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Comparison of the Frequency of Fibromyalgia Syndrome Between Those with and without Obstructive Sleep Apnea Syndrome

Obstrüktif Uyku Apne Sendromu Tanısı Olanlar ile Olmayanlar Arasında Fibromiyalji Sendromu Sıklığının Karşılaştırılması

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ABSTRACT Objective: Sleep disturbance plays an important role in the etiopathogenesis of fibromyalgia syndrome (FMS). This study aimed to compare the frequency of FMS between those with and without obstructive sleep apnea syndrome (OSAS). In addition, it was aimed to examine the relationship between polysomnography parameters and FMS. **Materials and Methods:** Twenty participants with OSAS (OSAS group) and 20 participants without OSAS (control group) were included in the study. All participants were evaluated for FMS diagnosis using the American College of Rheumatology FMS criteria. The chronic widespread pain levels of all participants were evaluated by the Numerical Rating Scale (NRS), their depression levels were evaluated by the Beck Depression Inventory (BDI), and their anxiety levels were evaluated by the Beck Anxiety Inventory (BAI). **Results:** The number of patients diagnosed with FMS, chronic widespread pain NRS levels, BAI scores, and chronic pain durations of the patients in the OSAS group were found to be significantly higher than in the control group. BDI scores of both groups were similar. Among the patients in the OSAS group, no significant difference was detected in terms of polysomnography parameters between patients with FMS and patients without FMS. **Conclusion:** In this study, the frequency of FMS in patients with OSAS was higher than in those without OSAS. This association should be kept in mind when evaluating patients with FMS and OSAS. In addition, in this study, it was determined that the presence of FMS did not affect the polysomnography parameters of patients with OSAS.

ÖZET Amaç: Uyku bozukluğunun, fibromiyalji sendromunun (FMS) etyopatogenezinde önemli rol aldığı bildirilmiştir. Bu çalışmada uyku bozukluğu ile karakterize bir hastalık olan obstrüktif uyku apne sendromu (OUAS) olan ve olmayan hastalarda, FMS sıklığının belirlenmesi amaçlanmıştır. Ayrıca polisomnografi parametrelerinin FMS ile ilişkinin incelenmesi amaçlanmıştır. **Gereç ve Yöntem:** Çalışmaya 20 OUAS'lı katılımcı (OUAS grubu) ile OUAS'ı olmayan 20 katılımcı (kontrol grubu) dahil edildi. Tüm katılımcılar Amerika Romatoloji Cemiyeti FMS kriterleri ile FMS tanısı açısından değerlendirildi. Tüm katılımcıların kronik yaygın ağrıları, Sayısal Derecelendirme Ölçeği ile; depresyon düzeyleri Beck Depresyon Envanteri (BDE) ile; anksiyete düzeyleri Beck Anksiyete Envanteri (BAE) ile değerlendirildi. OUAS'lı hastaların polisomnografi parametreleri kaydededildi. **Bulgular:** İki grup yaş, cinsiyet ve vücut kitle indeksi gibi demografik veriler açısından benzerdi. OUAS grubunda FMS tanılı hasta sayısı, hastaların kronik yaygın ağrı Sayısal Derecelendirme Ölçeği düzeyi, BAE skoru, kronik ağrı süresi kontrol grubuna göre anlamlı olarak daha yüksek olarak tespit edildi. Her iki grubun BDE skorları benzerdi. OUAS grubundaki hastalardan FMS'li hastalar ile FMS tanısı olmayan hastalar arasında polisomnografi parametreleri açısından anlamlı bir fark testpit edilmedi. **Sonuç:** Bu çalışmada OUAS'lı hastalardaki FMS sıklığı OUAS'ı olmayanlara göre daha yüksekti. FMS'li ve OUAS'lı hastaları değerlendirirken bu birliktelik akılda tutulmalıdır. Ayrıca bu çalışmada FMS varlığının OUAS'lı hastaların polisomnografi parameterlerini etkilemediği tespit edilmiştir.

