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Sleep Disturbance in Patients with Burning Mouth Syndrome: A Case-Control Study

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Aims: To examine sleep complaints in patients with burning mouth syndrome (BMS) and the relationships between these disturbances, negative mood, and pain. ***Methods:*** *Fifty BMS patients were compared with an equal number of healthy controls matched for age, sex, and educational level. The Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), the Hamilton Rating Scales for Depression (HAM-D) and Anxiety (HAM-A) were administered. Descriptive statistics, including the Mann-Whitney* U *test and hierarchical multiple linear regression analyses were used.* ***Results:*** *BMS patients had higher scores in all items of the PSQI and ESS than the healthy controls (*$P < .001$*). In the BMS patients, a depressed mood and anxiety correlated positively with sleep disturbances. The Pearson correlations were 0.68 for PSQI vs HAM-D (*$P < .001$*) and 0.63 for PSQI vs HAM-A (*$P < .001$*).* ***Conclusion:*** *BMS patients reported a greater degree of sleep disorders, anxiety, and depression as compared with controls. Sleep disorders could influence quality of life of BMS patients and could be a possible treatment target.*
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Key words: anxiety, depression, insomnia symptoms, pain, sleep

Burning mouth syndrome (BMS) is an idiopathic, chronic pain condition that affects more than 1 million individuals in the United States alone,[1] with an estimated prevalence ranging from 0.7% to 4.6%.[2,3] It usually occurs in the fifth to seventh decade of life and is more common in females than in males, with a ratio of approximately 3:1.[2,4]

The International Association for the Study of Pain and the International Headache Society define BMS as a "distinctive nosological entity," including all forms of burning sensation in the mouth and complaints described as a stinging sensation or pain, in the absence of specific oral lesions and without alterations in blood tests and/or instrument findings.[5]

In almost all patients, BMS is characterized by sensory symptoms (burning, pain, a foreign-body sensation such as sand granularity, a decrease of salivation, and itching) involving mainly the tongue and lips, followed by the hard palate, alveolar ridges, cheeks, and floor of the mouth,[6] which are not attributable to any organic pathologies and are not supported by clinical findings. The discomfort may range from minimal to severe and may significantly affect the patient's quality of life. It tends to persist for at least 4 to 6 months, to be constant and bilateral, and to be relieved with food consumption. Other complaints may be associated with the burning, such as dysgeusia, hyposmia, and/or dysosmia, which supports its designation as a syndrome.[7] The pathogenesis of BMS remains poorly understood, although both physiological and psychological factors have been hypothesized to be involved. Several studies have shown

an associated high prevalence of psychiatric symptoms and/or mental disorders in BMS patients, with good clinical responses to low-dose antidepressants and/or antianxiety medications.[7,8]

Neurophysiological and imaging studies have suggested that a dysfunction of the nigrostriatal dopaminergic pathway may play a role in the pathophysiology of BMS,[9,10] while other studies using functional magnetic resonance imaging (fMRI) have shown that patients with BMS have a specific qualitative and quantitative pattern of brain activation, leading to a net brain hypoactivity, suggesting that BMS patients may have a loss of function in the descending inhibitory serotonergic and noradrenergic pathways causing, or at least contributing to, chronic pain.[11]

Sleep is vital to health and quality of life, whereas poor sleep is associated with adverse health consequences[12] and worsening medical or psychiatric diseases (eg, chronic pain, dementia and depression).[13]

Insomnia is the most prevalent sleep problem and is characterized by a difficulty in falling or staying asleep, an early awakening or nonrestorative sleep in an individual who has adequate circumstances and opportunity for sleep.[14] Impaired sleep generally has a negative effect on mood, pain severity experience, daytime functioning, and general quality of life.[15–19] In particular, insomnia is often associated with somatic and pain symptoms.[20] The association between sleep disturbances and pain is complex because sleep and pain are both associated with the activation of a number of central nervous system regions, with several studies suggesting that the supraspinal regions, the thalamocortical pathways, or the anterior cingulate cortex may be involved in the sleep-pain interaction.[21,22] Although the mechanism has not been well studied, pain sensations could directly interrupt sleep. For example, chronic pain could cause a heightened arousal and vigilance, reducing the quality and quantity of sleep, and chronic pain and pain-related illness could cause cognitive and affective disturbances, which in turn cause insomnia.[23,24] Consequently, it appears that pain could influence sleep through direct and indirect pathways, with a high prevalence of sleep-related disturbances in chronic pain patients typically reported in the 50% to 70% range.[25] Moreover, insomnia is a common complaint in patients with pain symptoms related to their underlying medical disorders, such as rheumatoid arthritis and cancer.[26] More recently, LeBlanc et al[27] reported that a higher level of body pain was an important predictor for the incidence of insomnia,[28] with a close and bidirectional relationship between insomnia and pain.[29]

