

OBSTRUCTIVE SLEEP APNEA (OSA) AND DEPRESSIVE SYMPTOMS

Michele Dominici^{1,2}, Marleide da Mota Gomes¹

Abstract – Background: The relationship between obstructive sleep apnea (OSA) and depressive symptoms is ambiguous in the literature. **Purpose:** To investigate if there is a correlation between depressive symptoms and the severity of OSA. **Method:** A retrospective, cross-sectional study of data from 123 consecutive adults patients with neither mental illness nor psychotropic drugs intake, referred to a sleep laboratory for an evaluation of OSA. For the statistical analysis (uni- and multivariate), we used the following variables: gender and age, as well as scores based on several scales and indexes such as Beck Depressive Inventory (BDI), Epworth Sleepiness Scale (ESS), Body Mass Index (BMI) and Apnea-Hypopnea Index (AHI). **Results:** Univariate analysis found a weak but statistically significant negative correlation between BDI and AHI. However, with the multivariate logistic regression analysis model, the inverse relation between AHI and BDI no longer has statistical significance. **Conclusion:** There is no causal relationship between OSA and depressive symptoms in the population studied.

KEY WORDS: obstructive sleep apnea, depressive symptoms, Beck depressive inventory, apnea and hypopnea index.

Sintomas depressivos e síndrome de apnéia obstrutiva do sono

Resumo – Contexto: A relação entre apnéia obstrutiva do sono (AOS) e sintomas depressivos é ambígua na literatura. **Objetivo:** Investigar se há relação entre sintomas depressivos e intensidade da AOS. **Método:** Estudo transversal e retrospectivo com 123 pacientes adultos, consecutivamente atendidos em laboratório de sono, para avaliar AOS, sem transtornos mentais nem uso de psicotrópicos. Para análise estatística (uni e multivariada), utilizamos as seguintes variáveis: sexo e idade, além de escores de diversas escalas: Escala de Depressão de Beck (EDB), Escala de Sonolência diurna de Epworth (EPW), Índice de Massa Corporal e o Índice de Apnéia /Hipopnéia (IAH). **Resultados:** A análise univariada demonstrou fraca, mas estatisticamente significativa relação negativa entre EDB e IAH. Porém, na análise multivariada por regressão logística, esta relação inversa perdeu sua significância. **Conclusão:** Não há relação causal, em nossa população estudada, entre sintomas depressivos e intensidade de AOS.

PALAVRAS-CHAVE: apnéia obstrutiva do sono, sintomas depressivos, escala de depressão de Beck e índice de apnéia/hipopnéia.

It is known that it is difficult to determine the etiology of neuropsychological symptoms, and the DSM-IV¹ diagnosis of depression requires that five symptoms, which may include both psychological and somatic symptoms, be present, simultaneously and that one of these be either depressed mood or anhedonia. These depressive symptoms may overlap the symptoms of many medical illnesses^{2,3}, like obstructive sleep apnea (OSA)⁴. Therefore, judging whether a symptom is totally and fully related to the patient's medical condition might be a chal-

lenge in clinical practice, but is relevant to a correct clinical practice. OSA is defined by frequent episodes of obstructed breathing during sleep, and it is found in all age groups, but its prevalence increases with age⁵, and is higher in men than in women, by two to three folds⁶. Clinically, until 2005 OSA was defined by the presence of either snoring and excessive daytime sleepiness (EDS) or insomnia, and it was confirmed when a polysomnography recording determined an Apnea-Hypopnea-Index (AHI) of more than five per hour of sleep⁷. Based on the new clas-

¹Postgraduate in Psychiatry and Mental Health, Division of Neurophysiologic Clinics - Epilepsy Program of Neurological Institute/Federal University of Rio de Janeiro (UFRJ); ²Professor Fernando Pompeu Neurological Clinic, Rio de Janeiro RJ, Brazil. Michele Dominici was supported by a CNPq postgraduate scholarship (Pós-graduação em Psiquiatria e Saúde Mental do Instituto de Psiquiatria da UFRJ) and is a medical associate of Professor Fernando Pompeu Neurological Clinic as well.

