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ORIGINAL ARTICLE

The relationships between migraine, depression, anxiety, stress, and sleep disturbances

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Abstract To assess the relationships between migraine, depression, anxiety, stress, and sleep problems. Psychiatric conditions and sleep disturbances are common in migraineurs. Depression, anxiety, stress, migraine, and sleep problems frequently coexist as comorbidities. Eighty-seven episodic migraineurs (62 females, 25 males; 32.8 ± 6.9) and 41 control subjects (25 females, 16 males; 31.5 ± 5.6) were prospectively enrolled for the study. The participants completed a sociodemographic data form and a migraine disability assessment scale (MIDAS), depression, anxiety, stress scale (DASS), and Pittsburg Sleep Quality Index (PSQI). In migraineurs, a significant positive correlation was found between PSQI total scores and MIDAS scores (migraine related disability for at least three consecutive months) ($r = 0.\ 234$, $p = 0.04$). Only 24.1 % of migraineus ($n = 21$) had minimal or no disability, 75.9 % of the patients ($n = 66$) had more than a little disability according to MIDAS scores. PSQI total scores were also correlated with pain intensity over a three month period (MIDAS B) ($r = 0.221$, $p = 0.04$). While PSQI scores were found significantly different between migraineurs and control subjects (5.5 ± 2.9 vs 4.5 ± 2.5; $p = 0.04$), the correlation of all the DASS subscale scores between the groups was not statistically significant. Our findings showed that episodic migraine was a risk factor on its own for sleep disturbances without comorbid depression, anxiety, and stress. Moreover, migraine-related disability and pain intensity in migraine attacks were related to poor sleep quality.

Keywords Migraine · Depression · Anxiety · Stress · Sleep disturbances

Introduction

Migraine and sleep disorders are common in the general population. The lifetime prevalence of migraine in Turkey has been found to be 21.8 % in women and 10.9 % in men [1]. Sleep disorders also affect up to one-third of adults in the general population [2]. Therefore, many studies have focused on a search for associations between sleep and migraine [3–8]. Poor sleep quality is of clinical importance even among young migraineurs [9]. These associations could have a bidirectional relationship. Sleep disturbances, in the first place, can trigger migraine attacks and headaches in turn can cause sleep problems in patients prone to migraine [10]. Moreover, migraineurs have also reported sleep problems as a trigger factor in attacks, while sleep can also alleviate headache [11]. It is reported that sleep disturbances in migraineurs include excessive day time sleepiness (EDS), difficulty in initiating and maintaining sleep, early morning awakening, and daytime fatigue [12].

It is well known that migraine is comorbid with anxiety, depression, and stress [13, 14]. Migraine shares again a bidirectional relationship with these psychiatric conditions. Sleep disturbances can be a major symptom in these disorders; moreover anxiety, depression, and stress may also trigger migraine attacks [15, 16].

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According to previous studies, sleep disturbances in migraineurs should not be associated alone on the basis of co-morbid depression and anxiety [17, 18]. Understanding the interactions between the psychiatric conditions and sleep disturbances in migraineurs may help to further predict the prognosis and make plans for an effective treatment. The purpose of this study was to investigate the associations between migraine and depression, anxiety, stress, and sleep by using well-validated measures. This subject has already received some attention in the research literature, but compared with some of the existing literature [9, 19, 20] this study was conducted as a face to face interview, done by two neurologists at the outpatient's unit. In detail, we aimed to clarify whether migraineurs are more likely than healthy control subjects to have sleep disturbances and if so there is a positive correlation between these disturbances and the disability caused by migraine. In addition, we wanted to examine the impact of depression, anxiety, and stress on these findings.

