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ORIGINAL ARTICLE

Is There a Link Between Obstructive Sleep Apnea Syndrome and Fibromyalgia Syndrome?

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Abstract

OBJECTIVES: Fibromyalgia syndrome (FMS) is characterized by complaints of chronic musculoskeletal pain, fatigue, and difficulty in falling asleep. Obstructive sleep apnea syndrome (OSAS) is associated with symptoms, such as morning fatigueness and unrefreshing sleep. We aimed to investigate the presence of OSAS and objectively demonstrate changes in sleep pattern in patients with FMS.

MATERIAL AND METHODS: Polysomnographic investigations were performed on 24 patients with FMS. Patients were divided into two groups: patients with and without OSAS (Group 1 and Group 2, respectively). A total of 40 patients without FMS who presented to the sleep disorders polyclinic with an initial diagnosis of OSAS were included in Group 3. Based on their apnea hypopnea index (AHI), OSAS in the patients were categorized as mild (AHI, 5-15), moderate (30), or severe (>30).

RESULTS: OSAS was detected in 50% of patients with FMS. The most prominent clinical findings were morning fatigue and sleep disorder, which were similar in three groups. In polysomnography (PSG) evaluation, patients with FMS had mild (33%), moderate (25%), and severe (42%) OSAS. In correlation analyses, negative correlations were observed between fibromyalgia impact questionnaire (FIQ) and mean oxygen saturation, visual analogue scale (VAS), and minimum oxygen saturation, whereas a positive correlation was found between FIQ and desaturation times in patients with FMS.

CONCLUSION: Detection of OSAS in 50% of the patients with FMS, and similar rates of complaints of sleep disorder and morning fatigue of OSAS and FMS cases are important results. Detection of correlation between the severity of hypoxemia and FIQ and VAS scores are significant because it signifies the contribution of increased tissue hypoxemia to the deterioration of clinical status. Diagnosis and treatment of OSAS associated with FMS are important because of their favorable contributions to the improvement of the clinical picture of FMS.

KEYWORDS: Obstructive sleep apnea syndrome, fibromyalgia syndrome, polysomnography, sleep disorders, apnea hypopnea index, hypoxemia

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INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic health problem that presents with pain all over the body, with other symptoms, such as tenderness of the affected joints, muscles fatigue, sleep problems (waking up unrefreshed and excessive daytime sleepiness), and cognitive impairment [1]. Since its etiology is not fully known, its treatment is symptomatic. Patients with FMS are usually treated with various combinations of physiotherapy, psychotherapy, psychotrophic drugs, and analgesics. Treatment effectiveness in FMS is limited, and these patients frequently lead their lives with symptoms of chronic insomnia, sleep problems, fatigue, and pain [2].

Obstructive sleep apnea syndrome (OSAS) is a pathology with systemic effects that are characterized by associated symptoms of recurrent episodes of upper respiratory tract obstruction, hypoxemia, arousals during sleep, morning fatigue because of impaired sleep quality, morning headache, unrefreshing sleep, attention defict during daytime, impaired concentration, cognitive dysfunction, and depression [3]. Because of the similarities between the symptoms of FMS and OSAS, we aimed the presence of OSAS and objectively demonstrated the changes in sleep pattern in patients with FMS in this study.

MATERIAL AND METHODS

Cases and Study Design

This was a cross-sectional study and was performed between April 2013 and June 2014. Polysomnographic evaluation was performed on 24 patients who had predominantly complained of sleep disorder and were diagnosed with FMS in

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The Clinics of Physical Therapy and Rehabilitation in our hospital. Patients with FMS were divided into two groups: patients with and without OSAS (Group 1 and Group 2, respectively). A total of 40 patients who were evaluated with the an initial diagnosis of OSAS in the clinics of sleep disorder but were found to be devoid of FMS following assessments performed in the Department of Physical Therapy and Rehabilitation were determined as the control group (Group 3). Diagnosis of FMS was based on the criteria established by The American College of Rheumatology [4]. Data related to demographic characteristics, sleep patterns, medical history, medication use, and habits were retrieved using a standardized questionnaire survey administered before the sleep study.

