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The Evaluation of the Relationships Between Sleep Apnea Syndrome and Depression/Anxiety Disorder

Uyku Apne Sendromu ile Anksiyete ve Depresyon Birlikteliğinin Değerlendirilmesi

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ABSTRACT

AIM: *Sleep apnea syndrome (SAS) is commonly seen disorder in the population. There are many studies using different questionnaires to evaluate the patients who are diagnosed wit SAS and also suffering from depression and anxiety disorder; as there are many different questionnaires to evaluate these patients, the results of these studies have many discrepancies. We aim to research correlation of anxiety and depression with this study.*

METHODS: *134 cases were recruited for the polysomnographic evaluation and these cases are used as the subjects of this study. The participating patients are divided into two main groups: 51 cases with AHI<5 are selected as the control group and the remaining 83 cases with AHI>5 are named as the patient group. Later, these groups are subdivided into 3 more classes; the first one was the mild SAS patients consisting of 27 cases with AHI: 5–14.9, second one was the middle SAS patients consisting of 24 cases with AHI: 15–29.9 and finally the third one was the heavy SAS class which was consisting of 32 patients with AHI≥30. Hospital Anxiety Depression Test (HADT) was applied to all cases.*

RESULTS: *56.7% of the patients participating to the study were male and the remaining 43.3% of the patients were female. The mean age was 48.54±10.59. Control group the mean body mass index (BMI) was 30.11±4.84, patient group the mean BMI was 31.97±5.10. There was no statistically significant correlation between the depression and anxiety scores and AHI scores of the control and patient groups.*

CONCLUSION: *We used the HAD scale to evaluate excessive daytime sleepiness and the concurrence with depression and also to determine whether a correlation was present between the apnea-hypopnea index values and HAS scores in these patients in this study.*

Key words: *sleep apnea syndrome; anxiety; depression*

ÖZET

AMAÇ: *Uyku Apne Sendromu (UAS), toplumda yaygın olarak görülen bir hastalıktır. UAS'lu hastalarda, depresyon ve anksiyete birlikteliğini değerlendirmek farklı ölçeklerin kullanıldığı çalışmalar olmakla birlikte bu konuyla alakalı çelişkili sonuçlar bulunmaktadır. Bu çalışmamızda amaç UAS ile anksiyete ve depresyon korelasyonunu araştırmaktır.*

YÖNTEM: *Çalışmaya polisomnografik inceleme yapılan 134 olgu alındı. Apne-Hipopne İndeksi (AHİ) <5 olan 51 olgu kontrol grubu, AHİ ≥5 olan 83 olgu hasta grubu olarak oluşturuldu. Hasta grubu üç grup şeklinde sınıflandırıldı. 1) AHİ 5–14,9 olan 27 olgu hafif UAS; 2) AHİ: 15–29.9 olan 24 olgu orta düzey UAS; 3) AHİ ≥30 olan 32 olgu ağır UAS idi. Tüm hastalara, Hastane Anksiyete ve Depresyon ölçeği uygulandı.*

BULGULAR: *Çalışmaya dahil edilen hastaların 76 (%56,7)'si erkek, 58 (43,3)'ü ise kadındı. Hastaların yaş ortalaması 48,54±10,59 idi. HAD ölçeğinde kesme puanına göre depresyon tanısı alan olgu sayısı kontrol grubunda 18 (%35,29), hasta grubunda 30 (%36,14) kişiydi. Hasta grubunun alt grupları değerlendirildiğinde, Hafif UAS'de 10 (%37,03), Orta UAS'de 9 (%37,50), Ağır UAS'de 11 (%34,37) olgu olarak bulundu. Kesme puanına göre anksiyete tanısı alan olgu sayısı kontrol grubunda 19 (%37,25), hasta grubunda 27 (%32,53) kişiydi. Hasta grubunun alt grupları değerlendirildiğinde hafif UAS 9 (%33,33), orta UAS 8 (%33,33), ağır UAS 10 (%31,25) olarak bulundu. Kontrol ve hasta grubunun anksiyete ve depresyon skorları ile AHİ karşılaştırıldığında istatistiksel olarak anlamlı korelasyon yoktu (p>0,05).*

SONUÇ: *Çalışmamızda; HAD ölçeği kullanılarak gündüz aşırı uykululuğu, tanıklı apnesi ve horlaması olan hastalarda anksiyete ve depresyon birlikteliğini değerlendirmeyi ve bunun yanı sıra bu hastalarda apne-hipopne endeksi değerleri ile HAD puanlarının arasında korelasyonun olup olmadığını belirlemeyi amaçladık.*