Materials and methods

Subjects

Two hundred fourteen consecutive participants between September 2012 to August 2013 were evaluated, and 128 were ultimately enrolled. Eighty-seven participants aged between 18 and 55 years received the diagnosis of episodic migraine by two neurologists according to the International Classification of Headache Disorders, second edition [21]. Exclusion criteria were the recent use (i.e., within the 8 weeks preceding the study) of antidepressant, psychotropic and hypnotic drugs, acute and chronic psychosis, mental retardation, pregnancy, and illiteracy. Eighty-six patients were excluded due to ineligibility or unwillingness to participate in the study at the time. Forty-one healthy control subjects who had not met the criteria of migraine were included in the study.

The study protocol was conducted in accordance to the ethical principles stated in the "Helsinki Declaration" and approved by the Ethical Committee of Acibadem University School of Medicine. Written informed consent was obtained from all the participants before they enrolled on the study.

Materials

Sociodemographic data form

The participants answered a self-administered questionnaire that included information on sociodemographic features such as age, sex, educational, and marital status.

Assessment of migraine

The migraineurs were asked to fill out a form that focused on their migraine structure. The questions were designed to assess the duration, frequency, location, intensity, associated features and precipitating factors of their headache, and the amount and frequency of their use of analgesic drugs.

Migraine disability assessment scale (MIDAS)

The validated Turkish version of MIDAS was used to assess the level of disability associated with migraine [22]. It has five questions, evaluating the number of working days lost due to migraine over a three month period. MIDAS brings together information on migraine-related disability in terms of work/study, housework, and leisure activities on the days when the migraine attack is experienced [23]. The questions relate either to days of missed activity or days during which productivity is lowered by at least 50 %. The total of days is compiled and classified into four grades of severity. Depends on severity of MIDAS questionnaire: Grade I (scores ranging from 0 to 5), little or no disability; Grade II (scores ranging from 6 to 10), mild disability; Grade III (scores from 11 to 20), moderate disability; Grade IV (scores of 21 or higher), severe disability. MIDAS A evaluates headache frequency and MIDAS B assesses pain intensity (0 = no pain; 10 = very severe pain) over a three month course.

Depression, anxiety, stress scale (DASS)

The validated Turkish version of the depression, anxiety, stress scale was used to assess depression, anxiety, stress/tension [24]. It is a self-reporting instrument, presenting 42 items on three subscales each carrying 14 items [25]. Each item is rated on a four-point Likert scale showing the frequency or severity of the participants' experiences over the previous week.

Pittsburg Sleep Quality Index (PSQI)

The subjects filled out the validated Turkish version of the Pittsburg Sleep Quality Index for the assessment to sleep quality [26]. The PSQI has good reliability and validity in assessing the amount of sleep disturbance over the previous month [27]. The PSQI is a self-rating questionnaire, which contains 19 questions designed to evaluate 7 aspects of sleep, namely, (1) subjective sleep quality, (2) sleep latency, (3) sleep duration, (4) habitual sleep efficiency, (5) sleep disturbance, (6) use of sleep medication, and (7) daytime dysfunction. Each component of the PSQI was scored on a 0–3 scale, and the scores for the 7 aspects are

then combined in a global score somewhere between 0 and 21. Higher scores indicate worse sleep quality; any global score higher than 5 is sensitive and specific in making a distinction between poor and good sleepers [28]. PSQI total scores greater than 5 are defined in this study as indicating poor sleep quality.

Statistical analyses

Data are expressed as mean ± standard deviation (SD). Means and standard deviations were calculated for each variable. The data of categorical variables are shown as counts and percentages. An independent t test was used to compare variables. The correlations between the scales were evaluated using Pearson's correlation Analysis.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 13.0 (SPSS Inc., Chicago, IL, USA, 2005). The level of significance was set at $p < 0.05$.

Results

Sociodemographic and migraine clinical characteristics

Of the 87 migraineurs (32.8 ± 6.9), 62 were females (71.3 %; 33.7 ± 7.3) and 25 (28.7 %; 30.4 ± 5.5) were males. As regards their education level, 2 % of them ($n = 2$) had less than high school diplomas, 16 % ($n = 14$) had high school graduation diplomas, and 87 % of them ($n = 71$) had university degrees. Sixty-three percent of the migraineurs ($n = 54$) were married, 35 % of them ($n = 30$) were single, and 2 % of them ($n = 2$) were divorced. Thirteen migraineurs (15 %) had a past history of psychiatric disorders; 11 migraineurs suffered depression, and 2 of them anxiety.