For evaluating pain, the visual analogue scale (VAS) was used. Pain threshold was evaluated using an algometer. The pressure algometer used in this study (JTECH, Commander™) was connected to a dial that can measure pressure in kg or libres with a round rubber pressure measurement tip in the form of a disk of 1 cm diameter. By holding the dial, the operator can apply pressure on the predetermined points. During the assessments, at the first instance of pressure pain felt by the patient, the algometer was taken away from the body, and the value displayed on the indicator was recorded. Measurements were repeated for three times, and the average of these values was taken into consideration.

Back depression scale (BDS), back anxiety scale (BAS), and fibromyalgia impact questionnaire (FIQ) forms were completed by the study groups. BDS, which consists of a total of 21 questions, was developed in the year 1967 by Beck, and it is based on the evaluation of somatic, affective, and cognitive functions of the patient. It is designed in a questionnaire form, and the patients were requested to choose the responses most suitable to their condition. Each item consists of four sentences. These sentences are listed from neutral (0 point) to the most severe state (3 points). The maximum score is 63 points [5]. According to Beck et al., depression levels were classified based on BDS scores as follows: 0-13 points, no depression; 14-19 points, mild; 20-28 points, moderate; and 29-63 points, severe depression [6]. BAS is a Likert-type assessment scale consisting of 21 items, which measures the frequency of anxiety symptoms experienced by an individual. Each item is rated between 0 and 3 points. Higher total scores indicate the severity of anxiety experienced by an individual. Its validation and reliability studies have been performed in our country [7]. Based on BAS scores, 0-17 points, 18-24 points, and ≥25 points indicate mild, moderate, and severe degrees of anxiety, respectively. FIQ was developed by Burchardt et al. to measure the functional state of patients with FMS [8]. It measures physical function, feeling oneself good, inability to go to work, feeling uneasy at work, pain, fatigueness, morning fatigueness, stiffness, anxiety, and depression. Apart from feeling oneself good, lower scores indicate recovery or mild impact of the disease on the patient. FIQ is completed by the patient and takes approximately 5 min to complete. Validation and reliability studies of FIQ have been performed [9]. This study was in compliance with the principles outlined in the Declaration of Helsinki and was approved by the Local Ethical Committee. Written informed consent was obtained from all the patients.

PSG Evaluation

Overnight PSG was performed in all patients using a 55-channel polysomnograph (Alice® Sleepware, Philips Respironics, PA, USA) and included the following variables: electrooculograms (two channels), electroencephalograms (four channels), electromyograms of the submental muscles (one channel) and anterior tibialis muscle of both legs (two channels), electrocardiograms, airflow measurements (with oronasal thermistor and nasal cannula pressure transducer), body position sensor that discerns changes in the body position during sleep, and a snore sensor for the detection of snoring vibrations. Respiratory efforts of chest and abdominal muscles (two channels) were recorded using piezoelectric belts and arterial oxyhemoglobin saturation (SaO_2: one channel) using pulse oximetry with a finger probe. The recordings were scored according to the standard criteria of American Academy of Sleep Medicine (AASM). Apnea was defined as ≥90% decrease in the air flow amplitude persisting for at least 10 s relative to the baseline amplitude. AASM has provided two definitions for hypopnea. The recommended definition is a ≥30% decrease in the air flow amplitude relative to the baseline values associated with ≥4% oxygen desaturation, all sustaining for at least 10 s. Alternative definition is expressed as ≥50% decrease in the air flow amplitude relative to the baseline values associated with a ≥3% oxygen desaturation or arousal from sleep, all sustaining for at least 10 s. In our study, hypopnea was determined according to the alternative definition [10]. Apnea hypopnea index (AHI) was calculated as the number of apneic plus hypopneic episodes per hour of sleep. Patients with AHI of ≥5 events/h were diagnosed with OSAS. Based on their AHI scores, the patients were categorized into mild (AHI, 5-15), moderate (AHI, 15-30), and severe OSAS (AHI, >30) groups according to the AASM Task Force criteria [11]. Oxygen desaturation index (ODI) was defined as the total number of measurements of oxyhemoglobin desaturation of ≥4% within ≥10 s-<3 min from the baseline divided by the total sleep time.

