Original Article / Özgün Araştırma

The Prevalence of Fibromyalgia in Patients with Restless Legs Syndrome

Huzursuz Bacaklar Sendromlu Hastalarda Fibromiyalji Görülme Sıklığı

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Summary

Objective: To determine the prevalence of fibromyalgia (FM) in patients with Restless legs syndrome (RLS), and to evaluate the relationship of FM and the scales of quality of life.

Materials and Methods: Thirty patients aged between 18-65 years (20 females, 10 males) with RLS and 30 healthy control subjects (17 female, 13 male) participated in our study. The patients were assessed using the the RLS Severity Rating Scale. The Pittsburg Sleep Quality Index (PSQI), Beck Depression Inventory, Beck Anxiety Questionnaire, and Quality of Life Short form-36 (SF-36) were given to both the patient and control group. The American College of Rheumatology criteria were used to diagnose FM.

Results: The average age of the patients was 44.73 ± 11.23 years, the average age of the control group was 46.00 ± 12.23 years. The prevalence of FM was 36.7% in the patient group and 6.7% in the control group (p=0.01). PSQI, depression and anxiety scores were significantly worse in the patient group (p=0.0001; p=0.004; p=0.000). The patients with RLS had higher scores of mental health, social functioning, pain, and general perception of SF-36, and scale for the evaluation of quality of life (p=0.004; p=0.023; p<0.001; p=0.001; p=0.13); the scores for physical and emotional limitations did not differ between the patient and the control group. However, if a patient with RLS had additional FM symptoms, the general perception scores of the body were worse (p=0.029). When we compared the scores of the patients with both RLS and FM with the healthy group, the anxiety scores were the most increased (three times).

Conclusion: The prevalence of FM was frequent (36.67%) in patients with moderate and severe RLS. RLS impairs quality of life. However, coexistence of the two diseases only worsened patients' assessments of their own health score, and affected their anxiety scores the most.

Keywords: Fibromyalgia, Restless legs syndrome, Short form-36

Öz

Amaç: Çalışmamızın amacı Huzursuz bacaklar sendromlu (HBS) hastalarda fibromiyalji (FM) sıklığını belirlemek, yaşam kalitesi ölçekleri ve FM arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Çalışmamıza 18-65 yaş arasında HBS tanısı almış 30 hasta (20 kadın, 10 erkek) ve 30 sağlıklı kontrol (17 kadın, 13 erkek) katıldı. Hasta grubuna HBS Ağırlık Derecesi Ölçeği uygulanırken, hem hasta hem de kontrol grubuna Pittsburg Uyku Kalitesi İndeksi (PUKİ), Beck Depresyon Ölçeği, Beck Anksiyete Ölçeği ve Yaşam Kalitesi Kısa form-36 (KF-36) verildi. FM tanısı için Romatoloji Amerikan Koleji tarafından düzenlenen kriterler kullanıldı.

Bulgular: Hastaların yaş ortalaması 44,73±11,23 yaş, kontrol grubun yaş ortalaması 46,00±12,23 yaş idi. Hastaların %36,7'sinde FM varken, kontrol grubunun %6,7'sinde vardı (p=0,01). Hastaların PUKİ, depresyon ve anksiyete skorları anlamlı olarak daha kötüydü (p=0,0001; p=0,004; p=0,000). Yaşam kalitesini değerlendirme ölçeğine (KF-36) göre ise HBS'si olanlarda enerji, ruhsal sağlık, sosyal fonksiyon, ağrı ve genel algı puanları anlamlı olarak daha yüksekken (p=0,004; p=0,023, p=0,0001; p=0,001; p=0,13), fiziksel ve emosyonel kısıtlılık puanları arasında kontrol grubu ile fark saptanmadı. Ancak HBS olanlarda ek olarak FM varlığı sadece vücut genel algı değerinde kötüleşmeye neden olmaktaydı (p=0,029). HBS ve FM bulguları olan hastalar hiçbir hastalığı olmayan grupla karşılaştırılınca en çok anksiyete puanlarında (üç kat) artma olduğu tespit edildi.