Anahtar kelimeler: *uyku apne sendromu; anksiyete; depresyon*

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Introduction

Excessive daytime sleepiness, witnessed apnea and snoring generally suggest two kinds of disorders known as the sleep apnea syndrome (SAS) and the obesity-hyperventilation syndrome[1]. SAS is a common disorder in the population. There are three types named central, obstructive, and mixed and the obstructive type is the most common. Obstructive sleep apnea syndrome (OSAS) is characterized by full (apnea) or partial (hypopnea) upper respiratory tract obstruction attacks and arterial oxygen desaturation during sleep[2]. Central sleep apnea syndrome (CSAS) is characterized by the failure of the respiratory center to send commands to the respiratory muscles during sleep. There is no respiratory effort or intrathoracic change in CSAS in contrast to OSAS. The chest and abdominal movements also stop together with the respiration[3,4]. The airflow is interrupted without respiratory effort at first but this is followed by upper respiratory tract obstruction in mixed apnea. The prevalence of obstructive sleep apnea (OSAS) is 4% in adult males and 2% in adult females[5].

The Obesity-Hypoventilation syndrome is defined as excessive daytime sleepiness and hypoventilation that cause hypercapnia without any other neurological, muscular, mechanic or metabolic cause, generally in patients with a BMI ≥30. OSAS is also present in 90% of these patients[1].

Sleep continuity is disturbed, the superficial sleep duration increases and deep sleep duration decreases in these patients with complaints of excessive daytime sleepiness, witnessed apnea and snoring. These changes in sleep duration lead to neuropsychiatric symptoms such as excessive daytime sleepiness, tiring easily, psychomotor slowness, perception disturbances, forgetfulness, attention deficit, concentration problems, decreased interest, decreased work performance, and sexual problems[6–8].

Some studies have reported depression and decreased quality of life in SAS patients[9]. Depression is the most common mood disorder associated with SAS but most studies have found no such correlation[10]. There is no consensus on whether SAS causes mental changes or psychiatric disorders[11]. Some special scales are used to evaluate mood disorders in SAS patients[12]. The most commonly used scales for this purpose are the Beck Anxiety and Depression Scale and the Hospital Anxiety and Depression Scale (HAD).

We used the HAD scale to evaluate excessive daytime sleepiness and the concurrence with depression and also to determine whether a correlation was present between the apnea-hypopnea index values and HAS scores in these patients in this study.

Materials and Method

We included a total of 134 patients older than 16 years who had presented between June 2009 and July 2010 with one or more of the snoring, excessive daytime sleepiness or relative-reported apnea symptoms, had undergone Polysomnography (PSG), and had fully completed the HAD scale. Permission was obtained from the Harran University Faculty of Medicine Ethics Committee and all patients provided informed consent. Patients who suffered from a chronic pulmonary disorder such as asthma, any disorder that could affect cognitive functions such as bipolar disorder, mental retardation and schizophrenia, or who used any medication that would affect the sleep rhythm were excluded from the study. The Epworth sleep scale score was ≥9 in all patients[13].

The patients were administered the Hospital Anxiety and Depression Scale (HAD) in outpatient conditions before the PSG test. HAD is a four-item Likert-type scale developed by Zigmond and Snaith to determine the anxiety and depression risk of the patient and to measure the level and change in severity[14]. It contains a total of 14 questions with single numbers representing anxiety and even numbers depression. The patients respond by making marks on the scale. The scoring for items 1, 3, 5, 6, 8, 10, 11, 13 is in the form of 3, 2, 1, 0. Items 2, 4, 7, 9, 12, 14 are scored as 0, 1, 2, 3. The Turkish validity and reliability study for the scale has been conducted by Aydemir et al and the scale has been shown to be reliable when screening for depression and anxiety signs in those with a physical disorder[15]. Subscales for anxiety (HAD-A) and depression (HAD-D) are also present. The Turkish study has provided a cutoff point of 10/11 for the anxiety subscale and 7/8 for the depression subscale. Accordingly, patients with higher scores are considered at risk. The lowest score from either scale is 0 and the highest 21.

Our patients were followed up through the night with the Nihon Kohden polysomnography device. The acquired data were analyzed with the Polysmith V 5.0 software. The EEG records during PSG were obtained with four electrodes placed according to the international 10-20 system (C3/A2-C4/A1-O1/A2-O2/

A1). Right and left electrooculography, jaw electromyography and electrocardiography (ECG) were performed. Airflow was monitored with a nasal pressure cannula. Respiratory movements were evaluated with thoracic and abdominal belt measurements. Snoring was recorded with a snoring sensor. Sleep oxygen saturation was measured continuously with pulse oximetry. PSG recording was according to the the American Academy of Sleep Medicine sleep scoring (AASM) standard criteria[16].