Statistical Analysis

Chi-square tests were used to investigate the correlations (if any) between qualitative variables. Quantitative variables were presented as arithmetic mean ± standard deviation and qualitative variables as numbers and percentages. For the difference between the groups, the independent Samples t-test was used, and for the correlation analysis, the Pearson correlation coefficient was used. Covariance analysis was used to compare the differences among the groups. For multiple comparison, the Bonferroni test was used. P values were adjusted according to age and body mass index (BMI) values. P values less than 0.05 were considered to be statistically significant. Calculations were performed using a pre-prepared statistical software (IBM SPSS Statistics 19, (IBM SPSS; IBM Co., Somers, NY, USA).

RESULTS

A total of 64 patients (females, n=28, 44% and males, n=36, 56%) were included in the study. Mean age (48.39±9.47 years) and mean BMI (48.39±9.47 kg/m^2) of all the groups were also calculated. Groups 1, 2, and 3 consisted of 12, 12, and 40 patients, respectively. A significant intergroup difference was observed in terms of gender, age, and BMI of the patients. In this study, p values were adjusted according to age and BMI values. In patients with FMS (Groups 1 and 2), higher mean VAS, tender points, FIQ, and Beck anxiety-depression scores but lower mean algometry scores were found compared with those in patients without FMS (Group 3). The most predominant clinical findings were complaints of morning fatigue and sleep disorder, which were at similar rates in the three groups. No intergroup difference was detected for additional concomitant diseases, including diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease, and goiter (p>0.05). Demographic characteristics and FMS-related symptoms are indicated in Table 1.

The groups were compared with respect to PSG findings, and longer sleep latencies were seen in Group 2 (FMS positive, OSAS negative group) (p=0.004). Stages of non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep were similar between the groups with respect to their duration and percentages (p>0.05). Mean AHI and arousal index (ARI) scores were significantly different between the three groups (p<0.001), but mean AHI and ARI were similar between Group 1 (FMS positive, OSAS positive group) and Group 3 (FMS negative, OSAS positive group). OSAS has been detected in 50% of patients with FMS. Patients with FMS had mild (33%), moderate (25%), and severe (42%) OSAS (Group 1). In Group 3 (OSAS positive, FMS negative group), mild, moderate, and severe OSAS were seen in 15%, 20%, and 65% of the patients, respectively. PSG findings of the groups are shown in v 2. PSG findings of patients with FMS were evaluated, and alpha intrusions were detected in 11 of 24 patients. These activations were seen in NREM stages 2 and 3.

In correlation analyses, negative correlation was observed in all cases between sleep latencies and algometry scores (r=-0.28, p=0.022) (Figure 1). In patients with FMS, negative

