Acta Neurol Belg (2013) 113:61–65
DOI 10.1007/s13760-012-0135-9

ORIGINAL ARTICLE

Adolescents with chronic migraine commonly exhibit depressive symptoms

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Received: 19 June 2012 / Accepted: 8 September 2012 / Published online: 2 October 2012

Abstract Psychiatric comorbidity in patients with headache contributes to poorer prognosis, chronification of disease, poor response to treatment, increased cost of treatment, and decreased quality of life. The purpose of the present study was to evaluate the depressive symptoms in adolescents with chronic and episodic migraines and healthy adolescents. The study was performed between November 2010 and November 2011. All patients completed a detailed headache questionnaire comprising of demographical and clinical data and were instructed to fill out a headache diary over a 2-month period. The subjects ranged in age from 13 to 19 years. To evaluate depression symptoms, all of the subjects were asked to fill out the Beck Depression Inventory (BDI). A total of 137 participants were evaluated; 44 had episodic migraine (EM), 46 had chronic migraine (CM) and 47 were control subjects. Patients with a history of chronic migraine had significantly higher scores on the BDI than the other participants. Patients with chronic migraine had BDI scores that were 8.8 points higher than controls [95 % CI (β) = 5.0, 12.6] and 5.8 points higher than patients with EM [95 % CI (β) = 2.2, 9.4]. The main finding of this study was that chronic migraine is strongly associated with depression symptoms, regardless of demographic data. Comorbid depression may increase the total burden of migraine and diagnosis and treatment of depression in adolescents with migraine is likely to result in a better prognosis.

Keywords Migraine disorders · Comorbidity · Depression · Headache · Adolescent

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Introduction

Migraine is a significant, global problem for adults, children, and adolescents [1, 2]. Adolescents with migraine, specifically chronic migraine, are as acutely disabled as adults and require specifically designed treatment paradigms [3].

Psychiatric comorbidity in headache patients contributes to poorer prognosis, chronification of disease, poorer response to treatment, increased cost of treatment, and decreased quality of life [4]. Psychiatric comorbidity has been well defined in the adult migraine population [5, 6]. The occurrence of multiple psychiatric disorders with migraine has been repeatedly documented and includes affective and anxiety disorders such as depression, panic disorder, bipolar disorder, and obsessive–compulsive disorder [7].

A recent systematic review found inconclusive evidence that children and adolescents with migraine have increased anxiety and depression. There is limited clinical evidence showing that children and adolescents with migraine are more frequently diagnosed with dysthymia or depression compared to healthy children [8].

The purpose of the present study was to evaluate depressive symptoms in adolescents with chronic and episodic migraine and healthy adolescents.

Methods

The study was performed between November 2010 and November 2011 at the Federal University of São Paulo, Brazil. All of the migraine patients were recruited in the paediatric ambulatory department, and control subjects were recruited in schools. Subjects completed a detailed headache questionnaire comprised of demographical and clinical data and were instructed to keep a headache diary over a 2-month period.

The participants were divided into three groups: adolescents with episodic migraine (EM), adolescents with chronic migraine (CM), and healthy adolescent controls (CG). The subjects ranged in age from 13 to 19 years. Migraine was defined according to the diagnostic criteria of the International Classification of Headache Disorders, Second Edition (ICHD-2) [9] and CM was defined according to the 2006 appendix criteria [10].

The exclusion criteria were chronic disease, secondary headaches, continuous usage of any type of medication, drug addiction or abusive alcohol use, and any suffering from migraine or any other primary headache in control subjects. All subjects or their guardians provided written consent for the experimental procedure, which was approved by the Ethics Committee of The Federal University of São Paulo.

To evaluate depression symptoms all of the subjects were asked to fill out the Beck Depression Inventory (BDI), a 21-item scale used to evaluate the intensity of depressive symptoms. The internal consistency of the BDI was high (Cronbach's alpha coefficient = 0.8) [11]. Higher BDI scores are associated with higher levels of depression [12, 13] and depressive symptoms were stratified into high or significant levels (scores $\geq$20).

