

## FACULDADE DE MEDICINA DA UNIVERSIDADE DE COIMBRA

MESTRADO INTEGRADO EM MEDICINA – TRABALHO FINAL

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# "Qualidade de sono em adolescentes com enxaqueca"

ARTIGO CIENTÍFICO ORIGINAL

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### Abstract

**Objective:** to assess sleep quality in adolescents diagnosed with migraine headache.

**Methods:** a prospective, cross-sectional study was conducted in patients with migraine headache and healthy controls ranging in age from 13 to 18 years old. Sleep quality was determined, subjectively, using Pittsburgh sleep quality index, Cleveland scale and sleep questionnaire for adolescents. The Paediatric Migraine Disability Assessment was used to determine headache-related disability in adolescents with headache.

**Results:** 52 healthy controls (mean age 15.67 years; 51.9% females) and 30 patients (mean age 15.23 years; 56.7% females) were included in this study. Migraineurs reported more sleep difficulties with worse habitual sleep-efficiency (p=0.007) and more sleep disturbances (p=0.045). No correlation was found between headache-related disability and sleep difficulties or daytime sleepiness. Migraine sufferers also had a higher ratio of sleep deprivation (24.0% vs 11.6%, OR=2.40) and a higher prevalence of napping habits (16.67% vs 3.85% on school days, OR=5.00 and 23.33% vs 13.46% on other days, OR=1.96). Forty percent of patients vs 44.2% of controls felt that they were not getting enough sleep and 18.5% vs 25.0% felt sleepy during the day from a lot of times to everyday.

**Conclusion:** Migraineurs reported worse sleep quality than healthy controls, however, adolescents in general appear to have poor sleep quality. Sleep-hygiene measures should be promoted in this age group, in order to prevent the detrimental effects of a poor sleep quality at this phase of development.

**Keywords:** headache, migraine disorders, sleep quality, daytime sleepiness, sleep hygiene, adolescence, questionnaires.

## Introduction

Headache and sleep disturbances are common problems among adolescents and are often comorbid in the same subject (1-3).

Migraine is the second most common primary headache and it often begins during the early school-aged years (3%), however, higher rates occur in older adolescents (20%) and, during this stage, it affects more females than males (3–5). Furthermore, it is often a debilitating disorder and has a negative impact on overall health status, quality of life and society (3,4,6).

Sleep disturbances are a group of problems that interfere with the normal sleep pattern (affecting its quantity, quality or sleep-wake cycle regulation) and are pathological when maintained for so long that start interfering with individual's normal function (7).

Adolescence is an important and vulnerable stage, with significant brain maturation and puberty related biological and psychosocial changes. Being sleep an essential restorative function necessary for optimal mental and physical health, it plays an especially important role in this phase of development. Insufficient and poor quality sleep in adolescents can affect memory, learning, attention and other cognitive abilities and functions, as well as, physical growth, mental health status, social and neurobehavioral functioning. It can also contribute to obesity, anxiety, suicidal ideation, use of drugs and alcohol and diminished quality of life (8–13).

Disturbances in sleep are highly prevalent among migraine patients. Migraine often precedes the onset of sleep disturbances and, sleep disturbances also function as one of the most common "triggers" for migraine with sleep related symptoms, like tiredness and yawning, being particularly frequent in the premonitory phase before an attack (14,15).

The bidirectional relationship between primary headaches and sleep disturbances is complex and linked to common anatomical structures and neurochemical processes that are involved in the pathophysiology of both, however, its exact nature, magnitude and underlying mechanisms remain poorly understood (3,16,17). Headache episodes are known to occur during sleep, after sleep, and in relationship with various sleep stages. On the other hand, poor quality or inadequate duration (excess or lack) of sleep can trigger headache suggesting a causality or reinforcement in subjects with headache (17,18). Conversely, sleep has also been shown to relieve headache or even terminate the attacks in headache sufferers (2,3,16,18).