Previous studies on associations between pain and negative effects suggest that a negative mood may increase the perception of pain; they report a clear relationship between sleep disorders and negative mood,[30] with sleep problems being listed as a symptom of both major depression and anxiety disorders in the Diagnostic and Statistical Manual of Mental Disorders–IV, Text Revision.[31]

The association of a negative mood, such as anxiety or depression, with sleep disturbance could be related to common underlying pathophysiological mechanisms for sleep and mood regulation that make the individual vulnerable to both conditions.[30,32,33] In addition, a number of longitudinal studies indicate that poor sleep is a risk factor for major depression and anxiety.[34]

The relationship between pain, negative effects, and sleep is complex, and research has revealed contradictory data. Nicassio and Wallstone studied the relationship of pain and sleep with depression in 242 patients suffering from rheumatoid arthritis. On cross-sectional analysis, the regression results indicated that sleep disturbances and depression were closely associated. Depression was independent from pain when various demographic and functional impairments were controlled in the model, whereas longitudinal analysis indicated that pain influenced later sleep but sleep difficulty was not associated with pain assessed 24 months later.[35] In some studies, "poor sleepers" reported great pain but did not differ from "good sleepers" on measures of depression and anxiety. However, other studies reported that compared with "good sleepers," "poor sleepers" had higher scores on measures of depression and anxiety, pain intensity, and greater physical disability.[13,36,37]

Sleep disturbance in BMS patients is poorly documented, while mood disorders have been studied. The lack of research in this area may reflect the conventional approach of considering sleep disturbance as a symptom of an underlying disorder rather than an independent clinical entity worthy of attention. The role that sleep disturbances play in BMS is unknown. It was hypothesized that sleep disturbances affecting the quality of life could be considered worsening factors in patients with BMS. The purpose of this study was to examine sleep complaints in patients with BMS and the relationships between these disturbances, negative mood, and pain.

Materials and Methods

Participants and Procedure

This was a case-control clinical study carried out at the Oral Medicine Unit, Federico II University of Naples. Sixty-six BMS cases and 57 healthy subjects were screened to participate between May 2010 and December 2010. Fifty BMS patients (response rate 76%) and 50 healthy control subjects (response rate 88%) were included in the trial in accordance with the inclusion/exclusion criteria, undergoing a simple randomization procedure with IBM SPSS software. Both groups were frequency-matched for sex, age, and educational level. All patients received written information and provided their written informed consent for the management of personal data before their participation. The study was approved by the local Ethical Committee.

The inclusion criteria for BMS were *(1)* either sex, aged 18 or older; *(2)* the presence of chronic pain in the oral mucosa in the absence of hard and soft tissue lesions of any kind; *(3)* pain lasting more than 6 months, continuous throughout the day, with no paroxysm and not following any unilateral nerve trajectory; and *(4)* the absence of any abnormalities from the following laboratory investigations: salivary flow rates, laboratory tests, and tests for the detection of Candidiasis. The exclusion criteria encompassed patients presenting with organic conditions that could be considered a causative factor, such as diabetes, anemia, thyroid disease, iposcialia-related systemic disorders (eg, Sjogren's syndrome), contact allergies, psychotic illness, organic brain syndrome, or neurological disease; subjects with signs of parafunctional habits; or patients regularly treated with anxiolytic, antidepressant, anticonvulsant, or psychotropic drugs. Even in the absence of mucosal lesions, a local effect of dental materials related to contact hypersensitivity was excluded by means of patch tests when the symptoms had started after any dental rehabilitation. A final diagnosis of BMS was established only after all other possible causes of the oral complaints had been ruled out.

