ORIGINAL ARTICLE

Disease progression to chronic migraine: onset of symptoms of headaches, anxiety and mood disorders

Progressão da doença em enxaqueca crônica: Análise do início dos sintomas de cefaleia, ansiedade e humor

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ABSTRACT

Background: Psychiatric conditions, mostly anxiety and mood disorders, are common in patients with chronic migraine. There has recently been extensive debate on migraine progression, but little is known about the role of psychiatric disorders in this respect. **Objective:** In order to evaluate the role of psychiatric disorders in migraine progression, we analyzed the temporal profile of migraine, mood and anxiety disorders, and years since onset of symptoms in chronic migraine (CM) patients. **Methods:** Fifty CM patients diagnosed according to the International Headache Society (2004) criteria were interviewed and diagnosed for mental disorders using the Structured Clinical Interview for DSM-IV (SCID-I/P). **Results:** Anxiety disorders preceded the onset of episodic migraine, which was followed by depression and daily headaches. **Conclusions:** Psychiatric comorbidity evaluation in chronic migraine may lead to better patient management and clinical outcomes. Patients with a history of anxiety, episodic migraine, and depression may be at risk of developing CM. Early treatment of anxiety, mood disorders, and episodic migraine may prevent disease progression to CM.

Keywords: Anxiety disorders; Mood disorders; Disease progression; Comorbidity

RESUMO

Introdução: Ansiedade e depressão são condições clínicas comuns em pacientes com enxaqueca crônica. Um intenso debate em relação ao processo de cronificação da enxaqueca tem acontecido recentemente, mas pouca ênfase tem sido dada a comorbidade psiquiátrica. **Objetivos:** Para avaliar o papel das comorbidades psiquiátricas na progressão da enxaqueca, analisamos o perfil temporal de início dos sintomas de humor, ansiedade e dor nos pacientes com enxaqueca crônica. **Métodos:** Cinquenta pacientes diagnosticados de acordo com os critérios da Sociedade Internacional de Cefaleias (2004) foram entrevistados e diagnosticados para transtornos mentais de acordo com a entrevista estruturada para o DSM-IV (SCID-I/P). **Resultados:** Transtornos de ansiedade precederam o início das enxaquecas episódicas, que foram seguidas pelo aparecimento pelos transtornos de humor e sequencialmente a evoluçãoo/transformação para enxaqueca crônica. **Conclusões:** A avaliação das comorbidades psiquiátricas na enxaqueca crônica podem levar a um melhor diagnóstico e tratamento dos pacientes. Pacientes com história de ansiedade, enxaqueca e depressão podem ter risco de desenvolverem enxaqueca crónica. Tratamento precoce destas condições podem previnir a ocorrência da enxaqueca crônica.

Descritores: Transtornos de ansiedade; Transtornos do humor; Progressão da doença; Comorbidade

INTRODUÇÃO

Migraine is a chronic and sometimes progressive disorder characterized by recurrent episodes of headache and associated symptoms. Chronic migraine (CM) is debilitating and has a substantial impact on a patient's life;[1] it has recently been added to the second revised International Headache Society Classification (2004),[2] and redefined[3] under a broader concept of the disorder, accepting as migraine headaches occurring more than 8 days a month (previously 15 days), for more than three months. The diagnosis of medication overuse headache must be excluded.[4] Chronic migraine has been shown to be an early stage of chronification of transformed migraine.[5] CM is common in the general population[6] and accounts for up to 60% of consultations at tertiary headache centres.[7]

Mental disorders are common conditions among these patients and are associated with a high degree of disability, low level of satisfaction, and low quality of life.[8] Psychiatric comorbidities are also significant factors in the development and maintenance of chronic headaches.[9] Some degree of depression is found in 85% of CM patients, and severe depression in 25%.[10] Anxiety disorders affect 75% of CM patients,[11,12] but anxiety and mood disorders overlap in this condition.[13] CM is often difficult to treat and its refractoriness has been attributed to psychiatric comorbidity.[14]

Mental disorders were also found to be more common in migraine than in non-migraine individuals; relative risk for major depressive disorders was 2.2%, bipolar disorder 2.9%, generalized anxiety disorder 5.3%, panic disorder 3.3%, simple phobia, 2.4%, and social phobia, 2.0%.[15] Studies have consistently shown that migraine with aura is more closely associated with psychiatric comorbidity than migraine without aura.[16] Merikangas et al[17] observed that anxiety disorders generally preceded migraine, followed by mood disorder diagnoses, and postulated a syndromic relation between migraine, anxiety and depression involving a range of symptoms starting with anxiety (frequently in early childhood), followed by migraines and depressive episodes in adult life. CM has never been studied in this context.

Recent evidence suggests that a subgroup of migraine patients may have a clinically progressive disorder,[18-21] but little emphasis has been given to the putative role of psychiatric disorders in migraine progression.