The aim of our study was to assess and compare subjective sleep quality in a population of adolescents diagnosed with migraine headache, with or without aura, and one of healthy adolescents.

## Methods

One hundred and twenty-nine adolescents participated in this study. Ninety-one controls and thirty-eight patients. All the participants ranged from 13 to 18 years old. Data collection was made between May and June 2016 for controls and between May and December 2016 for patients.

#### **Controls**

All controls were recruited from two public schools at Coimbra (7<sup>th</sup> to 12<sup>th</sup> grade). The aims of the study were explained to the school director, teachers, parents and students. After obtaining written informed consent from parents and adolescents 18 years of age, students individually and anonymously completed the paper-pencil questionnaires in the classrooms.

Students with chronic illness, frequent headaches or shared bedroom were not included in this study.

Of the 91 students that answered the questionnaires, only 52 (57.14%) fulfilled the conditions to participate at the study. From the 52 controls, 94.2% (n=49) concluded Pittsburgh Sleep Quality Index and 88.5% (n= 46) the Cleveland Adolescent Sleepiness Questionnaire. At

Adolescent Sleep Questionnaire, questions were analysed individually therefore, even if they were not able to complete a question, the remaining ones were considered. All the controls completed the demographic questionnaire.

#### **Patients**

The patient population consisted of adolescents diagnosed with migraine according to the International Classification of Headache Disorder version-3 (ICHD - 3).

All the patients were randomly selected at the outpatient neuropediatric department of a tertiary care teaching hospital.

The aims of the study were explained to the parents and patients. After obtaining written informed consent from parents and adolescents 18 years of age, patients individually and anonymously completed the paper-pencil questionnaires during the appointment.

Migraineurs with coexisting chronic illness or that shared bedroom were not included in this study.

From the 38 patients that answered the questionnaires, only 30 fulfilled the conditions to participate in this study. From the 30 patients, 96.7% (n=29) concluded Pittsburgh Sleep Quality Index, 90.0% (n= 27) the Cleveland Adolescent Sleepiness Questionnaire and 73.3% (n=22) the Paediatric Migraine Disability Assessment. All the patients completed the demographic questionnaire.

#### **ETHICS**

This study was approved by the Local Institutional Ethics Committee. Written informed consent (parents and adolescents 18 years of age) were obtained from all patients and controls. Their participation in this study and filling of the questionnaires was voluntary and anonymity was assured.

#### MEASURES

**Demographic questionnaire:** was composed of a few questions about age, gender, school grade, existence of chronic illnesses, frequent headaches or shared bedroom.

**Pittsburgh sleep quality index (PSQI):** evaluates the sleep quality during the previous month and consists of 19 self-rated questions that assess a wide variety of factors relating to sleep quality, including estimates of sleep duration, latency and frequency and severity of specific sleep-related problems. These 19 items are grouped into seven component scores, each equally a 0-3 scale. The seven component scores are then summed to yield a global PSQI score, which range 0-21. PSQI global score > 5 provides a sensitive and specific measure of poor sleep quality, and it means that the subject is having severe difficulties at least two areas, or more moderate difficulties in more than three areas (19).

**Cleveland Adolescent Sleepiness Questionnaire (CASQ):** is composed of 16 questions that measure daytime sleepiness. Eleven questions assess sleepiness (11-55 scale) and 5 assess alertness (5-25 scale). Greater CASQ scores reflect increased daytime sleepiness (20).

Adolescent Sleep Questionnaire (ASQ): adapted from the questionnaire developed by Rebelo Pinto (2010). It includes a series of question that address two different components: 1) sleep self-perception and 2) sleep habits and routines (21).