The inclusion criteria for healthy subjects were *(1)* either sex, aged 18 or older; *(2)* the absence of oral mucosal lesions; *(3)* no history of psychiatric disorder; and *(4)* consultation at the department exclusively for dental disease (dental caries or periodontal disease). Conversely, the exclusion criteria encompassed *(1)* patients with unstable medical conditions or debilitating pathologies (eg, cancer, osteonecrosis, or autoimmune blistering disease) and *(2)* patients regularly treated with anxiolytic, antidepressant, anticonvulsant, and/or psychotropic drugs.

Sociodemographic data, age, education, occupation, and marital status were recorded for both BMS patients and healthy subjects. At admission, each subject underwent a medical anamnesis (including history, clinical features, and treatment), a general medical examination, an intraoral and extraoral examination, and laboratory tests (eg, full blood cell count, and serum levels of iron, ferritin, folate, vitamin B12, and glucose).

Three oral medicine specialists were responsible for determining the eligibility of the BMS patients and of the healthy individuals as controls, and for collecting all the demographic and medical data from both groups. After screening, the BMS patients and controls were evaluated by a psychiatrist from the Department of Neuroscience of the same University Hospital.

Upon admission, the BMS patients and healthy controls were assessed in accordance with the following evaluation battery scales: the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) for the assessment of sleep, the Hamilton Rating Scale for Depression (HRSD or HAM-D) and the Hamilton Rating Scale for Anxiety (HAM-A) for the evaluation of depression and anxiety, and the Numeric Rating Scale (NRS) for the measurement of oral pain symptoms.

All these scales were reviewed for completeness before collection and were administered in their Italian versions.

Sleep Scales

The Pittsburgh Sleep Quality Index. The PSQI is considered an essential measure of sleep and insomnia symptoms in treatment research, and it is a recommended assessment tool for epidemiological studies; it is a self-report questionnaire assessing sleep quality and disturbances over a 1-month time interval, and is designed to be used in clinical populations.[38] This instrument comprises 19 items, generating 7 "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Sleep pattern data (eg, bedtime, wake time, sleep onset latency, and sleep quantity) are also provided. Each item is scored from 0 to 3, with higher scores indicating poorer sleep or more frequent sleep problems. Items are combined to yield the 7 components (scores ranging from 0 to 3), and the sum of the scores for these 7 components yields 1 global score ranging from 0 to 21. Global scores above 5 distinguish poor sleepers from good sleepers with a high sensitivity (90% to 99%) and specificity (84% to 87%).[39] The psycho-

metrics of the PSQI were subsequently evaluated by Carpenter and Andrykowski[40] in four different patient populations, and the results indicated that the PSQI had a good internal consistency and construct validity. The PSQI has been translated into 48 languages and has been used in a wide range of population-based and clinical studies.

The Epworth Sleepiness Scale. The ESS is a simple, self-administered questionnaire that provides a measurement of the subject's general level of daytime sleepiness; the ESS was first introduced by John in 1991.[41] It does not require any instrumental evaluation, and is quick, inexpensive, flexible, and able to measure chronic sleepiness. The instrument comprises eight items assessing the propensity for sleep in eight common situations (eg, watching television, or talking with someone). Subjects rate their likelihood of dozing in each situation on a scale of 0 (would never doze) to 3 (a high chance of dozing). The ESS score is the sum of the eight items. The ratings can be added together to form a total score of 24, with a cut-off value of > 10 indicating excessive daytime sleepiness. Several studies have used the ESS and it is a well-validated questionnaire. Psychometric analyses of the ESS support its internal consistency and unidimensionality.[42] The ESS has been translated into 52 languages and has also been used in a wide range of population-based and clinical studies.

Depression and Anxiety Scales

The Hamilton Rating Scale for Depression. The HDRS (or HAM-D) is an inventory employed to detect and identify the intensity or severity of the signs and symptoms of depression.[43,44] The HAM-D is the most widely used clinician-administered depression assessment scale. It should be administered by a clinician experienced in working with psychiatric patients. Although the HAM-D form lists 21 items, the scoring is based on the first 17. Eight items are scored on a 5-point scale, ranging from 0 = not present to 4 = severe. Nine are scored from 0 to 2. Scores can range from 0 to 54. A total score is computed to reflect the degree of symptom severity. A score > 10 indicates impairment. Scores between 10 and 17 indicate mild depression, scores between 18 and 24 indicate moderate depression, and scores over 24 indicate severe depression. Many of the psychometric properties of the HAM-D are adequate and consistently meet established criteria. The internal, inter-rater, and re-test reliability estimates for the overall HAM-D are mostly good, as are the internal reliability estimates at the item level.[45]