Keywords: Obstructive sleep apnea; fibromyalgia; pain; sleep

Anahtar Kelimeler: Obstrüktif uyku apnesi; fibromiyalji; ağrı; uyku

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Fibromyalgia syndrome (FMS) is a disease that presents with sleep problems, fatigue, and chronic widespread pain. Mood disorders, cognitive dysfunction, joint stiffness, and muscle stiffness are other common symptoms observed in FMS.[1]

Obstructive sleep apnea syndrome (OSAS) is defined by more than five complete or partial upper airway obstructions per hour, leading to airway obstruction (apnea) or reduction (hypopnea) during sleep. Symptoms such as anxiety, depression, learning deficit, cognitive disorder, and excessive daytime sleepiness are observed.[2]

The pathophysiology of FMS has not been fully elucidated. Sleep disturbances are among the symptoms of FMS. But recently, the hypothesis has emerged that sleep disturbance is among its causal factors rather than a consequence of FMS.[1,3,4] Studies in healthy individuals have found that sleep deprivation leads to spontaneous pain, hyperalgesia, and mood changes, particularly an increased incidence of depression and anxiety.[1,5,6] In another study, it was reported that sleep discontinuity was more effective than sleep deprivation in the occurrence and exacerbation of psychiatric and somatic symptoms.[7]

Data revealing the relationship between OSAS, a disease that has common symptoms with FMS and causes sleep disturbance, and FMS are insufficient. This study aimed to compare those with and without OSAS in terms of FMS frequency. In addition, the secondary aim of this study is to examine the relationship between polysomnography (PSG) findings and FMS.

MATERIAL AND METHODS

The study was carried out at Kırşehir Ahi Evran University Faculty of Medicine, Department of Physical Medicine and Rehabilitation and Department of Chest Disease.

Twenty OSAS patients with OSAS symptoms for at least one year were consecutively included in the study. Polysomnographic recording was done overnight with the Philips Respironics Polysomnography device (1001 Murry Ridge Lane Murrysville, PA 15668 USA Respironics Deutschland Gewerbestrasse 17 82211 Herrsching, Germany). Patients with an apnea-hypopnea index (AHI)≥5/hour were diagnosed with OSAS.[8] The PSG included body position, thoracic and abdominal respiratory movements, finger pulse oximetry, nasal pressure transducer, oronasal thermistor, snoring, chin and leg electromyography, electro-oculogram, electroencephalogram, and electrocardiography. ≥30/hr AHI was considered severe, 15-30/hr AHI moderate, and 5-15/hr AHI mild OSAS.[8] Periodic leg movement (PLM) index score, the AHI score, mean oxyhemoglobin saturation levels, sleep efficiency, sleep latency times, rapid eye movement (REM) times, non-REM times, and non-REM Stage 3 times measured by PSG in patients with OSAS were recorded. Twenty individuals without OSAS symptoms or diagnosis were consecutively included in the control group. Participants in the control group were also interviewed with their bed partners and evaluated in terms of minor and major symptoms of OSAS. Individuals with OSAS symptoms were excluded from the control group. Recipients of anticonvulsive, antidepressants, or opioid analgesics within 2 weeks before evaluation were excluded in both the control group and the OSAS group. In addition, those who took nonsteroidal anti-inflammatory drugs in the 24 hours before the evaluation, those with chronic heart, kidney, lung, and thyroid diseases, and those with collagen tissue disease, infection, or inflammatory disorders that may cause pain were also excluded from the study in both groups.

Demographic information such as the age, height, weight, and gender of the patients was recorded. In addition, the number of FMS tender points of the patients and the duration of their current chronic pain were recorded in years. The level of chronic widespread pain in all patients in the last month was evaluated with a Numerical Rating Scale (NRS), anxiety levels were evaluated by Beck Anxiety Inventory (BAI), and depression status was evaluated by Beck Depression Inventory (BDI).[9-11] BDI is a scale consisting of 21 questions. It is used to assess the level of depression of individuals. A higher score indicates more severe depression.[11] BAI assesses participants' anxiety levels. It consists of 21 items. A high score means high anxiety.[10] Turkish validity and reliability of all these scales have been demonstrated.[12-14] All participants were evaluated

by the same physiatrist for the diagnosis of FMS with the 2016 American College of Rheumatology criteria.