Sonuç: Orta ve şiddetli HBS'li hastalarda FM sıktır (%36,67). HBS yaşam kalitesini bozmaktadır. Ancak iki hastalığın birlikteliği sadece hastaların kendi sağlıklarını değerlendirme skorlarını kötüleştirmekte ve en çok anksiyete skorlarını olumsuz etkilemektedir.

Anahtar Kelimeler: Fibromiyalji, Huzursuz bacak sendromu, Kısa-form-36

Introduction

Restless legs syndrome (RLS) is characterized by an irresistible need to move the legs. It appears when the patient is sitting or lying down, most often in the evening or at night (1). About 55% of patients describe their symptoms as painful and this condition was attributed to dysfunction of the dopaminergic system, which is responsible for the modulation of pain (2,3). Patients experience problems in central pain-modulatory processes in the long term, especially in dopaminergic and opioidergic descending pain inhibitory pathways (4). In a study conducted in young patients with RLS, shoulder and upper extremity pains were also common in addition to lower extremity pains (5). It was shown that patients with RLS, either treated or not, received significantly worse scores from Short form-36 (SF-36) health survey pain scale compared with the control group (4). The quality of life is low, and depressive symptoms and anxiety disorders are more common in patients with pain because of the more severe symptoms (6).

RLS is associated with many chronic pain syndromes. RLS is more frequent in patients with migraine, polyneuropathy, rheumatoid arthritis, and fibromyalgia (FM) (7). For the first time, RLS and leg cramps were reported more frequent in patients with FM in a study by Yunus and Aldag (8). The incidence of RLS in patients with FM was reported as 64% in later studies and this was 10 times higher than in controls (9,10). The demonstration of the efficacy of dopaminergic drugs in the treatment of both diseases has brought about the theory that they share the same pathogenesis (11).

In this study, we aimed to determine the frequency of FM in patients with RLS who were admitted to our neurology outpatient clinic, and to evaluate the relationship between quality of life scales and FM.

Materials and Methods

Thirty patients with RLS (primary/secondary distinction was not made) aged 18-65 years who were diagnosed according to the International RLS Study Group criteria and had normal neurologic examination findings, and 30 healthy controls participated in this study. The exclusion criteria were as follows: pregnancy, antidepressant use in the last week, and neurologic diseases such as epilepsy, Alzheimer's disease, Parkinson's disease, and multiple sclerosis. Patients were questioned about the use of dopamine agonists. The control group consisted of relatives of physicians and healthcare personnel who work in the neurology outpatient clinic, and graduate students. Neurologic examinations of the healthy controls were normal and they had no RLS symptoms.

The study was initiated following approval from the ethics committee and written consent was obtained from all patients. The "RLS Rating Scale" was administered to the patient group (12). This scale consisted of ten items and the total score was calculated by scoring each question from 0 to 4. Each question was graded from no impact (score 0) to very severe impact (score 4). The overall score ranged from 0 to 40 points; 1-10 points being mild, 11-20 points moderate, 21-30 points severe, and 31-40 points very severe.

The Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and SF-36 were administered to both the patient and control groups (13,14,15,16). The Turkish versions of BDI, BAI, PSQI, and SF-36 have been found highly reliable and valid (17,18,19,20).

The SF-36 was used to evaluate quality of life. This form evaluates the eight sections of health (physical functioning, physical role functioning, emotional role functioning, social role functioning, mental health, vitality, bodily pain, and general health perceptions) in 36 items. The scale provides separate scores for each subscale and total scores range from 0-100. A score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability.

The American College of Rheumatology 2010 criteria were used for the diagnosis of FM (Table 1) (21). The presence/absence of FM was questioned in the patient and control groups.