The Hamilton Rating Scale for Anxiety. The HAM-A is a rating scale developed to quantify the severity of anxiety symptomatology, often used in psychotropic drug evaluation.[46,47] It consists of 14 items, each defined by a series of symptoms. Each item is rated on a 5-point scale, ranging from 0 (not present) to 4 (severe), with a total score range of 0 to 56. A score of below 17 indicates mild severity, scores in the 18 to 24 range indicate mild to moderate severity, and from 25 to 30 indicate moderate to severe anxiety. It provides measures of overall anxiety, psychic anxiety (mental agitation and psychological distress), and somatic anxiety (physical complaints related to anxiety). It is also used as an outcome measure when assessing the impact of antianxiety medications, therapies, and treatments and is a standard measure of anxiety used in evaluations of psychotropic drugs.

Oral Pain Scale

A numerical rating scale (NRS-11) was used for the evaluation of oral symptoms.[48] This scale ranged from 0 to 10 (0 = no oral symptoms and 10 = the worst imaginable discomfort; therefore comprising 11 integers including 0). The NRS is a well-validated instrument and is recommended for more comprehensive pain assessment. The literature shows that the NRS and the visual analog scale (VAS) are equally efficient for the evaluation of pain[49]; the NRS may be preferred for its ease of use, standardized format, and better compliance. This scale was administered by interview undertaken by clinicians who asked the patients to assign a rating from 0 to 10 in order to quantify the pain. The patients were then questioned as to their goals and expectations with respect to their pain rating as a measure of satisfaction with the degree of analgesia.[50]

Statistical Analysis

Descriptive statistics, including means, standard deviations, medians, and interquartile range, were used to summarize all the variables. Considering the non-normality of the data analyzed, the Mann-Whitney *U* test was employed to test the significance of the study parameters between the BMS patients and controls. *P* values < .05 were considered to reflect statistical significance.

A series of hierarchical multiple linear regression analyses was performed to test the importance of disease-related and psychosocial factors to sleep quality after checking for demographic factors. Each hierarchical regression analysis computed whether the variance explained by the specific set contributed

Table 1 Demographic and Clinical Characteristics of BMS Patients and Control Subjects

	BMS patients	Control subjects	*P*
Demographic variables			
Age (mean ± SD)	57.98 ± 8.1	53.2 ± 8.6	.832
Years of education (mean ± SD)	8.4 ± 3.1	9.3 ± 2.9	.781
Sex (female:male)	38:12	38:12	—
Marital status (married:unmarried)	42:8	42:8	—
Job full-time (yes:no)	11:39	11:39	—
Clinical parameters			
Sleep quality, PSQI (median; IQR)	9.0; 6–14	4.0; 3–5	< .001**
Depression, HAM-D (median; IQR)	16.0; 10–24	5.0; 4–6	< .001**
Anxiety, HAM-A (median; IQR)	17.5; 13–27	5.0; 4–7	< .001**
Daytime sleepiness, ESS (median; IQR)	10.0; 7–12	3.0; 2–3	< .001**
Pain severity, NRS (median; IQR)	8.5; 8–10	—	—

IQR, interquartile range. The significance difference between medians was measured by Mann-Whitney *U* test. PSQI, Pittsburgh Sleep Quality Index; HAM-D, HAM-A, Hamilton Rating Scale for Depression, Anxiety; ESS, Epworth Sleepiness Scale; NRS, numerical rating scale.
**Significant $P \leq .01$.

significantly to the total variance in sleep quality after checking for the demographic set. A full model analysis was then computed with all the variables entered simultaneously into the model to determine the relative contributions of these variables to sleep quality.

Results

Table 1 summarizes the demographic and clinical parameters. There were 38 female patients (76%) and 12 male patients (24%).

PSQI Reliability

Table 2 shows the reliability analysis of PSQI in BMS patients. The Cronbach α measure 0.84 indicated a good overall reliability of the scale. All components presented an acceptable level of item-scale Pearson correlation. Item-scale correlation and Cronbach α index were used to verify the internal consistency, item by item, and the global reliability of the PSQI in BMS patients and controls.