Our own study analyzed the years since onset of anxiety-disorder symptoms, episodic migraine, mood disorders, and daily headaches in chronic migraine patients in order to evaluate the chronological relations between these conditions. We predicted that CM would be the next stage of disease progression after anxiety disorders, episodic migraine and mood disorders had set in.

METHODS

Fifty patients (forty women, ten men) were consecutively diagnosed with chronic migraine in accordance with the International Headache Society (2004)[2] criteria and enrolled in the study. Their mean age was 41.1 ± 11.6 years (SD), range 23-65 years, most being caucasians (45, 90%), with 4 black and 1 asian. Mean headache frequency was 22.2 ± 2.7 days/month, mean headache intensity (0-10 scale) was 8.1 ± 0.7. All patients had daily headaches (more than 15 headache days/month). All patients were enrolled at a tertiary headache centre in Sao Paulo and interviewed using the Structured Clinical Interview for DSM-IV SCID-I/P22;23 for psychiatric assessment. Patients were asked about the onset of anxiety symptoms and mood disorders using the standardized SCID interview procedure. Questions about the onset of symptoms of episodic and chronic migraine were asked by the same SCID interviewer, and responses were confirmed by the neurology team. We only included responses with significant degree of confidence by both patients and research team. The study protocol was approved by the local Ethics Committee and all patients gave written consent. We analyzed the onset of symptoms in different groups; all patients had a history of daily headaches and episodic migraine. We compared patients with both anxiety and mood disorders (22 patients, 44%), as well as patients with anxiety but not depression (16 patients, 32%), depression but not anxiety (6 patients, 12%), and no psychopathology (8 patients, 16%). A Student t-test and Mann-Whitney rank sum test were used to compare groups. Five percent was chosen as a minimum level of statistical significance for two-sided tests. Results were presented as mean ± standard deviation.

RESULTS

Forty-two patients (84%) met lifetime diagnostic criteria for some mental disorder; 38 (76%) presented an anxiety disorder; 25 (50%) presented a mood disorder; 22 (44%)

presented both anxiety and mood disorder; 26 (52%) presented generalized anxiety disorder; 3 (6%) presented panic disorder, 2 (4%) obsessive-compulsive disorder, 3 (6%) posttraumatic stress disorder and 27 (54%) specific or social phobia. Twenty-two (44%) presented major depressive episode, 14 (28%) of them had a recent, and 17 (34%) patients had previous episodes. Two patients met diagnostic criteria for dysthymic disorder, and 2 for bipolar II disorder.

Patients with both anxiety and mood disorders, episodic migraine, daily headaches onset and comorbidities presented the following features: mean years since onset of anxiety disorders was significantly earlier than migraine (27.1 ± 16.9 vs. 20.5 ± 11.1 years since onset, p=0.016), mood disorders (6.8 ± 1.9 years, p<0.001) and daily headaches (4.6 ± 2.8 years, p<0.001).

Migraine onset was significantly earlier than mood disorder and daily headaches onset, p<0.001, as was mood disorder onset compared to daily headaches onset (p<0.01).

Anxiety disorders preceded the onset of episodic migraine, which was followed by a mood disorder and daily headaches (Figure 1).

In patients with anxiety but not mood disorders, anxiety onset also preceded episodic migraine onset and daily headaches onset (23.7 ± 17.4 vs. 21.6 ± 11.2, p<0.01, vs. 5.5 ± 3.8, p<0.001). In patients with mood disorders alone, episodic migraine preceded depression symptoms (27.5 ± 8.2 vs. 4.2 ± 2.7, p<0.001). Mood disorder onset also preceded daily headaches, but only a trend toward significance was observed (4.2 ± 2.7 vs. 3.7 ± 2.8, p=0.054).

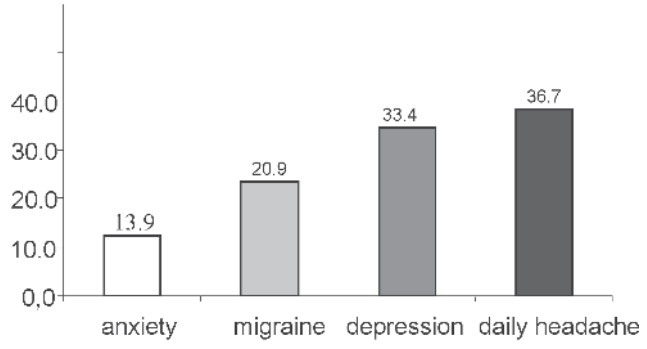

Figure 1. Mean onset age (years) of anxiety disorders, mood disorders, episodic migraine and daily headaches. Profiling migraine and comorbidities showed that mean ± SD onset age of anxiety disorders was significantly lower than that of migraine (13.9 ± 13.7 (range 0-44) vs. 20.9 ± 12.5 (range 4-54); onset of mood disorders (33.4 ± 10.1 (range 10-54); and CM (36.7 ± 11.3 (range 19-64). Mean onset age of migraine was significantly lower than that of mood disorders and CM, p<0.001, as it was for mood disorder onset compared to daily headaches onset (p<0.01).