**Paediatric Migraine Disability Assessment (PedMIDAS):** is the only validated measure of headache-related disability in children. It uses six questions to assess three functional disability domains: school attendance and function, participation in activities at home, and participation and function in recreational/leisure activities (3). PedMIDAS total score sums up the number of days reported in each of the questions. Total scores of 0–10 translate as "little to no disability", 11–30 as "mild disability", 31–50 as "moderate disability", and total scores higher than 50 as "severe disability" (6).

#### **STATISTICAL ANALYSES**

All data were analysed using the Statistical Package for the Social Sciences (SPSS), version 22. The analysis included descriptive analysis for quantitative variables and percentages for categorical variables. Comparisons involving quantitative variables were performed using t tests, however, when data were not normally distributed, comparisons were made using Mann-Whitney U test. Shapiro-Wilk test and Kolmogorov-Smirnov test were used on samples with less than 30 elements and on samples with 30 or more elements, respectively, to determine if the data had a normal distribution. Pearson qui-square test or Fisher's exact test (when 20% of expected frequencies were less than or equal to 5) and odds ratio were used to analyse crosstabs. Bivariate parametric correlations for continuous variables, using Spearman's rank correlation coefficient ( $r_s$ ) were used to asses any correlation between headache severity (PedMidas) and sleep quality (PSQI and CASQ).

## Results

Our results were based on 30 patients with migraine headache whose mean age was  $15.23 \pm 1.31$  years and 17 females (56.7%); and on 52 controls whose mean age was  $15.67 \pm 1.44$  years and 27 females (51.9%). Demographic variables in the two samples were equivalent (age: p=0.215; sex: p=0.678; grade: p=0.377).

Considering the PSQI total score and its items separately (table 1), migraine group reported more sleep difficulties when compared to controls. Differences were statistically significant at habitual sleep-efficiency (p=0.007) and at sleep disturbances (p=0.045) items. Sleep latency > 30 minutes was reported by 10.3% of adolescents with migraine vs 6.1% of controls (OR=1.769). Poor subjective sleep quality (PSQI>5) was reported by 37.9% of patients and by 32.7% of controls (OR=1.260). No significant correlation was found between headache-related disability (PedMidas total score) and sleep difficulties (PSQI total score) ( $r_s$ =0.344; p=0.127).

Regarding CASQ scores and subscales (Table 2), scores are higher in migraine group, but no statistical significant differences were found between the two samples. No significant correlation was found between headache-related disability (PedMidas total score) and daytime sleepiness (Cleveland total score) ( $r_s = 0.218$ ; p = 0.342).

Based on the disability scores of PedMidas, 9.1% migraineurs were severely affected by their headache, 9.1% were moderately affected, 36.4% were mildly affected and 45.5% had little to no disability related to their headache.

Sleep auto-perception answers are listed in table 3 and sleep patterns in table 4. The majority of adolescents, controls (57.1%) and patients (70.4%), reported having  $\geq$  8 hours of sleep on school nights. The percentage was even higher on "other nights" where 93.3% of controls and 92.7% of patients reported having 8 or more hours of sleep. However, sleep deprivation (difference in sleep duration  $\geq$  3 h between school nights and "other nights" – no school the next day), was present in 24.0% of patients and in 11.6% of controls (OR = 2.40; *p*=0.305).

## Discussion

Our findings, consistently with prior research, provide further support for the association between migraine headache and sleep disturbances among adolescents. Results show that migraineurs have poorer sleep quality and more daytime sleepiness, experiencing significantly more sleep disturbances and less sleep efficiency when compared to healthy controls (1,22). Though, neither sleep quality or daytime sleepiness were significantly correlated with headache severity. However, it should be noted that, adolescents in general appear to have poor sleep quality with significant sleep difficulties and daytime sleepiness, coming to report that they feel sleepy and that somnolence affects their daily life more often than migraineurs.

At sleep self-perception, as expected and though the differences were not significant, migraineurs classified their sleep as being "bad to very bad", "quite to very important" and as

having "many to some difficulties" regarding sleep, more often than healthy adolescents. Although, more controls felt that they did not get enough sleep. This corroborates the idea that Portuguese adolescents, in general, don't have a good sleep quality.