The lack of airflow in the mouth and nose for 10 seconds or more following the sleep analyses was defined as apnea. A decrease of more than 30% in the nasal cannula amplitude compared to the baseline or a decrease of more than 4% in saturation for 10 seconds or more compared to the pre-event baseline was defined as hypopnea. The total number of apnea and hypopnea episodes per sleep hour was defined as the Apnea-Hypopnea Index (AHI)[16].

The patients were divided into 2 groups according to their AHI. The 51 cases with AHI <5 made up Group 1 and the 83 cases with AHI ≥5 made up Group 2. Group 2 was subdivided according to the AHI index as follows: The 27 cases with AHI: 5–14.9 were in the Mild group, the 24 cases with AHI: 15–29.9 were in the Moderate group and the 32 cases with AHI: ≥30 were in the Severe Group.

All data were analyzed using the SPSS Version 11.0 (SPSS Inc. Chicago USA) computer software. The arithmetic mean and standard deviation (X±SD) were calculated. The significance of the difference between group means was compared with Student's t test and One-Way ANOVA. The relationship between the parameters was evaluated with Pearson's correlation analysis and a p value >0.05 was considered statistically significant.

Results

The 134 patients included in the study consisted of 76 (56.7%) males and 58 (43.3%) females. Table 1 presents the distribution of the groups by gender, age and body mass index (BMI). There was no significant difference between Group 1 and 2 regarding mean age, BMI, smoking, and alcohol use.

Table 2 presents the comparison of the anxiety and depression scores of the groups. The anxiety and depression scores were lower in Group 2 and its subgroups. However, there was no statistically significant difference.

The number of cases diagnosed with depression according to the cutoff score in the HAD scale was 18 (35.29%) in Group 1 and 30 (36.14%) in Group 2. Evaluation of Group 2 subgroups revealed depression in 10 mild (37.03%), 9 moderate (37.50) and 11 severe (34.37%) cases. The number of cases diagnosed with anxiety according to the cutoff score was 19 (37.25%) in Group 1 and 27 (32.53%) in Group 2. Evaluation of the subgroups revealed anxiety in 9 mild (33.33%),

Table 1. *Demographic features of the groups*

	Group 1 (51) Mean±SD	Group 2 mild (N=27) Mean±SD	Group 2 moderate (N=24) Mean±SD	Group 3 severe (N=32) Mean±SD	p
Gender (M/F)	28/23	15/12	12/12	21/11	0.659
Age (years)	45.41±11.72	46.07±11.98	48.91±10.05	50.34±9.63	0.532
BMI (Kg/m^2)	30.11±4.84	30.88±4.03	31.50±3.59	33.25±6.53	0.498

SD, standard deviation.

Table 2. *Comparison of the anxiety and depression scores between groups*

	Group 1 (N=51) Mean±SD	Group 2 mild (N=27) Mean±SD	Group 2 moderate (N=24) Mean±SD	Group 3 severe (N=32) Mean±SD
Anxiety score	7.66±3.92	6.14±4.02 (p=0.416)	6.50±4.31 (p=0.669)	6.34±4.49 (p=0.492)
Depression score	7.43±3.71	6.66±3.29 (p=0.784)	6.54±2.43 (p=0.720)	6.53±3.67 (p=0.649)

8 moderate (33.33%) and 10 severe (%31.25) SAS cases. There was no statistically significant correlation between the anxiety and depression score and the AHI values of the control and patient groups (p>0.05) (Table 3).

Table 3. *Correlation analysis of SAS severity and anxiety and depression in the groups.*

	Depression r / p	Anxiety r / p
Group 1	0.031 / 0.829	-0.13 / 0.926
Group 2 Mild	0.306 / 0.120	0.312 / 0.113
Group 2 Moderate	0.019 / 0.931	0.149 / 0. 487
Group 3 Severe	0.230 / 0.205	-0.202 / 0.268

Discussion

We did not find a statistically significant correlation between the Apnea-hypopnea index and anxiety and depression scores in patients with symptoms of excessive daytime sleepiness, witnessed apnea and snoring in our study. Several studies have used various scales in various regions to evaluate the concurrence of depression and anxiety in patient groups. Most of these studies have been conducted with SAS patients with symptoms of excessive daytime sleepiness, witnessed apnea and snoring who had AHI values over 5 on polysomnography.