Data analysis

The Chi-square test (χ^2) (without Yates correction) was used for categorical data comparisons. The mean values of the two patient groups were compared using the independent Student's t test (t). An ANOVA (one-way analysis of variance) (F) was used when there were three samples. When the ANOVA resulted in significant differences, Bonferroni's multiple comparison test was performed to determine which groups differed significantly.

Multiple linear regression analysis was performed to verify the relationship between migraine status (as the independent variable) and BDI (as the dependent variable). The mean values ± standard deviations are reported. A p value of <0.05 is considered statistically significant, and all tests were two-tailed. Ninety-five percent confidence intervals (CI) were calculated for the differences between means. Statistical analyses were performed using the statistical package for social sciences (SPSS) 11.5.1 for Windows. CIs for the resampling method were calculated using the statistical package R.

Results

A total of 173 subjects were recruited to the study. Of these, 36 subjects were excluded: 8 refused to participate, 6 did not give a reliable history, and 22 met at least one criterion for exclusion. The analysis of the remaining 137 subjects is shown below, of which 44 had EM, 46 had CM, and 47 were CG.

There were significant differences between the three groups regarding age [$F(2.155) = 10.5$, $p < 0.001$]. Control patients were older (16.1 ± 1.8 years) than subjects with EM [15.6 ± 2.2 years, 95 % CI (difference) = 0.1, 2.5] and CM [15.4 ± 2.3 years, 95 % CI (difference) = 1.0, 3.3]. In addition, the proportion of women was higher in the chronic migraine group (CM = 46 %, CG = 28 %, EM = 25 %, $\chi^2(2) = 9.71$; $p = 0.008$).

Clinical characteristics of migraine

The age of onset for headache in EM patients was 5.7 ± 2.8 years with a median attack duration of 7.9 h. In the CM group, the age of onset was 5.8 ± 3.0 years with a median duration of 7.6 h. There were no significant differences regarding age of onset [$t(105) = 0.08$, 95 % CI = −1.09–1.17, $p = 0.949$] or the duration of headache episodes [$t(105) = -0.96$, 95 % CI = −4.75–1.65, $p = 0.330$]. The presence of aura was similar in the CM and EM groups (48 vs. 36 %, $\chi^2(1) = 1.87$; $p = 0.171$), but the intensity of pain was significantly higher in the CM group than that in the EM group [7.3 ± 1.6 vs. 6.1 ± 1.9, $t(105) = 2.86$, 95 % CI (difference) = −0.3, −1.6, $p = 0.005$].

BDI

The mean BDI scores of the three groups differed significantly [$F(2.154) = 9.54$, $p < 0.001$]. Patients with CM had more depressive symptoms (15.4 ± 9.8) than EM patients [9.4 ± 8.1, 95 % CI (difference) = 1.2, 9.7] and the CG group [7.8 ± 9.2, 95 % CI (difference) = 3.2, 11.7]. However, the mean BDI score was not significantly different between the CG and EM groups [95 % CI (difference) = 2.4, 6.3].

Multiple logistic regression analyses were performed to verify if the relationship between migraine status (as independent variables) and BDI scores (as the dependent variable) was independent of age and sex (Table 1).

CM was strongly positively associated with BDI scores, independent of age or sex. Patients with CM had BDI scores that were 8.7 points higher than controls and 5.8 points higher than patients with EM.

Discussion

Medical comorbidities associated with migraine influence several factors such as patient's quality of life, functioning, and psychological well-being. Therefore, it is crucial to assess the prevalence and impact of these conditions in migraine patients. Although the association between psychiatric disorders and migraine is not yet clear, a greater understanding of their relationship may contribute to our understanding of the underlying aetiologies of both conditions, extend our comprehension of the development of psychopathology, and function as a tool for improving nosology [14]. In patients with migraine, depression can exacerbate the impact of the disease and complicate treatment. Signs and symptoms of depression may be underdiagnosed in these patients because they may present differently in individuals without migraine [15].

The probability of a patient with migraine to have depression is 2.2–4 times higher than individuals without migraine [16, 17]. Guidetti et al. [18] observed the comorbidity between migraine and depression in adolescents and young adults with chronic migraine, with a mean age of 17.9 years, and concluded that these factors negatively influenced the progression of migraine.