Regarding sleep patterns, migraineurs reported going to bed earlier and sleeping during more time than controls. Considering that they are being followed on our department, where they are frequently advised to avoid headache triggers as a preventive measure for migraine attacks, it is probably that they are more aware of the importance of a good sleep schedule. Despite this, migraine patients had a higher ratio of sleep deprivation and a higher prevalence of napping habits. It is known that migraine attacks could be relieved with daytime naps but, consequently, they can negatively affect the normal sleep-wake cycle, predisposing to sleep disturbances (23).

Adolescents who suffer from migraine headache complained more frequently of anxiety/stress, sadness, anger and lack of relaxation when going to bed. Additionally, they also reported drinking caffeinated drinks, smoking and eating heavy meals (3 hours before bedtime) more often than controls which all may interfere with reasonable bedtime rituals (8). Cigarette smoking and caffeinated drinks, in addition to being considered migraine triggers, are associated with insufficient and poor sleep quality and, subsequently, increased daytime sleepiness (24–26). Current cigarette smoking status was associated with increased odds of long sleep latency, daytime dysfunction, and sleep medicine use. On the other hand, caffeine leads to release of dopamine, activation of central nervous system and increases wakefulness, however, its effects vary across individuals and are influenced by tolerance levels and genetics. Thus, caffeine consumption has only been found to reduce sleep quality in caffeine-sensitive individuals (27).

A high percentage of migraine sufferers reported practicing a sport or intense physical exercise 3 hours before bedtime. Exercise has been cited as a common migraine trigger and, despite being recommended to get regular exercise as an essential sleep hygiene measure, its practice should be avoided 5 hours before bed (25,28,29).

#### Strengths

Migraine headache diagnosis was made according to strict ICHD-3 criteria and, to the best of our knowledge, this is one of the few studies to compare sleep quality between migraineurs and healthy adolescents and, the first using a Portuguese adolescent population. A further strength of our study is that sleep quality was assessed using three different tools, thus evaluating its difference domains: PSQI (sleep difficulties), CASQ (daytime sleepiness) and ASQ (sleep self-perception, habits and routines).

### Limitations

Limitations of this study are the small sized samples, the tertiary care recruitment (referral bias), the self-reported and subjective sleep information, the longer time of data collection for patient's sample and the fact that a significant percentage of migraineurs reported little to no disability related to their headache. A further limitation could be due to PedMidas bias with underestimation for non-school days and overestimation of the exact number of days when compared to a headache diary (recall bias) (6). Another weakness of the study could be the failure to best characterize migraine headache by assessing its subtypes (with and without aura), duration and frequency of attacks.

### Conclusion

Since sleep disturbances represent a potentially modifiable vulnerability to headache and vice versa, the clinical evaluation of adolescents with migraine headache should include a careful analysis of sleep habits and patterns and, the evaluation of the presence of sleep disturbances in order to, develop better treatment methods for both sleep and headache (17,18,30).

This study highlights the need to apply sleep hygiene measures not only on migraineurs, but also on general Portuguese adolescent population, to avoid the short and long-term detrimental effects of a poor sleep quality during this phase of development. These measures include maintaining a consistent sleep/wake schedule 7 days per week, conformity of time spent in bed to the time necessary for sustained and individually adequate sleep, sleep in a dark environment, avoid daytime naps, restriction of stimulants (caffeine, nicotine...), foods and alcohol, which tend to disrupt sleep, before bedtime (17,29,31).

Conflict of interest: the authors declare that they have no conflict of interests.

Author's contribution: IF and AV were involved in patient data collection and consultation. JT was involved in the controls data collection, data entry, data analysis and writing the article. All authors read and approved the final manuscript.