Table 1. Demographic and clinical findings of study groups

	Group 1 FMS (+) OSAS(+) (n=12)	Group 2 FMS (+) OSAS(-) (n=12)	Group 3 FMS(-) OSAS (+) (n=40)	p
Age (year)[a]	51.75±8.00[a]	39.92±8.25[b]	50.88±8.3[a]	<0.001
Gender				
Female, n (%)	9 (75)[a]	12 (100)[a]	7 (17.5)[b]	<0.001
Male, n (%)	3 (25)[a]	0 (0)[a]	33 (82.5)[b]	
BMI (kg/m^2)*	40.66±11.53[a]	28.65±5.20[b]	32.28±5.42[b]	<0.001
Chronic pain duration (year)*	6.00±4.54	2.46±2.71	2.3±5.98	0.122
VAS*	7.00±1.00[a]	7.00±1.00[a]	2.00±3.00[b]	<0.001
TP*	14.00±3.00[a]	15.00±3.00[a]	2.00±3.00[b]	<0.001
Algometry*	19.07±4.06[a]	18.28±4.96[a]	21.95±3.54[b]	0.007
FIQ*	80.19±16.22[a]	69.31±14.15[a]	25.38±23.2[b]	<0.001
BDS*	19.00±7.00[a]	20.00±12.00[a]	6.00±5.00[b]	<0.001
BAS*	19.00±7.00[a]	31.00±14.00[a]	10.00±7.00[b]	<0.001
Symptoms, n(%)				
Chronic widespread pain	10 (90.9)[a]	10 (83.3)[a]	8 (20)[b]	<0.001
Sleep disorder	11 (100)	10 (83.3)	35 (87.5)	0.401
Fatigue, weakness	11 (100)[a]	12 (100)[a]	23 (57.5)[b]	0.001
Concentration disturbance	8 (72.7)[a]	8 (66.7)[ab]	12 (30)[b]	0.009
Headache	9 (81.8)[a]	12 (100)[a]	16 (40)[b]	<0.001
Paresthesia	8 (72.7)	6 (50)	18 (45)	0.265
Stiffness	8 (72.7)[a]	10 (83.3)[a]	10 (25)[b]	<0.001
Swelling sensation	9 (81.8)[a]	10 (83.3)[a]	9 (22.5)[b]	<0.001
Morning fatigue	11 (91.6)	10 (83.3)	26 (65)	0.064

*Mean±standard deviation. FMS: fibromyalgia syndrome; BMI: Body Mass Index; VAS: visual analogue scale; TP: tender points; FIQ: fibromyalgia impact questionnaire; BDS: Back depression scale; BAS: Back anxiety scale

[a,b]Each different superscript indicates the statistical significance

Table 2. Polysomnographic findings of study groups

	Group 1 FMS (+) OSAS(+) (n=12)	Group 2 FMS (+) OSAS(-) (n=12)	Group 3 FMS(-) OSAS (+) (n=40)	p
Total sleep time (minute)	377.42±52.65	353.04±61.78	363.34±53.35	0.551
Sleep latency (minute)	15.00±11.66[a]	31.88±28.07[b]	14.88±10.32[a]	0.004
REM (minute)*	62.67±31.93	56.71±21.39	64.23±30.15	0.736
(%)	16.09±7.43	16.18±6.05	17.05±7.12	0.879
Stage 1 (minute)*	40.08±21.42	26.33±12.89	45.98±28.57	0.067
(%)	10.95±5.71	8.01±5.07	12.86±8.48	0.147
Stage 2 (minute)*	153.13±21.12	148.21±35.2	151.44±45.9	0.954
(%)	41.22±7.53	42.02±7.23	41.62±10.73	0.980
Stage 3 (minute)*	121.54±48.28	121.79±48.8	101.94±47.31	0.285
(%)	31.73±10.51	33.82±11.37	28.12±12.99	0.320
Sleep Efficiency (%)	82.13±12.1	78.06±12.19	79.07±11.03	0.646
AHI	33.86±28.93[a]	2.09±1.72[b]	43.83±26.68[a]	<0.001
ARI	36.49±22.25[a]	7.12±3.48[b]	49.57±23.65[a]	0.001
Desaturation (%)	23.15±31.87	0.16±0.33	12.82±23.53	0.062
ODI	31.43±28.41[a]	2.21±1.98[b]	38.78±32.43[a]	0.001
Minimum O_2 saturation in night (%)	73.25±14.39[a]	90.42±3.82[b]	76.45±13.48[a]	0.002
Average O_2 saturation in night (%)	91.42±5.82[a]	95.67±1.07[b]	92.25±4.07[a]	0.025
Severity of OSAS n (%)				
Mild	4 (33)	-	6 (15)	
Moderate	3 (25)	-	8 (20)	0.277
Severe	5 (42)	-	26 (65)	

*Sleep stages are given as minute and % of total sleep time. REM: Rapid Eye Movement; AHI: Apnea-Hypopnea Index; ARI: Arousal Index; ODI: oxygen desaturation index; Desaturation (%): Sleep time of SpO_2<90%