Sleep Quality

The global and component scores for the PSQI were significantly different between cases and controls (Tables 1 and 3). Patients with BMS had higher mean PSQI scores, indicating a poorer sleep quality for these patients compared to the healthy controls. Forty patients (80%) were poor sleepers, with a PSQI global score of > 5.

Table 2 Reliability Analysis of PSQI Scale in BMS Patients and Control Subjects

	Item-Scale ρ correlation	
PSQI Components	BMS patients	Control subjects
Subjective sleep quality	0.58	0.51
Sleep latency	0.76	0.32
Sleep duration	0.60	0.43
Habitual sleep efficiency	0.62	0.36
Sleep disturbances	0.54	0.03*
Use of sleep medications	0.31	0.61
Daytime dysfunction	0.63	0.17*
Cronbach α	0.84	0.65

*Poor correlation between a single item and the global scale ($\rho < 0.3$).

Patients with Poor Quality of Sleep. Among BMS patients, the clinical parameters of good (PSQI < 5) and poor (PSQI > 5) sleepers were compared. Depression ($P < .001$), anxiety ($P < .001$), and daytime sleepiness ($P < .001$) were found to be significantly different between the two groups, while pain severity was not ($P = .214$) (Table 4).

Dependence of Sleep Quality. As shown in Table 5, depression (HAM-D), anxiety (HAM-A), and daytime sleepiness (ESS) correlated positively with sleep quality, while pain severity did not. In addition, the years of education correlated negatively with sleep quality.

Table 3 Comparison of Components of PSQI in BMS Patients and Control Subjects

	BMS patients			Control subjects			
PSQI components	Median	IQR	Range	Median	IQR	Range	*P*
Subjective sleep quality	1	1–2	0–3	1	1–1	0–2	.002**
Sleep latency	1	1–2	0–3	0	0–1	0–2	< .001**
Sleep duration	1	0–2	0–3	1	1–1	0–2	.199
Habitual sleep efficiency	1	0–2	0–3	1	0–1	0–3	.015*
Sleep disturbances	1	1–2	0–3	0	0–1	0–3	< .001**
Use of sleep medications	3	0–3	0–3	0	0–0	0–3	< .001**
Daytime dysfunction	1	1–2	0–3	0	0–1	0–4	< .001**

IQR, interquartile range. The significance difference between medians was measured by Mann-Whitney *U* test. *Significant .01 < $P \leq .05$, **Significant $P \leq .01$.

Table 4 Comparison Between Good and Poor Sleepers for BMS Patients

	PSQI ≤ 5 (n = 23)			PSQI > 5 (n = 27)			
	Median	IQR	Range	Median	IQR	Range	*P*
Depression (HAM-D)	8.5	6–9	3–12	18	13–25	6–39	< .001**
Anxiety (HAM-A)	6.5	4–9	3–18	20	15.5–30	5–48	< .001**
Daytime sleepiness (ESS)	6.0	6–6	6–8	11	8–12	6–16	< .001**
Pain severity (NRS)	8.0	7–9	6–10	9	8–10	4–10	.214

PSQI, Pittsburgh Sleep Quality Index; IQR, interquartile range; HAM-D, HAM-A, Hamilton Rating Scale for Depression, Anxiety; ESS, Epworth Sleepiness Scale; NRS, numerical rating scale. The significance difference between medians was measured by Mann-Whitney *U* test. **Significant $P \leq .01$.

Table 5 Dependence of Sleep Quality with Clinical Parameters and Demographic Characteristics for BMS Patients

	Pearson coefficient		*P*
Clinical parameters			
Depression (HAM-D)	0.68		< .001**
Anxiety (HAM-A)	0.63		< .001**
Daytime sleepiness (ESS)	0.85		< .001**
Pain severity (NRS)	0.18		.213
Demographic characteristics			
Age	0.03		.858
Years of education	–0.32		.022*
	Median; IQR		
Sex	Female 9.0; 6–15	Male 8.5; 6–10.5	.368
Marital status	Married 9.0; 7–15	Unmarried 6.0; 5–9	.126

HAM-D, HAM-A, Hamilton Rating Scale for Depression, Anxiety; ESS, Epworth Sleepiness Scale; NRS, numerical rating scale; IQR, interquartile range. For the numerical variables, *P* values were obtained by Pearson correlation test. For the qualitative characteristics, *P* values were obtained by Mann-Whitney *U* test. *Significant .01 < $P \leq .05$, **Significant $P \leq .01$.