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Dr. Michele Dominici – Avenida Prado Jr 307/604 - 22011-040 Rio de Janeiro RJ - Brasil. E-mail: micheledominici@gmail.com

sification (ICSD-2)⁸, the symptoms associated with OSA have added fatigue with the same AHI or without a specific symptom, but with an AHI of more than 15/h.

The abnormal respiratory events of OSA usually are accompanied by arousals from sleep, with frequent arousals being the most important factor resulting in EDS⁹. Even if patients are often not aware of this repetitive sleep interruption, they usually do not feel restored in the morning. Other nocturnal symptoms can include restlessness, nocturia, excessive salivation and sweating, gastroesophageal reflux, as well as headache, and dry mouth, or dry throat in the morning, on awakening. OSA is a relatively common chronic disease that is often associated with a severe reduction in the quality of life with symptoms other than EDS, which greatly impact daytime functioning, such as irritability, difficulty concentrating, cognitive impairment, depressive symptoms, and other psychological disorders¹⁰. Thus, OSA patients frequently report symptoms of fatigue and depression in addition to significant EDS.

The literature on OSA paints an ambiguous picture of the role of depression in sleep apnea. There are perhaps two general positions on the issue of depression. The first one maintains that higher levels of depression do exist¹¹⁻¹⁷, and the second position, though less common, maintains that higher levels of depression do not exist in this population¹⁸⁻²⁰. Measuring depressive symptoms is a common, important task in research and clinical settings. Several depressive symptom severity scales have been developed and validated, such as the Beck Depressive Inventory (BDI)²¹.

The purpose of this study is assessing: the presence and intensity of depressive symptoms in a population suspected of having OSA, with no previous mental illness diagnosis and/or use of psychotropic drugs; the correlation or non-correlation between the intensity of OSA, measured by AHI, and the depressive symptoms measured by the BDI.

METHOD

A retrospective, cross-sectional study of data from 123 consecutive patients with ages ranging from 18 to 65 (inclusion criteria) referred to a sleep laboratory for an evaluation of OSA over a period from March 2007 through July 2007 who had been subjected to an overnight polysomnography (PSG). Patients using psychotropic drugs or diagnosed as having a psychiatric illness, including depression, were excluded.

All patients have signed the informed consent, and the ethical committee of the Neurological Institute of the Federal University of Rio de Janeiro approved the project, in compliance with the ethical standards.

Excessive daytime sleepiness was assessed by applying the Epworth Sleepiness Scale (ESS)²², and the depressive symptoms, by BDI, both applied during the PSG. For overnight polysomnography, AHI was used for the diagnosis and assessment of severity of OSA. OSA, EDS, body mass index (BMI), co-morbidity, AHI

and demographic data were subjected to univariate and multivariate analyses in order to ascertain the predictive factors for depression symptoms.

The ESS asks the individual to rate the likelihood of falling asleep in eight specific situations, on a 0–3 scale, with 0 meaning no chance at all of falling asleep, and 3 representing a high chance of falling asleep. Therefore, the scale goes from 0 to 24. There is a fixed scoring recommendation of 10 as a probably excessive daytime sleepiness.

The BDI is a commonly used 21-item measure of depression. Each item consists of four statements describing increasing intensities of depression. The items are rated on a 0–3 scale, reflecting how the participants have felt over the previous week. Possible scores range from 0 to 63; higher scores reflect a more severe depressive symptomatology.

Standard polysomnography in our laboratory uses a Brazilian polysomnography equipment (Meditron) and the following protocol: after the patient is acclimated to the facility, he/she is fitted with EEG (C3/A2, C4/A1, O2/A1, O1/A2), electro-oculographic (right outer canthus/A1, left outer canthus/A2), and chin electromyogram electrodes for sleep staging, according to the criteria outlined by Rechtschaffen and Kales²³; electrodes are placed on both legs, in order to monitor the myoclonic activity; uncalibrated inductive plethysmography bands are used to monitor chest and abdominal movements; a nasal pressure transducer is used to monitor the airflow; pulse oximetry is assessed at the finger to evaluate oxygen saturation; ECG leads are placed to monitor the cardiac rhythm; concurrent monitoring of audio, video, and body position supplements the other measured parameters.