The protocol was approved by the ethics committee of Kırşehir Ahi Evran University Faculty of Medicine (date: February 11, 2020, no: 2020-02/13) and performed in accordance with the ethical standards of the 1975 Declaration of Helsinki. All participants gave written informed consent after a comprehensive explanation of the relevant procedures was provided.

STATISTICAL ANALYSIS

Statistical analyzes of the study were performed with the SPSS version 21.0 software for Windows (IBM Corp., USA). Data were expressed as percentage, standard deviation, and mean. Normality assumption was tested using the Shapiro-Wilk and the Kolmogorov-Smirnov tests. The Chi-square test and the Fisher's exact test were used to compare qualitative data. Group means were compared with the Student's t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. $p<0.05$ was considered statistically significant. G-power 3.19.4 (Version 3.1.9.6; Universitat Kiel, Germany) was performed for post hoc power analysis. For both groups with 20 patients in each group with 9/20 prevalence in OSAS group and 1/20 FMS prevalence in the control group with odds ratio: 9.0; 81.3% power ratio was obtained at $\alpha=0.05$ level.

RESULTS

Forty-five individuals were evaluated for eligibility for the study. Five participants were excluded because they met the exclusion criteria. As a result, the study was carried out with 40 participants (20 in OSAS group, 20 in control group). Both groups were similar in terms of gender, age, and body mass index. The number of patients diagnosed with FMS in the OSAS group, general body pain NRS levels, BAI scores, and chronic pain durations were found to be significantly higher than in the control group (Table 1).

When the patients in the OSAS group were divided into two separate subgroups, with and without FMS, there was no significant difference between the two subgroups in terms of PSG parameters (Table 2).

The possible factors that may increase the risk of FMS in OSAS patients were analyzed using binary logistic regression. PSG parameters and stage of OSAS were not associated with the risk of FMS in the OSAS group ($p>0.5$) (Table 3). BAI and BDI were also not associated with an increase in the risk of FMS in OSAS patients ($p>0.05$) (Table 4).

DISCUSSION

In this study, the number of patients diagnosed with FMS, anxiety levels, duration, and levels of chronic pain were found to be higher in patients with OSAS than in patients without OSAS.

TABLE 1: Comparisons of clinical and demographic data of control and OSAS groups.

	OSAS n=20 $\bar{X}$±SD	Control n=20 $\bar{X}$±SD	p value
Age	53.3±10.9	50.75±9.6	0.436[a]
BMI	31.6±3.9	30.3±3.6	0.267[a]
Male	16 (80%)	16 (80%)	1.000[b]
Female	4 (20%)	4 (20%)	
Chronic widespread pain NRS	3.3±3.0	0.6±2.0	0.002[a]
Beck Anxiety Inventory	22.9±16.6	9.9±8.5	**0.004[a]**
Number of tender points	7.6±7.6	2.1±3.7	0.063[c]
Beck Depression Inventory	11.4±12.6	11.5±7.7	0.336[c]
Chronic pain duration	4.8±7.2	0.6±2.2	**0.002[c]**
Number of patients diagnosed with FMS	9 (45%)	1 (5%)	**0.003[d]**

[a]Student t-test; [b]Fisher's exact test; [c]Mann-Whitney U test; [d]Chi-square test; OSAS: Obstructive sleep apnea syndrome; SD: Standard deviation; BMI: Body mass index; NRS: Numerical Rating Scale; FMS: Fibromyalgia syndrome.

TABLE 2: Comparisons of clinical and demographic data of control and OSAS groups.