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# Appendix

Table 1- Comparison of PSQI items and total score between migraineurs and controls

	Migraineurs	Controls	<i>p</i> -value*
Subjective quality sleep,	1.03±0.68	0.90±0.55	0.432
mean (SD)			
Sleep latency, mean	1.14±0.95	1.02±0.80	0.709
(SD)			
Sleep duration, mean	0.41±0.87	0.41±0.67	0.556
(SD)			
Habitual sleep	0.48±0.91	0.06±0.24	0.007
efficiency, mean (SD)			
Sleep disturbances,	1.21±0.66	0.94±0.43	0.045
mean (SD)			
Use of sleep	0.17±0.60	0.14±0.61	0.524
medication, mean (SD)			
Daytime dysfunction,	1.14±0.83	1.20±0.87	0.830
mean (SD)			
PSQI total score, mean	5.59±3.64	4.67±2.17	0.324
(SD)			
<b><i>PSQI</i> &gt; 5</b> , % ( <i>n</i> )	37.9 (11)	32.7 (16)	-

\* Mann-Whitney test

Table 2 - Comparison of Cleveland subscales and total scores between migraineurs and controls

	Migraineurs	Controls	<i>p</i> -value
Alertness, mean (SD)	13.33±5.31	12.54±5.06	0.529*
Sleepiness, mean (SD)	19.70±7.56	18.35±5.11	0.279**
Cleveland total score,	33.04±11.45	30.89±7.91	0.348*
mean (SD)			

\* T-student test

\*\* Mann-Whitney test

	Migraineurs, % (n)	Controls, % (n)
Do you get enough sleep?		
No	40.0 (12)	44.2 (23)
You are the kind of person that sleeps		
very bad	3.3 (1)	-
bad	10.0 (3)	3.8 (2)
reasonably	26.7 (8)	26.9 (14)
well	40.0 (12)	48.1 (25)
very well	20.0 (6)	21.2 (11)
In your opinion, sleep is		
little important	3.3 (1)	5.8 (3)
fairly important	6.7 (2)	13.5 (7)
quite important	66.7 (20)	40.4 (21)
very important	23.3 (7)	40.4 (21)
Regarding sleep, you are used to have		
no difficulties	26.7 (8)	23.1 (12)
few difficulties	53.3 (16)	59.6 (31)
some difficulties	13.3 (4)	11.5 (6)
many difficulties	6.7 (2)	5.7 (3)

Table 3 - Sleep self-perception answers

Table 4 - Sleep patterns and routines analysis

	Migraineurs	Controls
Bedtime		
on school nights, median (range)	22:30 (20:00 - 24:00)	23:00 (21:30 - 1:30)
on other nights, median (range)	23:30 (21:00 – 2:00)	24:00 (22:30 - 3:00)
Rising time		
on school days, median (range)	7:17 (6:00 – 8:00)	7:25 (5:50 - 8:20)
on other days, median (range)	10:00 (7:30 – 12:00)	10:00 (6:00 - 14:00)
Total of sleep hours		
on school nights, mean (range)	8:02 (5:00 - 11:30)	7:40 (6:00 – 10:00)
on other nights, mean (range)	9:38 (7:00 – 12:30)	9:04 (5:30 - 12:00)
Do you use to take a nap		
on school days?		
<i>Yes</i> , $\% (n)^{1}$	16.67 (5)	3.85 (2)
in the afternoon (n)	4	2
at night (n)	1	_
on other days?		
<i>Yes</i> , $\% (n)^2$	23.33 (7)	13.46 (7)
in the afternoon (n)	6	5
at night (n)	-	2
in the afternoon (n) at night (n)	6 -	5 2