Sleep staging was scored according to the criteria of Rechtschaffen and Kales. Arousals were scored as defined in the American Sleep Disorders Association Atlas Task Force report on EEG arousals²⁴. An apnea was defined as a reduction of the measured airflow parameter to 10% of the baseline, lasting at least 10 s. Hypopnea was defined as any reduction of the measured airflow parameter lasting at least 10 s, accompanied by a 4% decrease in the oxygen saturation measured, or a contiguous arousal. AHI is defined as the total number of apneas and hypopneas per hour of sleep.

Statistical analysis

Means with standard deviations or percentages were used to describe the sample. Comparisons between groups with the unpaired Student t test or Mann-Whitney U test were performed for continuous variables, where appropriate, and for categorical variables with the chi-square test. Spearman correlation coefficient was used to measure the association between numerical variables. Logistic regression analysis was used to identify independent predictors of EDB>10. The statistical analysis package used was SAS version 6.04 (SAS Institute Inc, Cary, NC, USA). All statistical tests were two-sided, and p values less than 0.05 were considered significant.

Table 1. Population studied according to major characteristics.

Variable	Category	N	%
Gender	Masculine	92	74.8
	Feminine	31	25.2
BMI	≤ 28	67	54.5
	29–34	38	30.9
	> 34	18	14.6
BDI	≤ 10	84	68.3
	> 10	39	31.7
ESS	≤ 10	58	47.2
	> 10	65	52.8
AHI (1)	≤ 5	21	17.1
	6–30	47	38.2
	> 30	55	44.7
AHI (2)	≤ 15	42	34.1
	16–30	26	21.1
	> 30	55	44.7
Comorbidity	Absent	58	47.2
	Present	65	52.8

BMI, body mass index; BDI, Beck depressive inventory; AHI, apnea and hypopnea index; ESS, Epworth sleepiness scale.

RESULTS

Table 1 describes the population studied and its general characteristics. We stratified the AHI in two groups, due to the different classifications proposed by the International Classification of Sleep Disorders (ICSD-2)

Table 2. Correlation among several characteristics.

		BDI	ESS	AHI
ESS	r_s	0.134		
	p	0.14		
AHI	r_s	-0.272	0.172	
	p	0.002	0.057	
Age	r_s	-0.167	0.039	0.291
	p	0.065	0.67	0.001
BMI	r_s	-0.082	0.133	0.535
	p	0.37	0.14	0.0001

r_s , Spearman coefficient; p, descriptive level; BDI, Beck depressive inventory; ESS, Epworth sleepiness scale; AHI, apnea and hypopnea index; BMI, body mass index.

and the presence of any clinical comorbidity or absence thereof.

The unvaried numerical analysis shows that AHI has a positive correlation with the age and BMI, as expected, but has a negative statistical significant correlation with BDI, as shown in Table 2.

When we changed the numerical analysis for the categorical analysis, this inverse correlation between AHI and BDI remained, even if we changed the AHI category degrees (Table 3).

However, with the logistic regression analysis model, the inverse relation between AHI and BDI has no longer statistical significance when we include ESS, BMI, comorbidity, age and gender, although the feminine gender alone is an important independent risk factor (Table 4).

Table 3. Relationship between several variables and depression (all of them dichotomized).

Variable	Category	BDI				Category
		≤ 10		> 10		
		n	%	n	%	
Gender	Masculine	71	84.5	21	53.9	< 0.0001
	Feminine	13	15.5	18	46.2	
BMI	≤ 28	47	56.0	20	51.3	0.18
	29–34	28	33.3	10	25.6	
	> 34	9	10.7	9	23.1	
ESS	≤ 10	42	50.0	16	41.0	0.5
	> 10	42	50.0	23	59.0	
AHI (1)	≤ 5	12	14.3	9	23.1	0.042
	6–30	28	33.3	19	48.7	
	> 30	44	52.4	11	28.2	
AHI (2)	≤ 15	25	29.8	17	43.6	0.042
	16–30	15	17.9	11	28.2	
	> 30	44	52.4	11	28.2	
Comorbidity	Absent	43	51.2	15	38.5	0.18
	Present	41	48.8	24	61.5	

BDI, Beck depressive inventory; ESS, Epworth sleepiness scale; AHI, apnea and hypopnea index; BMI, body mass index.