Six migraineurs ($n = 7$) had migraine with aura and 93 % of them ($n = 81$) had migraine without aura. The mean duration of migraine was 8.9 ± 6.6 years. The number of attacks per month was 4.2 ± 2.9. The mean duration of migraine attacks was 1.6 ± 0.8 days. The mean pain intensity of the migraineurs was 7.5 ± 1.2 (on the numerical analog scale, ranging between 0 and 10). Five migraineurs (5.7 %) suffered from vertigo with or without migraine attacks. Sixty-seven migraineurs (77 %) complained of nausea and 16 migraineurs (18 %) reported vomiting as an accompanying symptom of their migraine attacks. Table 1 shows MIDAS grades of the migraineurs. Only 24.1 % of migraineurs ($n = 21$) had minimal or no disability, 75.9 % of the migraineurs ($n = 66$) had had more than a little disability within past three months. The MIDAS A score in the migraineurs was 16.5 ± 10.8, and their MIDAS B score was 7.5 ± 0.1.

Table 1 MIDAS grades of the migraineurs

MIDAS grade	%
Grade I (little/no disability ($n = 21$)	24.1
Grade II (mild disability) ($n = 16$)	18.4
Grade III (moderate disability ($n = 25$)	28.7
Grade IV (severe disability ($n = 25$)	28.7

N number of subjects, *MIDAS* migraine disability assessment scale

Of the 41 healthy control subjects (31.5 ± 5.6), 25 were females (61 %) and 16 males (39 %). Regarding their education level, 7 % of them ($n = 3$) had little, 37 % of them ($n = 15$) had graduated from high school, and 56 % of them ($n = 23$) had a university degree. Seventy-one percent of the control subjects ($n = 29$) were married, 27 % of them ($n = 11$) were single, and 2 % of them ($n = 2$) were divorced. None of the control subjects had a past history of psychiatric disorders.

DASS subscales and PSQI scores

Table 2 shows the DASS depression, anxiety, stress, and PSQI scores and a statistical comparison between the migraineurs and the control subjects. While the PSQI scores were found significantly different between the two groups (5.5 ± 2.9 vs 4.5 ± 2.5; $p = 0.04$), the correlation of all the DASS subscale scores was not statistically significant between the groups. Table 3 displays the prevalence of depression, anxiety, and stress levels of the migraineurs and control subjects according to DASS. Thirty-three migraineurs (37.9 %) and 13 control subjects (31.7 %) had some level of depression ($p = 0.298$). Forty-eight migraineurs (55.2 %) and 14 control subjects (34.1 %) had abnormal DASS anxiety scores ($p = 0.234$). Thirty-seven migraineurs (42.5 %) and 14 control subjects (34.1 %) had higher than normal stress levels ($p = 0.105$).

In the migraineurs, a significant positive correlation was found between the PSQI total scores and the MIDAS scores (migraine related disability for at least three consecutive months) ($r = 0.23$, $p = 0.03$) (Table 4). The Pearson correlation test did not show any association of PSQI with MIDAS A ($r = 0.09$, $p = 0.398$), the number of migraine attacks per month ($r = 0.04$, $p = 0.971$). The PSQI total scores also correlated pain intensity over a three month period (MIDAS B) ($r = 0.22$, $p = 0.04$). Table 4 illustrates the correlation between the PSQI total and the scores for the/seven aspects with MIDAS and MIDAS B in migraineurs. MIDAS scores were found to be correlated with sleep latency ($r = 0.22$, $p = 0.04$), sleep disturbance ($r = 0.33$, $p = 0.002$), and daytime dysfunction ($r = 0.24$, $p = 0.03$). The MIDAS B scores were also associated with habitual sleep efficiency ($r = 0.35$, $p = 0.001$) and sleep disturbance ($r = 0.23$, $p = 0.03$).