Table 6 Multiple Linear Regression Model Predicting Sleep Quality in BMS Patients

	Model 1		Model 2		Model 3		Model 4		Model 5	
	Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*	Beta (SE)	*P*
Predictors										
Age	−0.02 (0.09)	.785	0.10 (0.06)	.131	0.09 (0.07)	.198	−0.01 (0.09)	.944	0.01 (0.06)	.144
Years of education	−0.53 (0.23)	.026*	−0.48 (0.16)	.004**	−0.39 (0.18)	.034*	−0.49 (0.24)	.043*	−0.46 (0.16)	.007**
Sex: Female	0.71 (1.63)	.665	1.15 (1.12)	.309	1.46 (1.25)	.247	0.77 (1.64)	.642	1.24 (1.15)	.286
Marital status: Married	−2.72 (1.71)	.120	−0.57 (1.22)	.641	−0.64 (1.35)	.637	−2.58 (1.74)	.145	−0.49 (1.24)	.693
Depression (HAM-D)			0.39	<.001**					0.32 (0.11)	.005**
Anxiety (HAM-A)					0.29 (0.05)	<.001**			0.07 (0.09)	.452
Pain severity (NRS)							0.37 (0.47)	.440	−0.13 (0.36)	.720
R^2 (%)	16.2	.088	61.5	<.001**	52.7	<.001**	17.3	.125	62.0	<.001**
R^2 change (%)			45.3	<.001**	36.5	<.001**	1.1	.440	45.8	<.001**

SE, standard errors of beta estimates. HAM-D, HAM-A, Hamilton Rating Scale for Depression, Anxiety; ESS, Epworth Sleepiness Scale; NRS, numerical rating scale. *P* values were obtained by hypothesis test on regression coefficients. *Significant $.01 < P \leq .05$, **Significant $P \leq .01$.

Association with Sleep Quality. The results of the hierarchical multiple linear regression analyses predicting sleep quality are shown in Table 6. Model 1 (the demographic model) tested the contribution of demographic variables to disturbed sleep. Model 2 (the depression model) tested the contribution of depressed mood to poor sleep quality after controlling for the demographic variables. Model 3 (the anxiety model) tested the contribution of anxiety mood to poor sleep after checking for the demographic variables. Model 4 (the pain model) tested the contribution of pain severity after checking for the demographic variables. Model 5 is the standard regression analysis where all of the variables were entered simultaneously into the model to assess the relative contributions of these variables to sleep quality. This model takes into account the interrelations between the predictor variables as well as the effects of the predictor variables on the outcome variable (PSQI).

The first model testing the contributions of demographic variables to sleep quality was not found to be statistically significant ($R^2 = 16.2\%$, $P = .088$). The addition of depression (model 2) and anxiety (model 3) resulted in a significant increase in the R^2 value ($\Delta R^2 = 45.3\%$, $P < .001$ for depression, $\Delta R^2 = 36.5\%$, $P < .001$ for anxiety) while the addition in model 4 of pain (NRS) did not contribute significantly to poor sleep quality. The final full model (the standard multiple regression analysis) in which all of the variables were entered simultaneously could explain 62% of the variance in sleep quality.

The analysis of dependence reported in Table 5 highlights a strong correlation between the PSQI and the ESS. This result is consistent with the similar nature of the two scales, and therefore the ESS can be considered as a proxy variable of the PSQI. For this reason, the ESS was excluded from the set of predictors considered in the hierarchical multiple linear regression analysis reported in Table 6.

Discussion

Previous studies have demonstrated that sleep disorders occur in up to 27% of the primary-care population and more frequently (ranging from 51% to 75%) in the elderly and in patients with advanced medical illness.[51,52] In clinical populations, the prevalence of sleep disturbance has been estimated to be about 51% of patients who experience chronic low back pain, 75% of those with fibromyalgia, and 70% of those with rheumatoid arthritis.[53]

In the present study, the prevalence of poor sleep in patients with BMS was 80%, with the global PSQI and all of the component scores significantly higher in BMS patients compared to controls. This clearly depicts the poorer sleep quality of BMS patients when compared to healthy subjects. While in previous studies it has been reported that sleep disorders can increase pain, which in turn may cause sleep disorders,[54–57] the measurement of pain (NRS) in this study was similar in both groups, good and poor sleepers. Forty patients (poor sleepers) had a clinically significant depressed mood and anxiety. None of these patients was taking antidepressants. This could be due to the probable underestimation of depression and anxiety in diseases such as BMS.