	With FMS n=9 $\bar{X}$±SD	Without FMS n=11 $\bar{X}$±SD	p value[a]
PLM index	45.1±27.6	34.1±16.7	0.305
Apnea-hypopnea index	51.0±31.8	27.9±23.7	0.087
Mean oxyhemoglobin saturation	93.0±3.1	93.8±1.8	0.756
Sleep efficiency	83.2±11.7	77.3±11.3	0.095
Sleep latency	9.4±9.3	18.8±18.7	0.137
REM time	25.1±20.7	24.0±14.5	0.761
Non-REM time	336.5±48.4	297.8±68.3	0.080
Non-REM Stage 3 time	67.2±37.8	75.3±44.6	0.761

[a]Mann-Whitney U test; OSAS: obstructive sleep apnea syndrome; FMS: Fibromyalgia syndrome; SD: Standard deviation; PLM: Periodic leg movement; REM: Rapid eye movement.

TABLE 3: Logistic regression analysis of polysomnography parameters with increased risk of FMS in OSAS patients.

	B	SE	Wald	df	p value	Exp(B)	95% Confidence interval
PLM index	0.027	0.047	0.325	1	0.569	1.027	0.937-1.126
Apnea-hypopnea index	-0.088	0.095	0.855	1	0.355	0.916	0.761-1.103
Mean oxyhemoglobin saturation	-0.726	0.580	1.567	1	0.211	0.484	0.155-1.507
Sleep efficiency	-0.009	0.081	0.014	1	0.907	0.991	0.845-1.162
Sleep latency	0.022	0.077	0.080	1	0.777	1.022	0.879-1.18
REM latency	-0.017	0.011	2.352	1	0.125	0.983	0.962-1.005
REM time	-0.016	0.058	0.081	1	0.776	0.984	0.879-1.101
Non-REM time	-0.004	0.015	0.056	1	0.813	0.996	0.967-1.027
Non-REM Stage 3 time	0.021	0.031	0.454	1	0.501	1.021	0.961-1.086
Stage of OSAS	0.203	2.149	0.009	1	0.925	1.225	0.018-82.686
Constant	72.302	55.127	1.720	1	0.190	2.511	

FMS: Fibromyalgia syndrome; OSAS: Obstructive sleep apnea syndrome; SE: Standard error; df: Degree of freedom; PLM: Periodic leg movement; REM: Rapid eye movement.

TABLE 4: Logistic regression analysis of BAI and BDI scores with increased risk of fibromyalgia syndrome in OSAS patients.

	B	SE	Wald	df	p value	Exp(B)	95% Confidence interval
BAI	0.064	0.053	1.458	1	0.227	1.066	0.961-1.181
BDI	0.051	0.085	0.369	1	0.544	1.053	0.892-1.243
Constant	-2.082	1.041	4.000	1	0.56	0.125	

BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; OSAS: Obstructive sleep apnea syndrome; SE: Standard error; df: Degree of freedom.

In the study of Terzi and Yılmaz, the myalgic score measured by pressure algometry (dolorimetry) in patients with OSAS was significantly higher than the control group.[15] Similarly, widespread pain levels were found to be higher in the OSAS group compared to the control group in the current study. Not using an algometer for pain measurement is one of the limitations of the current study, but comparing the frequency of FMS diagnosis and considering PSG parameters are the strengths of this study. In their study, Atan and Atan divided the patients with FMS into two groups as those with OSAS and those with simple snoring. They found that the fibromyalgia impact questionnaire (FIQ) values of the simple snoring group were higher than the group with OSAS. They also found that there was no significant relationship between PSG parameters and FIQ.[16] Similarly, in the present study, no significant relationship was found

between the presence of FMS and PSG parameters. However, unlike the study of Atan and Atan, the participants in the present study were not only patients with FMS. The purpose and design of this study were different. The current study aimed to determine whether OSAS increases the frequency of FMS by comparing the frequency of FMS between patients with OSAS and patients without OSAS.[16]

