

Fatigue, sleep–wake pattern, depressive and anxiety symptoms and body-mass index: analysis in a sample of episodic and chronic migraine patients

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Abstract Migraine clinical presentation and life-time course can be highly heterogeneous, with a subgroup of patients developing chronic migraine; moreover, migraine clinical spectrum is expanded by the association with different coexisting conditions and interictal dysfunctions. The aim of this study was to systematically evaluate migraine clinical features, daily functioning parameters, sleep pattern, presence of depressive-anxiety symptoms and body mass index (BMI) in a sample of 75 episodic and 75 chronic migraine without aura patients. Migraine-related disability, fatigue, daily sleepiness, subjective sleep quality, anxiety and depressive symptoms were, respectively, evaluated using the following questionnaires: Fatigue Severity Scale (FSS), Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index (PSQI), Generalized Anxiety Disorder 7-item Scale (GAD-7), Patient Health Questionnaire 9-item Scale (PHQ-9). Mean FSS score ($p < 0.001$), PSQI score ($p = 0.015$), GAD-7 score ($p = 0.019$), PHQ-9 score ($p < 0.001$) and BMI score ($p = 0.012$) were significantly higher in chronic compared to episodic migraineurs. Additionally, a correlation analysis carried out in the total sample of 150 migraine patients documented a statistically significant, positive correlation between monthly frequency of migraine attacks and FSS score ($p < 0.001$), PSQI score ($p = 0.006$), GAD-7 score ($p = 0.019$), PHQ-9 score ($p < 0.001$) and BMI score ($p = 0.049$). Data from the present report seem to expand the concept of migraine as a continuum or spectrum, with

greater occurrence of fatigue, poor sleep quality, anxiety-depressive symptoms and higher BMI score in chronic compared to episodic migraine patients; further investigation is certainly necessary to better define the biological basis and mechanisms associated with migraine transformation from episodic to chronic pattern.

Keywords Episodic migraine · Chronic migraine · Fatigue · Sleep quality · Psychiatric disorders · Body-mass index

Introduction

Migraine is a common primary headache disorder, whose clinical presentation can be highly heterogeneous, as well as life-time disease course, with a subgroup of patients developing chronic migraine, defined as headache occurring on 15 or more days per month for more than 3 months and having the features of migraine headache on at least 8 days per month [1]. It has been hypothesised that migraine represents a spectrum disorder, in which migraine can progressively evolve from episodic to chronic pattern in susceptible individuals over a variable period of time, ranging from months to years. Furthermore, it seems that migraine clinical spectrum is expanded by the association with different comorbid/coexisting conditions, among which psychiatric and sleep disorders, chronic pain conditions and obesity, possibly reciprocally interacting and contributing to modulate migraine clinical expression [2].

Taking this scenario into consideration, the aim of this study was to systematically evaluate different clinical parameters, among which migraine clinical features, occurrence of fatigue, daily sleepiness, sleep pattern, presence of depressive and anxiety symptoms and body

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mass index (BMI), in a consistent sample of episodic and chronic migraine patients.

Methods

A cross-sectional study was carried out at the Institute of Neurology, University of Pisa, between October 2013 and February 2015, enrolling 150 migraine without aura patients (ICHD-3 beta criteria); 75 patients fulfilled criteria for episodic migraine and 75 for chronic migraine [1]. In the group of chronic migraine patients, 67 subjects also fulfilled diagnostic criteria for the diagnosis of Medication-Overuse Headache, according to ICHD-III beta criteria [1].

Inclusion criteria were: age ≥ 18 years; normal neurologic evaluation; brain MRI examination without pathological findings; absence of migraine preventive treatment for at least 3 months before study inclusion. Exclusion criteria were: comorbidity with other primary or secondary headaches; positive history of comorbid medical disorders; chronic medication use, other than migraine symptomatic drugs.

Data regarding age, gender, disease duration and body mass index (BMI) score were collected; monthly frequency of migraine attacks was obtained according to the previous 3 months headache diaries. Migraine Disability Assessment Score (MIDAS) questionnaire was used to assess migraine-related disability in a 3-month period [3]. The occurrence of fatigue was evaluated using the Fatigue Severity Scale (FSS); a score greater than 27 is indicative of pathological levels of fatigue [4]. The Epworth Sleepiness Scale (ESS) provided a measurement of the patient's subjective habitual level of daytime sleepiness (cut-off >10) [5]. Subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), a self-rated questionnaire evaluating sleep quality over a 1-month time interval; a score greater than 5 is indicative of poor sleep quality [6]. Finally, the Generalized Anxiety Disorder 7-item scale (GAD-7) and the Patient Health Questionnaire 9-item Scale (PHQ-9) [7, 8] were respectively used to evaluate anxiety and depressive symptoms; a score greater than 10 was considered indicative, respectively, of anxiety and depressive symptoms of moderate-severe degree. In episodic migraine patients, clinical and psychological features were explored in the interictal period.

Informed consent was obtained from all the individual participants included in the study.