[a,b]Each different superscript indicates the statistical significance

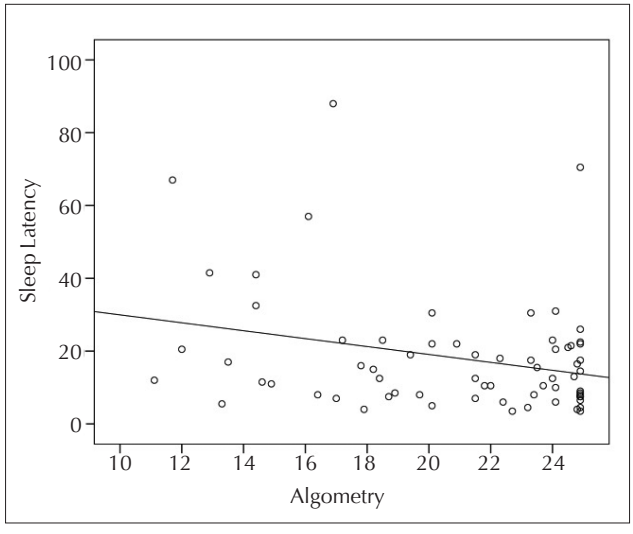

Figure 1. Correlation between sleep latency and algometry

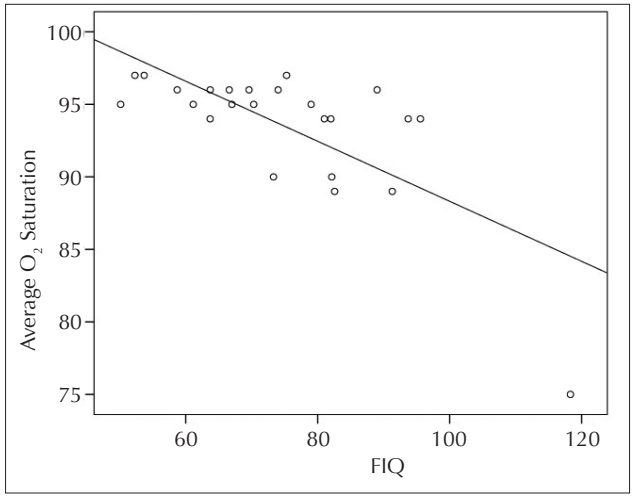

Figure 2. Correlation between average O_2 saturation and FIQ
FIQ: fibromyalgia impact questionnaire

correlations were observed in FIQ and average oxygen saturation (r=-0.71; p<0.001) (Figure 2), VAS and average oxygen saturations (r=-0.458, p=0.02), and VAS and minimum oxygen saturations (r=-0.438, p=0.032) (Figure 3), while a positive correlation was observed between FIQ and desaturation times (r=0.69, p<0.001) (Figure 4).

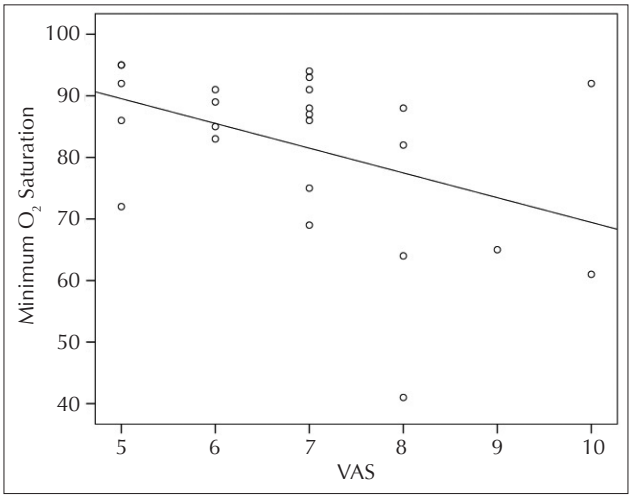

Figure 3. Correlation between minimum O_2 saturation and VAS
VAS: visual analogue scale