<sup>1</sup> OR=5.00

<sup>2</sup> OR=1.96

in the morning, afternoon	1	-
and at night (n)		
At night, 3h before bedtime, you use		
<i>to</i>		
drink caffeinated soft drinks		
never, % (n)	65.5 (19)	70.6 (36)
sometimes, $\%(n)$	27.6 (8)	29.4 (15)
a lot of times, $\%(n)$	6.9 (2)	-
every day, % (n)	-	-
drink coffee or caffeinated tea		
<i>never</i> , % ( <i>n</i> )	79.3 (23)	88.2 (45)
sometimes, % (n)	20.7 (6)	11.8 (6)
a lot of times, $\%$ (n)	_	-
<i>every day, % (n)</i>	_	-
smoke		
<i>never</i> , % ( <i>n</i> )	93.1 (27)	100 (51)
sometimes, % (n)	_	-
a lot of times, $\%$ (n)	3.4 (1)	-
<i>every day, % (n)</i>	3.4 (1)	-
drink alcohol		
<i>never</i> , % ( <i>n</i> )	96.6 (28)	94.1 (48)
sometimes, % (n)	3.4 (1)	5.9 (3)
a lot of times, $\%(n)$	-	-
<i>every day, % (n)</i>	-	-

eat "heavy" meals		
never, $\%(n)$	44.8 (13)	41.2 (21)
sometimes, % (n)	48.3 (14)	35.3 (18)
a lot of times, $\%(n)$	3.4 (1)	21.6 (11)
every day, $\%(n)$	3.4 (1)	2.0 (1)
practice a sport or intense physical		
exercise		
<i>never</i> , % ( <i>n</i> )	60.0 (18)	44.2 (23)
sometimes, $\%(n)$	30.0 (9)	32.7 (17)
a lot of times, $\%(n)$	10.0 (3)	17.3 (9)
every day, $\%(n)$	-	5.8 (3)
At bedtime, do you use to feel		
relaxed/rested		
<i>never</i> , % ( <i>n</i> )	18.5 (5)	10.0 (5)
sometimes, % (n)	59.3 (16)	40.0 (20)
a lot of times, $\%(n)$	11.1 (3)	34.0 (17)
every day, $\%(n)$	11.1 (3)	16.0 (8)
tired/exhausted		
<i>never</i> , % ( <i>n</i> )	10.0 (3)	11.9 (5)
sometimes, $\%(n)$	43.3 (13)	54.8 (23)
a lot of times, $\%(n)$	30.0 (9)	14.3 (6)
every day, $\%(n)$	16.7 (5)	19.0 (8)
anxious/stressed		
<i>never</i> , % ( <i>n</i> )	25.9 (7)	44.0 (22)

sometimes, % (n)	51.9 (14)	36.0 (18)
a lot of times, $\%$ (n)	18.5 (5)	14.0 (7)
every day, % (n)	3.7 (1)	6.0 (3)
sad		
<i>never</i> , % ( <i>n</i> )	53.6 (15)	68.0 (34)
sometimes, $\%$ (n)	39.3 (11)	26.0 (13)
a lot of times, $\%(n)$	3.6 (1)	6.0 (3)
<i>every day, % (n)</i>	3.6 (1)	-
angry		
<i>never</i> , % ( <i>n</i> )	50.0 (14)	68.0 (34)
sometimes, $\%(n)$	42.9 (12)	24.0 (12)
a lot of times, $\%(n)$	7.1 (2)	4.0 (8)
<i>every day, % (n)</i>	-	-
During the day, do you feel sleepy?		
<i>never,</i> % ( <i>n</i> )	44.4 (12)	15.4 (8)
sometimes, % (n)	37.0 (10)	59.6 (31)
a lot of times, $\%$ (n)	7.4 (2)	19.2 (10)
every day, % (n)	11.1 (3)	5.8 (3)
Do you feel that your daily activities		
are affected by somnolence?		
<i>never, % (n)</i>	53.3 (16)	42.3 (22)
sometimes, % (n)	33.3 (10)	46.2 (24)
a lot of times, $\%$ (n)	13.3 (4)	9.6 (5)
every day, % (n)	-	1.9 (1)

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