Table 4. Logistic regression analysis for BDI > 10.

	Significant variation	Coefficient	Standard error	p value	RR	CI 95%	
1	Female	1.544	0.441	0.001	4.7	2.0	11.1

DISCUSSION

We excluded patients with comorbidity psychiatric illnesses and who were taking psychoactive drugs, but patients with other clinical comorbidity were not excluded. In fact, we did that because most of the papers looking at this relationship did not do it, and it can be a bias in two ways – first, patients with sleep apnea can better their condition or worsen it depending on the psychotropic drug that is taken and, second, a depressive patient under medication can improve his/her depressive symptoms.

The choice of a scale instead of a professional evaluation has been seen with criticism since depressive symptoms frequently change in the course of the day²⁵, most often resulting in a better mood in the evening, a fact which, by itself, may impair the results interpretation. However, our aim was to evaluate the depressive symptoms instead of diagnosing depression; therefore, we believed that a validated screening test could be more suitable to our purpose and, according to the clinical guideline from the Annals of Internal Medicine, the feedback of screening results to healthcare providers usually increases the recognition of depression, especially major depression, by a factor of two to three²⁶.

The scale for depression (BDI) used in this study suffered some modifications in its new version and was not standardized for OSA, but the standard general version in Brazil is still the first one.

Regarding the plausible coexistence of OSA and depressive symptoms, we may recall sleep fragmentation and oxygen desaturation during sleep. Sleep fragmentation is a direct consequence of the recurrent microarousals associated with apneas and hypopneas, and the nocturnal hypoxemia is due to the intermittent drops in oxygen saturation caused by the respiratory events. Sleep fragmentation is the primary cause of EDS in OSA patients, and is suggested as the cause of the depressive symptomatology in OSA²⁷.

At the neurotransmitter level, the serotonergic system has a central role as a neurobiological substrate underlying impairments in the regulations of mood, sleep-wakefulness cycle, and upper airway muscle tone control during sleep. Depression is associated with a functional decrease of serotonergic neurotransmission, and it is mostly responsible for the alterations in sleep^{28,29}.

OSA physiopathology involves numerous factors, one of the most important being the abnormal pharyngeal collapsibility during sleep. Serotonin delivery to the upper airway dilator motor neurons has been shown to be reduced depending on the vigilance state. This leads to reductions in the dilator muscle activity specifically during sleep, which may contribute to sleep apnea³⁰. However, whereas the role of serotonin in mood disorders has been largely documented, its involvement in the pathophysiology of sleep apnea remains to be elucidated.

On the other hand, our findings in the univariate analysis suggested that OSA could be a protective factor for depression; in fact, it could be explained as the effect of sleep restriction in the improvement of depressive symptoms in patients with depression³¹, and OSA is a model of sleep restriction considering the multiple arousals associated to the respiratory events, although contrary to most of the works published. Rejection by means of the logistic regression model analysis reinforces the opinion that the univariate analysis has several limitations and can be misleading when it excludes other important factors.

Methodological considerations render the comparison between investigations difficult. Some of the different findings among studies can be explained by differences in the sample size, population studied, gender distribution, age, psychotropic medication intake, presence of mental disease, and AHI cut-off point, as well as by a variability in terms of the questionnaires and scales used to assess the depressive symptomatology.

Another difficult analysis occurs when the general approach compares AHI to depressive symptoms like BDI or others, since we know that even the symptom that has made OSA a syndrome (sleepiness) has only a poor correlation with AHI³². This fact underlines the complexity and multifactor causality of the depressive symptoms generation.

Although there is a biological plausibility between OSA and depressive symptoms, the findings in our selected population studied were mainly related to gender, as a reflection of the prevalence in the whole population. Consequently, we propose that patients with depressive symptoms and OSA be referred to a psychiatrist, as well as a sleep specialist, and the assessment and treatment of mood symptoms – not just the treatment of OSA itself – might be done, especially in women.

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