DISCUSSION

The findings of our study of the pattern of psychiatric comorbidity symptoms and headaches in CM matched those of Merikangas et al[24] who reported that anxiety disorders preceded migraine, which preceded onset of depression, but did not record daily headaches in young adults aged 27-28 in Zurich (whereas the mean age of our participants was 41.1 ± 11.6, range 23-65). Perhaps the younger age of the Zurich population explains the absence of daily headaches as a common symptom. We also found that the last step in the symptom progression from anxiety disorders to episodic migraine and mood disorders may be migraine chronification and a daily pattern. Even when anxiety patients without mood disorder were compared with mood disorder patients without anxiety, the same pattern was observed: anxiety preceded episodic migraine onset in the former group, and episodic migraine preceded mood disorders onset in the latter. The small sample size of the latter may explain why depression onset was not significantly different to daily headaches onset, but a trend toward significance was found at p=0.054.

CM may also be transformed to a wide spectrum of symptoms, as elegantly reported by Bigal et al[25] who suggested that the frequency of migraine attacks is high in the early stages of migraine chronification, but the frequency of nonmigraine headaches increases as the illness progresses. Early descriptions of transformed migraine mentioned anxiety and mood disorders as key elements for developing daily headaches from episodic migraines.[26,27]

Our findings suggest that CM may be the result of a combination of anxiety and mood disorder symptoms in an episodic migraineur, but prospective studies are required to draw causal inferences. In this context, CM would be a truly neuropsychiatric condition. Another possibility is that CM is a broader syndrome, involving anxiety manifested frequently in early childhood, adolescence or young adulthood, followed by episodic migraines and then depressive disorders in adult life. There may well be genetic predisposition for this disease progression. Other comorbid conditions such as sleep disorders, fibromyalgia, and other functional somatic syndromes require further investigation to better define their

role and level within a broader concept of disease progression, which would hypothetically include these syndromes.

Progression of symptoms in headache is common. A longitudinal epidemiologic study found that 3% of individuals with episodic headache (frequency from 2 to 104 days per year) progressed to chronic daily headache (CDH, episode frequency >180 days per year) in the course of a year.[28] The study concluded that the incidence of CDH in subjects with episodic headache is 3% per year. A one-year follow-up of 532 consecutive episodic migraine patients (<15 days per month) found that 64 (14%) developed chronic daily headache.[29]

Despite its clinical relevance, the evidence of risk factors for migraine progression is limited. The prevalence of CDH has been reported to decrease slightly with age and to be higher in women [odds ratio (OR) = 1.65 (1.3 to 2.0)] and in divorced, separated, or widowed individuals [OR = 1.50 (1.2 to 1.9)]. Social risk factors have also been described: the risk of CDH in individuals with less than high-school education was threefold that of a college-educated sample [OR = 3.56 (2.3 to 5.6)].[30] CDH was also associated with a self-reported diagnosis of arthritis [OR = 2.50 (1.9 to 3.3)], diabetes [OR = 1.51 (1.01 to 2.3)],[31] previous head trauma[32] and medication overuse.[33] Interestingly, the highest risk factor described for development of CDH was obesity [OR = 5.53 (1.4 to 21.8)].[34] A study comparing 41 migraineurs with 41 medication overuse headache (MOH) patients found that the latter showed excess risk of suffering from mood and anxiety disorders associated with use of psychoactive substances. Psychiatric disorders occurred significantly more often before rather than after the transformation from migraine to medication overuse headache (MOH).[35]

Most studies failed to explore one of the main issues in migraine management: psychiatric comorbidity. Our sample, although relatively small, showed a consistent pattern of disease progression based on the onset of symptoms described by patients. Recollection bias may be present, but previous studies have utilized and validated the same method.[14] The ideal methodology would be a prospective study, but long term follow-up (decades) is also very difficult.

This paper raises the possibility of early pharmacological or non-pharmacological intervention for adolescents or young adults with anxiety disorders in order to prevent the future onset of migraine.

CONCLUSION

Psychiatric disorders, mostly anxiety and mood disorders, are common in patients with CM. Anxiety disorders may occur before the onset of episodic migraine and be followed by depression and finally daily headaches.

Psychiatric evaluation for CM patients may enhance patient management and clinical outcomes. Even though the present findings are limited by the cross-sectional design of this study, the data suggests that anxiety disorders may be an important risk factor for subsequent migraine and that both anxiety and mood disorders play an important role in migraine progression to CDH.

Therefore, early treatment of anxiety disorder and/or episodic migraine may prevent long term complications, such as depression and CM.

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