Statistical Analysis

Descriptive statistical methods (mean, standard deviation, minimum, maximum) were used for data analysis.

Regarding differences, t-test was used for normal distribution and the Mann Whitney-u test was used for non-normal distribution. Chi-square and Fisher's exact tests were used for fractional data. The effects of variables were assessed using multinomial logistic regression analysis and Spearman's correlation analysis. The findings were evaluated at a confidence interval of 95% and significance level of 5%. SPSS version 10.0 was used.

Results

The data and statistical values of the patient and control groups are presented in three tables (Table 2, 3, 4).

Among all variables, the presence of FM in the patient group was found as the only risk factor to statistically significantly increase "general health perceptions" scale 1.02 times. For the

control group, none of the variables were found as statistically significant risk factors.

The effects of variables on individual diseases and FM were investigated using multinomial logistic regression analysis. Compared with the "control group with FM", the depression,

anxiety, SF-physical, SF-vitality, SF-mental health, SF-social role, SF-pain and SF-general perceptions scores were statistically significantly increased approximately 2 times, PSQI scores were statistically significantly increased approximately 1.5 times, and anxiety scores were statistically significantly increased approximately 3.5 times in "RLS patients with FM".

Compared with "control group without FM", SF-physical role functioning and SF-emotional role functioning scores were statistically significantly increased approximately 2 times in "control group with FM".

Compared with "control group without FM", PSQI, SF-physical, SF-vitality, SF-social role functioning and SF-pain scores were statistically significantly increased approximately 2 times and anxiety scores were statistically significantly increased approximately 3 times in "RLS patients with FM".

The likelihood of FM among controls was 0.07 and the likelihood of FM among patients was 0.37. The power of the study was 0.72 with 0.05 error. This power is within acceptable statistical limits.

A statistically significant correlation was found between the RLS Rating Scale and PSQI (p=0.003), SF-physical functioning (p=0.004), SF-emotional (p=0.032), SF-vitality (p=0.032), SF-mental health (p=0.011), SF-social role functioning (p=0.011), and SF-pain (p=0.005). There were no statistically significant differences between patients with and without FM in terms of the RLS Rating Scale (p=0.011).

Table 1. Criteria for the diagnosis of fibromyalgia
Criteria
1. Widespread pain index ≥7 and symptom severity scale score ≥5, or widespread pain index 3–6 and symptom severity scale score ≥9
2. Symptoms present at a similar level for at least 3 months
3. The patient has no disorder that would otherwise explain the pain
Ascertainment
1. Widespread pain index: Number of areas in which the patient has had pain over the last week (score between 0 and 19) Shoulder girdle, left-right; hip, left-right; jaw, left-right; upper back Upper arm, left-right; upper leg, left-right; chest; lower back Lower arm, left-right; lower leg, left-right; abdomen and neck
2. Symptom severity scale score Fatigue Waking unrefreshed Cognitive symptoms Somatic symptoms in general

Table 2. Comparison of the demographic characteristics and survey data of the patient and control groups					
		Patient		**Control**	**p value**
Age (years)		44.73±11.23		46.00±12.23	0.680
		Number	**%**	**Number**	**%**	
Sex	Female	20	66.7	17	56.7	0.430
	Male	10	33.3	13	43.3	
FM	Yes	11	36.7	2	6.7	**0.010**
	No	19	63.3	28	93.3	
		Mean	**SD**	**Mean**	**SD**	
PSQI		8.73	4.48	4.77	2.49	**<0.001**
Depression		14.03	8.22	8.13	7.95	**0.004**
Anxiety		15.97	10.43	6.57	6.56	**<0.001**
SF-physical functioning		62.17	26.02	86.50	17.72	**<0.001**
SF-physical role functioning		77.83	36.07	89.17	26.00	0.191
SF-emotional role functioning		82.08	35.88	81.21	35.53	0.876
SF-vitality		42.60	16.20	57.17	17.55	**0.004**
SF-mental health		47.77	17.73	59.20	17.43	**0.023**
SF-social role functioning		62.08	23.78	85.42	19.44	**<0.001**
SF-bodily pain		53.00	27.42	77.00	24.99	**0.001**
SF-general health perceptions		48.68	24.71	65.00	20.47	**0.013**
SD: Standard deviation, FM: Fibromyalgia, PSQI: Pittsburgh Sleep Quality Index, SF: Short form						

