11	18	15	33	
Total	52	48	100	

Table 4: Correlation between presence of pre-ictal headache and patterns of therapy for epilepsy

Treatment	Pre-ictal		Total	*P*-value
	No	Yes		
Mono drug	28	3	31	0.337
Dual drug	38	15	53	
Multidrug	12	4	16	
Total	78	22	100	

Table 5: Correlation between presence of post-ictal headache and patterns of therapy for epilepsy

Treatment	Post-ictal		Total	*P*-value
	No	Yes		
Mono drug	13	18	31	0.585
Dual drug	31	22	53	
Multidrug	8	8	16	
Total	52	48	100	

Table 6: Correlation between presence of interictal headache and semiology of seizures

Seizure type	Interictal		Total	*P*-value
	No	Yes		
Generalized tonic-clonic seizures	38	52	90	0.637
Complex partial seizures	5	5	10	
Total	43	57	100	

Table 7: Correlation between presence of interictal headache and duration of epilepsy

Duration in years	Interictal		Total	*P*-value
	No	Yes		
<5	22	24	46	0.675
6–10	12	9	21	
>11	9	24	33	
Total	43	57	100	

Table 8: Correlation between presence of interictal headache and duration of epilepsy

Treatment	Interictal		Total	*P*-value
	No	Yes		
Mono drug	14	17	31	0.585
Dual drug	24	29	53	
Multidrug	5	11	16	
Total	43	57	100	

Intraictal headache was not found in any patients in our study population. Even various studies in literature also consider that cases of epileptic headache (ictal headache) were rare and can be seen in children than in adults, as mentioned in Mainieri *et al.*[8] Moreover, the term epileptic headache is also not used in the current ICHD and International League Against Epilepsy (ILAE) classification. ILAE also consider ictal headache as a form of autonomic aura.

The most common among peri-ictal headache was post-ictal headache which accounts for 48% in our study population and incomparable with 12–52% other studies.[2,9-14] Migraine was the most common type of headache among post-ictal headaches, with significant $P < 0.0001$ Table 1 in accordance with other studies in the literature.[1,5] However, the duration of epilepsy and drug-resistant epilepsy (multidrug therapy) does not correlate with the presence of peri-ictal (pre-ictal, and post-ictal) headache Tables 2-5 ($P = 0.667$, 0.73, 0.337, and 0.585, respectively) in contrast with other studies in the literature.[15,16]

Interictal headache was more prevalent among epilepsy patients than peri-ictal headache, being found in 57% of patients among our study population. Migraine was the most common type accounting for 61% in accordance with 60% in a study by Wang *et al.*[14] TTH and unclassifiable type of interictal headache in epilepsy patients account for 21% and 17%, respectively. Semiology, duration of seizure, and presence of drug-resistant seizures do not correlate significantly with the occurrence of an interictal headache Tables 6-8 ($P = 0.637$, 0.675, and 0.585).

In total, the strong association of peri-ictal and interictal migrainous headache attacks and epilepsy was established in this study. Recent studies also support this association by various theories such as genetic and membrane channel theory.[17] Altered membrane channel creating between the imbalance of excitatory and inhibitory impulses in the brain leading to a common risk for both migraine and epilepsy. Cortical spreading depression is also found to be another pathophysiology underlying common to both epilepsy and migraine with aura.[17] Furthermore, studies suggest epilepsy can also occur as a stressful event triggering the occurrence of other headaches such as TTH.[18,19] Our study further validates this association with data and considering the common pathophysiology through various studies, treating these patients with common antagonistic drugs and alleviating the symptomatology can further prove the association further.

CONCLUSIONS

Interictal headache (57%) was the most common among our study population, followed by postictal headache (48%). Migraine was the common type of headache among all categories of peri-ictal and interictal headaches. The strong association of migraine among epilepsy patients and the high prevalence of interictal and post-ictal headache in epilepsy patients are established and strengthened by our study. Our study highlights that the presence of migraine and other types of headache during interictal and peri-ictal period should be anticipated in epilepsy patients and should be addressed early as ignoring can add to the morbidity of the patient.

Early anticipation of headache and proper simple measures like history taking can lead to early detection of this comorbidity in epilepsy patients. Early detection can influence the choice of antiepileptic drug; thereby selecting a common therapy leads to control of both epilepsy and headache reducing the morbidity and mortality among patients.

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