Table 2 DASS depression, anxiety, stress, and Pittsburg Sleep Quality Index scores and comparison of the migraineurs and control subjects

Groups	DASS depression		DASS anxiety		DASS stress		PSQI	
	Mean ± SD	*p*	Mean ± SD	*p*	Mean ± SD	*p*	Mean ± SD	*p*
Migraineurs ($n = 87$)	8.9 ± 8.0	0.3	9.3 ± 6.9	0.23	8.0 ± 0.9	0.10	5.5 ± 2.9	**0.04**
Control ($n = 41$)	7.3 ± 8.4		7.6 ± 8.8		8.2 ± 1.2		4.4 ± 2.5	

DASS depression anxiety stress scale, *PSQI* Pittsburg Sleep Quality Index, *n* number of subjects, *SD* standard deviation, *bold* indicates means $p < 0.05$

Bold indicates means $p < 0.05$

Table 3 Prevalence of depression, anxiety, and stress levels of migraineurs and control subjects according to DASS

DASS subscales	Normal *n* (%)		Mild *n* (%)		Moderate *n* (%)		Severe *n* (%)		Extremely severe *n* (%)	
	M	C	M	C	M	C	M	C	M	C
Depression	54 (62.1)	28 (68.3)	15 (17.2)	6 (14.6)	9 (10.3)	2 (4.9)	6 (6.9)	4 (9.8)	3 (3.4)	1 (2.4)
Anxiety	39 (44.8)	27 (65.9)	14 (16.1)	3 (7.3)	18 (20.7)	4 (9.8)	8 (9.2)	3 (7.3)	8 (9.2)	4 (9.8)
Stress	50 (57.5)	27 (65.9)	12 (13.8)	4 (9.8)	13 (14.9)	5 (12.2)	9 (10.3)	5 (12.2)	3 (3.4)	–

DASS depression anxiety stress scale, *n* number of subjects, *M* migraineurs, *C* control group

Table 4 Correlation of Pittsburg Sleep Quality Index total and 7 component scores with MIDAS and MIDAS B

	C1 *p*	C2 *p*	C3 *p*	C4 *p*	C5 *p*	C6 *p*	C7 *p*	TS *p*
MIDAS	0.24	**0.04**	0.67	0.31	**0.002**	0.88	**0.03**	**0.03**
MIDAS B	0.35	0.94	0.12	**0.001**	**0.034**	0.34	0.37	**0.04**

MIDAS migraine disability assessment scale, *MIDAS B* pain intensity (0 = no pain; 10 = very severe pain), *C* component, *TS* total score, *bold* indicates $p < 0.05$

bold indicates $p < 0.05$

Discussion and conclusions

Migraine maintains a complex relationship with comorbid conditions, such as sleep disturbance, depression, anxiety. Interactions between migraine, sleep disturbances, and psychiatric comorbidities in migraineurs were analysed in this study. Episodic and chronic migraine have different effects on the quality of life, and higher rates of psychiatric comorbidities are also seen in patients with chronic migraine [3], we did not include chronic migraine patients in this study.

In this study, 75.9 % of the migraineurs had mild/moderate/severe disability related to migraine within the past three months. A number of attacks per month in migraineurs were 4.2 ± 2.9, and the mean pain intensity of their migraine attacks was higher than moderate (7.5 ± 1.2). The mean age and educational status of the migraine and the control groups did not differ from each other.