Previous studies have commonly reported a higher presence of negative mood in both chronic pain populations and individuals with sleep problems.[32] However, previous findings of the interrelationships between sleep, pain, and negative mood have been inconsistent in the existing literature.[58,59] Some studies have reported higher levels of depression and/or anxiety among chronic pain patients with sleep disturbances; other studies have not found these relationships.[13,37,58–60]

In the present study, the association between depression, anxiety, daytime sleepiness, and sleep quality in BMS patients, which was evident and significant on bivariate analysis, remained significant in standard multiple regression analyses. Therefore, depression and anxiety could be important risk factors of sleep disturbance in BMS patients.

It is possible that high levels of negative mood may increase or perpetuate the impact of sleep disturbances in BMS patients, possibly through mechanisms of increased physiological or cognitive arousal or dysregulated diurnal patterns (eg, decreased physical and social activities during the day, increased time in bed combined with high levels of daytime sleepiness). These symptoms and behaviors are common in the clinical pictures of both depression and anxiety. Additionally, it is not difficult to see how a negative mood and sleep disturbances can each act to increase the other, leading to a cycle that perpetuates itself if there is no intervening action to disrupt it.[61,62]

In previous studies, the association between pain symptoms and sleep disturbances has been demonstrated based on epidemiological data,[37] with controversial data on the worsening effect of poor sleep on chronic pain complaints.[18,19,63] Morin et al also reported that chronic pain preceded or coincided with a complaint of poor sleep in approximately 90% of patients in an outpatient pain clinic.[59] In that study, pain was considered the causal factor of sleep disturbances and generally improved with pain management. There is a lack of data in the literature on the relationship between sleep quality and pain intensity; however, even if the correlation between sleep disturbances and the intensity of pain symptoms needs to be addressed, it is possible to consider that a prolonged period of pain and a long history of unsuccessful treatment can, in time, worsen sleep quality. In a previous study that analyzed anxiety, depression, and pain in BMS patients, the authors demonstrated that pain increases along with anxiety and depression, and not with illness duration.[64] Although pain, sleep disturbance, and psychological distress are frequently observed in various chronic pain conditions, it is difficult to determine which of these conditions begins first. There is controversy as to whether psychogenic factors are primary or secondary events, because chronic pain conditions may affect and alter the subject's psychological profile.[65,66]

Treatment of BMS includes the administration of low doses of benzodiazepines, including clonazepam.[67,68] The mechanism of action of these drugs in BMS is unknown. However, it is known that these medications have an effect on sleep and have also been used in the treatment of insomnia.[69] It is possible that this effect on promoting sleep may partially explain the mechanism of action of these drugs in BMS.[69–71] The results from the present study suggest a new direction for etiological and interventional research in BMS, but larger prospective studies are needed to add to our knowledge of the causative role of sleep in BMS. In addition, a suitable therapy to improve sleep quality could be evaluated as an intervention for BMS.[72]

Study Limitations

There are several limitations to the current study. First, because of the small size of the sample, composed largely of women (76%), and because this study was performed in a single tertiary care center, the results may not be generalizable. Second, the pain rating scales in the BMS patients suffer from a ceiling effect, with many pain ratings near or at the top of the scale. For this reason, pain rating scales could be inadequate to assess pain intensity and its correlation with sleep quality. Third, only the intensity and not the type and pattern of pain has been considered. The type of pain may be equally important in the evaluation of patients, and may be an important determinant of sleep quality. And last, this was a case-control study, unsuitable to evaluate the prospective relationships between pain, sleep, and psychological disorders.

Conclusions

This study has confirmed the comorbidity of sleep disturbance and psychological distress in a sample of BMS patients. In contrast, pain intensity did not correlate with sleep quality. The study has demonstrated that sleep disturbance is a common problem among BMS patients and has highlighted the importance of assessing sleep variables in clinical evaluation and, possibly, in treatment. Future studies should try to gain an understanding of the pathophysiological relationships between these sleep disturbances, anxiety and depression, and their biological background.

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