Guilleminault et al. have reported high depression scores in sleep apnea patients in their 1977 study[17]. Many later studies have found a positive correlation between the severity of SAS and the intensity of depression and anxiety. Schwartz et al. have found depression in 41% of their SAS patients and have started antidepressant treatment in 39%[18]. Another study evaluating the relationship between quality of life and depression has found worse quality of life in severe SAS patients and depression in half of this group[19]. Aloia et al. have reported that SAS patients suffer from a constant desire to sleep, depression and attention deficit due to the apnea, hypopnea and leg movements[20]. Similarly, Pillar et al. found a higher rate of anxiety and depression in female patients with severe SAS compared to those with mild SAS but they stated that this result was due more to sleeplessness than SAS. They also found that the SAS severity was not correlated with the presence of depression and anxiety in male SAS patients[11]. A study from our country reported interesting results: the lowest depression scores were found in SAS patients and there was a negative correlation between SAS severity and the depression score. The study showed that severe SAS was associated with a low anxiety score. Fidan et al. have associated these results with the effect on the cognitive functions of the patients[21].

There are also some studies stating no relationship between SAS and anxiety and depression as in our study. In other words, many studies have stated that the relationship between SAS and depression is not significant or present except for a few studies reporting their concurrence. Bliwise et al did not find a significant relationship between SAS and depression in their study on 336 subjects[22]. Cassel et al believe that the notion of a relationship between SAS and psychiatric disorders is due to misinterpretation. They have stated that the survey type used could affect the result[23]. Millman et al. found no relationship between the severity of the disorder and the depression score but 45% of SAS patients complained of depression[24]. They also found no relationship between SAS severity and psychological signs in their other study evaluating the relationship between SAS and psychological disorder severity[25]. Two recent studies have found no correlation between anxiety and depression severity in SAS patients[26,27].

There are only a few studies associating SAS and anxiety. Yue et al. have found high anxiety and depression scores in SAS and have suggested that this could be associated with the severely disturbed sleep[28]. Another study found that SAS can cause severe daytime sleepiness due to sleep deprivation, leading to decreased quality of life and increased anxiety and depression in future years[29]. Similarly, Platon and Sierra have reported a weak relationship between SAS and anxiety[30].

Several pathophysiological mechanisms have been suggested to explain the development of depression and anxiety in SAS patients with symptoms of apnea, snoring and excessive daytime sleepiness. The limbic system that contains important neuroanatomical structures such as the thalamus, hypothalamus, hippocampus, pineal gland, the pituitary and amygdala is an important region among the subcortical structures of the brain and is responsible for memory and changes in mood. The amygdala, one of the limbic structures, is a neuroanatomical structure with the most important

role in fear and anxiety development. The lateral hypothalamus, the dorsomedial vagus nucleus, nucleus ambiguus, the parabrachial nucleus, the ventral tegmental area, locus ceruleus, pedinculopontine nucleus, nucleus reticularis and the hypothalamic paraventricular nucleus that have neuronal connections with the amygdala are the main neuroanatomical structures with a role in the development of normal and pathological anxiety signs[31,32]. The depression and anxiety that can develop in the obesity-hypoventilation syndrome can be explained with similar mechanisms. The intermittent hypoxia and the oxygen desaturation that patients with sleep respiration disorders suffer can cause neuronal damage that can result in excessive daytime sleepiness. Subcortical white matter intensity increases indicating advanced damage in the brain parenchyma and especially the structures mentioned above have been found in patients with severe SAS. It is possible that this is correlated with neuropsychological and depression-related scores[20].

Many postmortem and neurological imaging studies also indicate prefrontal cortex and hippocampus atrophy and neuronal loss in patients suffering from anxiety and depression[33]. A model that associates the interrupted sleep and intermittent hypoxemia in SAS patients with prefrontal cortex dysfunction has recently been suggested. This model states that the prefrontal region becomes functional during sleep and is especially sensitive to sleep interruption and that hypoxemia creates a cellular environment that is not conducive for repair processes to take place. This model also postulates that the interruption of sleep and intermittent hypoxemia decrease the efficacy of the sleep-connected repair processes. These changes result in disturbed functional hemostasis in the central nervous system and a change in the survival times of the neurons and glial cells in some parts of the brain[17].

Our study has several limitations. We did not perform capnographic evaluation in Group 1 patients although they had excessive daytime sleepiness, witnessed apnea and snoring and a mean BMI of 30.11 kg/m^2. We therefore felt that the most probable diagnosis was the obesity-hypoventilation syndrome as they were symptomatic and the BMI value was high, even though the AHI index was ≤5. It would also have been more appropriate to use patients with no symptoms and an AHI index ≤5 with PSG in the control group.

In conclusion, we feel studies on larger patient populations that also include non-symptomatic healthy individuals and that take into account all additional risk factors should be conducted although we did not find a statistically significant difference between the patient groups' anxiety and depression values.

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