Previous studies have confirmed that mood and anxiety disorders are two to ten times more prevalent in migraineurs than in the general population also higher than 25 % of patients with migraine meet the criteria for mood disorders and anxiety [29–31]. Based on the information taken from participants, 15 % of migraineurs had a past history of psychiatric disorders, whereas none of the control subjects had a past history of psychiatric disorders. However, in our study, the migraineurs and the control subjects showed some levels of depression (37.9 vs 31.7 %), anxiety (55.2 vs 34.1 %), and stress (42.5 vs 34.1 %). Although anxiety and stress correlate with many conditions, in our study migraineurs showed no statistical difference in their DASS-depression, anxiety, and stress scales from that shown by the healthy control subjects. At the same time, the migraineurs had poor sleep quality, according to PSQI scores and also based on previous studies [3–8]. Zhu et al. [32] reported that migraine history and comorbidity with anxiety and/or depression predicted poor sleep quality. Our

findings confirm the study of Vgontzas et al. [17] that comorbid depression and anxiety disorders are not the only link that explains the correlation between migraine and sleep disturbances.

Based on our study, the numbers of migraine attacks per month and headache frequency were not correlated with poor sleep quality in migraineurs; however, pain intensity and migraine related disability were associated with sleep problems in these patients. The total MIDAS scores correlated with sleep latency ($r = 0.22$, $p = 0.04$), sleep disturbance ($r = 0.37$, $p = 0.002$), and daytime dysfunction ($r = 0.24$, $p = 0.03$). MIDAS B scores were also associated with habitual sleep efficiency ($r = 0.35$, $p = 0.001$) and sleep disturbance ($r = 0.23$, $p = 0.03$). In previous studies, Seidel et al. [33] demonstrated that the quality of sleep decreased in migraineurs, Kelman et al. [11] reported that migraineurs had difficulty in initiating (53 %) and maintaining (61 %) sleep, and Karthik et al. [10] also found that 66.7 % of migraineurs had poor sleep quality compared to 7.8 % of healthy control subjects, as determined by a PSQI score. Moreover, these patients had difficulties with sleep initiation, sleep maintenance, and early morning awakening. Excessive day time sleepiness was not searched in this study; however, we would point out that EDS is also frequently reported by migraineurs [10, 34, 35].

Many theories have been suggested to explain the etiology of the link between migraine and psychiatric conditions, such as shared environmental or genetic factors, latent brain state, and unidirectional or bidirectional causal models [13, 29, 36]; however, none of these theories has been explained accurately underlying this comorbidity yet. Serotonergic dysfunction is well known in an etiology of migraine [37, 38], and serotonin has also been known to play a role in the initiation and maintenance of sleep and in modulating mood [39, 40]. Furthermore, dopaminergic dysfunction also underlies the comorbidity of migraine and depression pathophysiology [41, 42]. In a recent review, the author suggested a migraine attack as a brain state such as sleep, wakefulness, and attention [43]. Clinical symptoms, electrophysiological, and functional imaging studies show that multiple brain networks are either activated or inactivated during a migraine attack in addition to activation of the pain network, so a migraine attack might be considered as a pathological brain state. This consideration may provide an expanded framework for understanding migraine. Moreover, neurochemical mediators such as adenosine, melatonine, and orexin (hypocretin) play a role in the pathogenesis of sleep and headache [44]. Finally, several similar brain areas in diencephalon and brainstem and neurotransmitters are involved in the pathogenesis of depression, anxiety, stress, sleep regulation, and migraine. The comorbidity of sleep disturbances, psychiatric conditions, and migraine could be a manifestation of common underlying pathways.

Understanding the interactions between these conditions in migraineurs might be important to avoid poor clinical outcomes and may help to define the best treatment options and to predict the chronification of migraine. A size of our migraine patients is small. Furthermore, we evaluated sleep disturbances and psychiatric conditions only by a self-reported questionnaire. A history of past psychiatric condition was taken from participants based on their own judgements alone. These were the main limitations of our study. In conclusion, further prospective studies are needed to define the precise nature and direction of the relationship between these conditions. Evaluating not only the coexisting psychiatric conditions in migraineurs but also their sleep problems is the pragmatic recommendation for daily practice by neurologists, in order to achieve better and more effective treatment.

Conflict of interest The authors declare that they have no conflict of interest.

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