The statistical analysis was carried out using SPSS version 14.0 for Windows. The data are shown as arithmetic means with standard deviations (SD) for continuous variables. The statistical analysis was performed using unpaired Student *t* test for multiple comparisons for

continuous variables and Chi square test with continuity correction for categorical variables. A correlation analysis was carried out by means of the ρ coefficient of Spearman. The significance level was set at $p = 0.05$. All tests were two tailed.

Results

One hundred and fifty migraine without aura patients according to ICHD-III beta criteria [1] were enrolled. The sample was constituted by 75 patients with episodic migraine (13 males, 62 females) and 75 with chronic migraine (10 males, 65 females); no statistically significant differences were detected in gender distribution between episodic and chronic migraineurs ($p = 0.650$).

Mean age ($p = 0.012$), disease duration ($p < 0.001$), BMI score ($p = 0.012$) and MIDAS score ($p = 0.005$) were significantly higher in chronic compared to episodic migraineurs. Furthermore, mean FSS score ($p < 0.001$), PSQI score ($p = 0.015$), GAD-7 score ($p = 0.019$) and PHQ-9 score ($p < 0.001$) were significantly higher in chronic migraine patients compared to episodic patients. Data are reported in detail in Table 1.

A correlation analysis (ρ coefficient of Spearman) carried out in the total sample of 150 migraineurs documented a statistically significant, positive correlation between monthly frequency of migraine attacks and patients age ($\rho 0.375$, $p < 0.001$), disease duration ($\rho 0.360$, $p < 0.001$), BMI score ($\rho 0.177$, $p = 0.049$), MIDAS score ($\rho 0.353$, $p < 0.001$), FSS score ($\rho 0.370$, $p < 0.001$), PSQI score ($\rho 0.247$, $p = 0.006$), GAD-7 score ($\rho 0.208$, $p = 0.019$) and PHQ-9 score ($\rho 0.314$, $p < 0.001$). The correlation analysis failed to provide statistically significant correlations between monthly frequency of migraine attacks and ESS score.

Discussion

The results of the present study mainly showed higher migraine-related disability, BMI score, greater occurrence of fatigue, poor sleep quality and anxiety-depressive symptoms in chronic compared to episodic migraine patients. Furthermore, a statistically significant, positive correlation between monthly frequency of migraine attacks and migraine-related disability, BMI score, occurrence of fatigue, poor sleep quality and presence of anxiety and depressive symptoms was evidenced. In this study we failed to show statistically significant differences in mean EDSS score between episodic and chronic migraine patients, as well as a correlation between monthly frequency of migraine attacks and ESS score; these data are in

Table 1 Mean \pm SD values of the different parameters analyzed in the study are reported in detail

	Episodic migraine (mean \pm SD)	Chronic migraine (mean \pm SD)	<i>p</i>
Migraine frequency (days/month)	5.6 \pm 3.2	23.2 \pm 6.3	<0.001
Patients' age (years)	37.9 \pm 10.1	47.2 \pm 13.2	<0.001
Disease duration (years)	16.1 \pm 11.1	25.8 \pm 13.3	<0.001
MIDAS score	24.4 \pm 23.5	37.9 \pm 28.5	0.005
BMI score (kg/m ²)	23.1 \pm 3.3	24.6 \pm 3.7	0.012
FSS score	28.2 \pm 14.7	39.7 \pm 16.2	<0.001
ESS score	5.5 \pm 3.1	5.5 \pm 3.8	0.727
PSQI score	5.9 \pm 5.2	6.8 \pm 3.6	0.015
GAD-7 score	9.4 \pm 5.5	11.5 \pm 4.9	0.019
PHQ-9 score	6.4 \pm 4.6	10.1 \pm 5.9	<0.001

agreement with previous literature data documenting a lack of daytime vigilance level impairment also in migraineurs with poor sleep quality [9, 10].

Chronic migraine is a highly disabling condition, with significant impact on quality of life and elevated socio-economic costs; it has been estimated that about 3 % of individuals with episodic migraine progress to chronic migraine over the course of a year [11]. It has been hypothesized that migraine represents a spectrum disorders, clinically involving a life-time disease course, with a subgroup of patients progressing from episodic to chronic pattern. Furthermore, the literature data suggested that the process of migraine chronification is associated with progressive changes in nociceptive pathways caused by recurrent migraine attacks, with greater impairment in cortical processing of sensory stimuli and cortical hyperexcitability in chronic compared to episodic migraine [2].

Data from the present report expand the concept of migraine as a continuum or spectrum, with greater occurrence of fatigue, poor sleep quality, anxiety and depressive symptoms and higher BMI score in chronic migraine patients. Further research is certainly necessary to better define the biological basis underlying the complex and multidirectional relationship between migraine, fatigue, sleep and appetite regulation and anxiety and depressive symptoms, as well as their role in the process of migraine transformation from episodic to chronic pattern.

Compliance with ethical standards

Conflict of interest The authors declare the absence of conflict of interest.

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