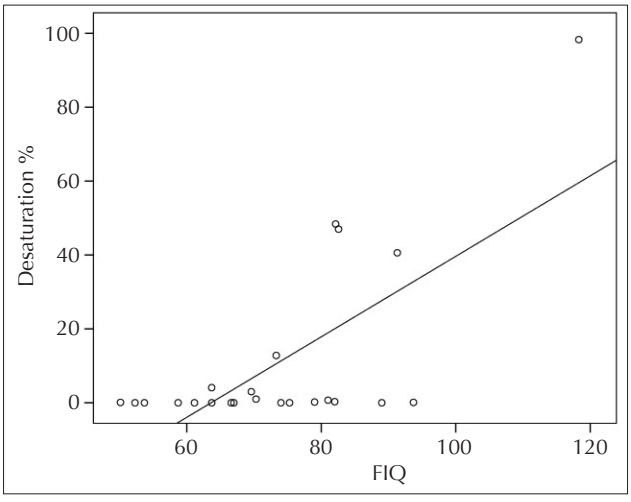

Figure 4. Correlation between desaturation times and FIQ
FIQ: fibromyalgia impact questionnaire

DISCUSSION

The salient findings of the present study are as follows. First, OSAS was detected in 50% of patients with FMS. The second outcome is distraction of attention to common symptoms of sleep disorder and morning fatigue in both FMS (Group 1, Group 2) and OSAS (Group 3). The third result is the detection of a significant correlation between the degree and severity of hypoxemia as retrieved from the records of PSG, FIQ, and VAS scores, which are characteristic measures of FMS. These outcomes were significant because they demonstrated the contribution of increased tissue hypoxia to clinical deterioration in FMS.

Fibromyalgia syndrome is a chronic painful condition with unknown etiology characterized by tender trigger points, with painful response to pressure, widespread pain, and muscular hypersensitivity [12]. Other frequently seen concomitant symptoms include fatigue, joint stiffness, sleep disorders, depression, and anxiety [13]. Fibromyalgia syndrome can affect the quality of life via induction of functional impairment [14]. Its prevalence is estimated to range between 2% and 4% [15-18]. It is observed in 3.4%-4.9% of females and 0.5%-1.6% of male patients with a female/male ratio of 6-9/1 [15,19].

In FMS, non-restorative sleep and morning fatigue are the most prominent symptoms [20-22]. The patients indicated their sleep as unrefreshening when they woke up, which signifies impaired sleep quality even if their sleep duration was normal. Impaired sleep quality is associated with fibromyalgia pain. Dysfunctional changes in the central nervous system (CNS) caused by chronic pain have been held responsible for sleep disorder. It has been suggested that in FMS, increased sympathetic activity in CNS and release of proinflammatory cytokines from glial cells adversely affects sleep quality. On the other hand, sleep has been suggested to have an impact on fibromyalgia symptoms, with an underlying immunological pathogenesis, and effects of mediator cytokines, such as TNF-α and IL1-β, involved in the sleep regulating regions of CNS on the the emergence of FMS symptoms have also been indicated [23]. In our study, complaints of sleep disorders were found in similar patients with FMS and OSAS. Similarly, the rates of morning fatigue, which is one of the most predominant symptoms of FMS, were not different between the groups. It should not be forgotten that the complaints of sleep disorder and morning fatigue, which are common symptoms of both FMS and OSAS, are extremely important because they are not related only to the underlying disease but are associated with other pathologies. Another outcome of our study is that sleep architecture is impaired in patients with FMS. PSG findings of the groups were compared, and longer sleep latencies were detected in patients with FMS and in those without OSAS (Group 2). In other words, these patients had difficulty in falling asleep, which is thought to be related to fibromyalgia pain. Indeed, in correlation analyses, a negative and significant correlation was observed between the algometry (pain threshold) and sleep latency, and the patients experienced difficulties in falling asleep as their pain threshold lowered. Similar distribution rates for NREM and REM stages of sleep in all groups were also remarkable. Indeed, increased duration of superficial sleep at the expence of deep (slow wave) sleep in patients with FMS demonstrates impaired sleep quality in these patients.