Depression may also be associated with other types of headaches. Some studies have proposed that it may be more related to the frequency of the headache than the subtype itself [17]. However, for other forms of headache, the bidirectional relationship with depression does not seem to exist as it does with migraine. Breslau et al. conducted an epidemiological study that followed, for three and a half years, individuals between 22 and 55 years. They observed that each disorder increases the risk for the other by about three times, and this situation was not observed with other types of headache. They also assessed the presence of mood disorders and anxiety in relation to migraine and other aches such as arthritis and back pain, with 28 % of individuals with migraine considered depressed, while only 12.3 % of patients without migraine fulfilled the same criteria [19, 20].

Table 1 Multiple linear regression analysis to verify associations between the diagnostic groups and depressive symptoms, controlling for sex and age

	β	SE	t	95 % CI (β)	p
EM × C (ref)	2.99	1.82	1.64	−0.60–6.59	0.102
CM × C (ref)	8.82	1.92	4.60	5.03–12.60	<0.001*
CM × EM (ref)	5.82	1.83	3.18	2.21–9.44	0.002*
Age	0.76	0.30	2.50	0.16–1.36	0.014*
Sex	−0.92	1.61	−0.57	−4.11–2.26	0.567

Asterisk indicates statistical significance

Some theories propose mechanisms to justify the co-occurrence of migraine and depression. One such example is based on the presence of a polymorphism in the gene 5-HTT, which would lead to decreased levels of the serotonin transporter and thus increase the patient's risk of depression. This polymorphism would also influence the patient's sensitivity to stress and anxiety [4, 21]. The same gene has been associated with susceptibility to migraine and frequency of attacks [22]. Because both migraine and depression exhibit a reduction in serotonin levels and both present a strong response to selective inhibitors of serotonin reuptake, it is likely that these diseases share a dysfunction in the central availability of serotonin; however, this mechanism is not well understood [23, 24].

Based on the observation that migraine and mood disorders are as much as 2–3 times more common in women after puberty [25], it is believed that comorbidity is also influenced by hormonal factors. Ovarian hormones modulate several neurotransmitters in women, which can lead to mood changes in menstrual, postpartum and perimenopausal periods. Subjects with migraine often have seizures associated with decreasing levels of oestrogen. The abrupt decline in oestrogen levels would lead to an "up-regulation" of the sympathetic system and a "down-regulation" of the serotoninergic and GABAergic systems [26].

As well as other painful disorders, migraine could lead to worry and dysphoria, increasing the risk for depression. Conversely, depression could lead to the occurrence of headache and other somatic conditions or interfere with an individual's ability to cope with pain. Similar to what is observed in migraine, the frequency of depression episodes increases with time and can progress to chronification. This occurs through the phenomenon of central sensitisation, one of the theories that considers the factors that contribute to chronic migraine [27].

The first studies pertaining to the psychology of children with migraine attempted to identify the personal characteristics of children with this type of headache. Bille [28] suggested that children with migraine were more anxious, sensible, fearful, susceptible to frustration, methodic, and had less physical resistance. These differences were more pronounced in girls.

Maratos and Wilkinson [29] observed high levels of anxiety, depression, and conflicted relationships in the

parents of children with migraine. Guidetti et al. [30] identified the presence of exclusion sentiments and repressed hostility in family relationships.

The main finding of this study was that CM was strongly positively associated with BDI scores in adolescent populations, regardless of demographic data and pain intensity. Scores were significant to differentiate control groups of patients with chronic migraine, showing higher levels of depression in the latter group. Our result is in full agreement with population studies previously conducted, in which the prevalence of depression was higher in cases of chronic migraine compared to episodic, reaching up to 57 % [17, 31–33]. Mercante et al. [34] analysed patients with chronic migraine and could verify that 85 % had some degree of depression, 25 % of these cases of depression were severe. In the same study, particular aspects of depression were also evaluated, and showed that 40 % of patients had some degree of suicidal thoughts.

The total burden of migraine may be increased when migraine is found in conjunction with depression. The diagnosis and treatment of depression in adolescent migraine patients is essential for a better prognosis.

Acknowledgments This study was sponsored by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

Conflict of interest The authors report no conflicts of interest.

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