Yildirim and Alp found that patients with OSAS+FMS had higher malondialdehyde (an oxidative stress marker) levels and lower antioxidative parameters (glutathione peroxidase, catalase, and superoxide dismutase) compared to those with only OSAS and the control group.[17] Altıntop Geçkil and Aydoğan Baykara divided female OSAS patients into two groups, with and without FMS. PLMs, desaturation index (CT90), and sleep latency were found to be higher in the group with FMS compared to the group without FMS.[18] The study of Altıntop Geçkil and Aydoğan Baykara and Yildirim and Alp are useful studies in determining the effects of FMS on patients with OSAS, but they were not designed to answer the question of whether OSAS increases the frequency of FMS.[17,18] Köseoğlu et al. performed PSG examination on patients with FMS and found that 50% of the patients had OSAS.[19] Çetin et al. performed PSG examination on patients with FMS and healthy volunteers without FMS. They found OSAS at a rate of 36% in patients with FMS. In addition, PSG examinations revealed less N1 sleep, higher AHI, higher arousal index, more arousal, and more awakening in patients with FMS than in healthy controls.[20] According to the literature review by the authors on the relationship between OSAS and FMS, there are many studies investigating the frequency of OSAS in patients with FMS or investigating the effect of FMS in patients with OSAS, as the examples given above. However, the literature is quite insufficient to reveal whether OSAS increases the frequency of FMS. Although the prevalence of FMS in the general population is 0.5% in men and 3.4% in women, Marvisi et al. found that 15% of 900 OSAS patients, mostly men, met the FMS criteria. There was no control group in their study.[21] Unlike this study, the frequency of FMS in patients with OSAS was compared with the control group without OSAS in the current study. In the current study, the frequency of FMS was found to be 45% in patients with OSAS and it was found to be significantly higher than in the control group. The difference in the results of these two studies may be due to the differences in the evaluation criteria of the studies and the differences in the cultural, clinical, and demographic parameters of the study populations.

FMS is a syndrome characterized by widespread body pain, cognitive disorders, mood changes, fatigue, and sleep disturbances. Its prevalence has been reported as 0.5%-5%.[22] The etiology and pathogenesis of FMS are not clear. It is controversial whether sleep disturbance, which is common in FMS, is a consequence of the disease or a causal factor.[23] In the study of Moldofsky et al., one of the first studies on this subject, it was shown that individuals with fibrositis (the terminology used in the past for FMS) had sleep disorders and that the same symptoms could be induced in healthy individuals who were deprived of sleep. In addition, the "non-restorative sleep syndrome" hypothesis has been put forward for FMS.[24] Subsequent studies have found that improving sleep quality can improve FMS fatigue and pain.[23,25] Current data on this subject support a bidirectional relationship between FMS and sleep disorder, but it has been reported that sleep disorder begins before pain.[1,23] It has been reported that sleep deprivation in healthy individuals leads to mood changes and hyperalgesia.[5] Smith et al. claimed that this effect is related to sleep continuity disorder rather than sleep deprivation.[7] It has been reported that sleep disruption and sleep discontinuity are more frequent and associated with pain in FMS.[26] It has also been shown that poor quality sleep and sleep deprivation can lead to hyperalgesia by increasing the sensitivity of peripheral nociceptors by increasing interleukin (IL)-6.[5] IL-6 is one of the mediators associated with FMS.[27] In addition, a decrease in growth hormone occurs as a result of sleep fragmentation in OSAS.[28] Decreased growth hormone is also one of the factors held responsible for FMS.[29] All these mechanisms may explain the positive relationship between OSAS and FMS in the results of the current study. Because OSAS is characterized by sleep interruptions, sleep deprivation, and poor quality sleep as a result of recurrent upper airway obstructions during sleep.[15,30]

The small number of patients and the lack of pain measurement with an algometer are the limitations of this study. However, comparison with a control group without OSAS to show the frequency of FMS in patients with OSAS is one of the strengths of this study.

CONCLUSION

In this study, the frequency of FMS in patients with OSAS was found to be higher than in those without OSAS. This association should be kept in mind when evaluating patients with OSAS and FMS. In addition, it was determined in the study that FMS did not contribute independently to the PSG parameters of patients with OSAS. Further studies with larger sample sizes are needed on this subject.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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