In patients with FMS, impairment of especially NREM stage of sleep is seen [24]. First, in the year 1975, PSG reports indicated the presence of alpha intrusions in NREM deep sleep in patients with FMS [25]. Phasic alpha activity, which causes sleep fragmentation, is seen in 50% of the patients [26]. In addition, cyclic alternating pattern episodes observed in these patients were found to be correlated with the severity of fibromyalgia symptoms, such as pain, fatigue, unrefreshing sleep, and depressive mood [27]. In our study, PSG findings of patients with FMS were evaluated and alpha intrusions were detected in 11 of 24 patients. These activations were seen in NREM stages 2 and 3. Another outcome related to this finding is the detection of mean ARI scores that were higher than the mean AHI scores, which defied any correlation in patients with FMS. Arousals often occur after apnea-hypopnea during sleep. It is a phenomenon that causes disruption of sleep continuity. In our study, higher number of arousals unrelated to respiratory events was detected in patients with FMS. These findings signified that this phenomenon leads to sleep fragmentation with ensuing impairment of sleep quality.

In FMS, increased sympathetic activity is seen, which is sustained during the sleep period [28]. In records of actigraphy, in addition to impaired sleep pattern, increase in nighttime activity was seen similar to daytime activity [29]. In OSAS, autonomic dysfunction and increased sympathetic discharge were also observed [30]. In conclusion, both pathologies impair sleep quality and abnormally increase heart rate variability, which will lead to emergence of vitally important pathologies. Therefore, OSAS and FMS concomitancy is an extremely important association because in addition to its adverse effects on the quality of life, it contributes to the mortality rates. In our study, detection of OSAS in 50% of the patients with FMS indicates the importance of this association.

In patients with FMS, the effect of hypoxia on tensile strength of muscles was investigated. The data obtained suggested that tissue hypoxia develops because of increased capillary perfusion and increase in the demand for oxygen by muscle tissue rather than enhanced muscle strain [31]. In another study, muscle metabolism was evaluated during aerobic and anaerobic exercises and lower maximum oxygen consumption was detected in patients with FMS. Besides, in these patients, muscles used aerobic metabolism less frequently and reached anaerobic threshold earlier [32]. These outcomes emphasize tissue oxygenation in fibromyalgia. In our study, patients with FMS had severe oxygen desaturations. Another outcome of our study is the detection of a positive correlation between FIQ and desaturation times (the time interval where nocturnal oxygen saturation is below 90%) and a negative correlation between mean and minimum oxygen saturation in patients with FMS. As mean and minimum oxygen saturation drops and desaturation time increases (ie. as oxygenation deteriorates), FIQ scores increase. This result was important because it emphasized the contribution of increased tissue hypoxia with resultant muscular dysfunction to clinical deterioration. Similar correlations were also observed between VAS and average and minimum oxygen saturations. We did not evaluate the contribution of effective OSAS treatment (ie. continuos positive airway pressure, CPAP) on the improvement of symptoms in patients with FMS associated with OSAS, which constituted the most important limitation of our study. This condition was stemmed from the scarce number of patients requiring CPAP treatment. Other limitation of this study is that the data was collected from a single region and the study had a small sample size.

In conclusion, because of similar symptoms, patients with FMS should be evaluated for OSAS. Also, FMS might occur in patients with OSAS. Additional contributions of diagnosis and treatment of concomitant OSAS to the treatment of patients with FMS can be suggested. Prospective studies with larger patient population that will evaluate treatment efficacy will shed light on this subject.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.İ.K., A.İ., A.K.; Design - H.İ.K., A.İ.; Supervision - H.İ.K., A.K.; Resources - S.O., O.Ç., S.İ.; Materials - S.O., O.Ç., S.İ.; Data Collection and/or Processing - H.İ.K., A.İ., S.O.; Analysis and/or Interpretation - O.D., H.İ.K., A.İ., A.K., S.İ.; Literature Search - H.İ.K., A.İ., A.K., S.İ., S.O., O.Ç.; Writing Manuscript - H.İ.K., A.İ., A.K., S.İ., O.D.; Critical Review - A.K., A.İ., O.D.; Other - S.O., O.Ç., S.İ., O.D.

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