Discussion

Spontaneous remission can be observed within one year in patients with mild forms of RLS (60% of patients) (22). Therefore, patients who present to physicians are patients with moderate to severe symptoms. Although RLS symptoms in more than half (56.7%) of the patients in our study were severe, 23.3% had moderate and 20% had very severe scores. It is known that the diagnosis of RLS predisposes to depression and anxiety disorders and that they occur more frequently with increased disease severity (23,24). Clinical depression is 2-4 times more frequent in patients with RLS than in controls (25). This is not an extension of chronic insomnia, it is a comorbidity (26). Sleep-related disorders are present in 43.4% of patients with RLS (27). Polysomnography studies revealed longer sleep-onset latencies and higher arousal indices in patients with RLS (6,28).

One of the objectives of our study was to examine the effects of RLS on depression, anxiety, and sleep in patients admitted to our clinic. Consistent with previous studies, sleep quality was significantly worse (2 times), and depression (3 times) and anxiety scores (2.5 times) were higher in the patient group. In addition, a significant correlation was observed between the severity of RLS and PSQI scores. This supports that quality of sleep is disrupted with increased severity of the disease.

The main feature of SF-36 is that it is a self-assessment scale. The short completion time and assessment of the positive aspects of health status, as well as the negative aspects are among the advantages of this scale (29). In our study, the physical functioning (difficulty in fulfilling physical activity), vitality (feeling tired and exhausted), mental health (irritability and anxiety), social role functioning (the interruption in normal social activities due to physical and emotional problems), bodily pain and general health perception (belief in having a poor and increasingly worsening health) scores were significantly lower in the patient group. Abetz et al. (30) previously assessed 85 patients with every-night RLS symptoms using SF-36. Although significant decreases were observed in all scales of SF-36, the most worsened was observed in the "vitality" and "physical functioning" subscales (30). In social studies with larger patient groups, the deterioration in physical and emotional role functioning subscales of SF-36 was more than in patients with type-2 diabetes mellitus, osteoarthritis, and depression (31). However, although RLS caused mental and physical health deterioration in our study group, it did not cause any limitations. One reason for this situation could also be due to differences in the methodology used in these studies. We obtained information face-to-face with patients admitted to our clinic in our study, whereas Kushida et al. (31) reported that they made phone inquiries for the SF-36.

Physical role functioning, emotional role functioning, vitality, mental health, social role functioning, and bodily pain subscales were affected with increasing severity of RLS. However, it did not cause changes in the physical functioning and general health

Table 3. Dopamine agonist use rates of the patient group and the percentage of severity of Restless legs syndrome disease

		Number	Percentage (%)
Dopamine agonist	Yes	3	10.0
	No	27	90.0
RLS severity	Mild	0	0.0
	Moderate	7	23.3
	Severe	17	56.7
	Very severe	6	20.0
RLS: Restless legs syndrome			

Table 4. Comparison of survey data of patient and control groups in terms of presence and absence of fibromyalgia

	Patient					Control				
	FM +		FM -			FM +		FM -		
	Mean	SD	Mean	SD	p value	Mean	SD	Mean	SD	p value
PSQI	10.55	4.20	7.68	4.40	0.109	5.00	2.83	4.75	2.52	0.866
Depression	17.55	7.67	12.00	8.02	0.052	7.50	0.71	8.18	8.23	0.707
Anxiety	18.18	10.84	14.68	10.25	0.400	9.00	1.41	6.39	6.76	0.315
SF-physical functioning	57.27	30.28	65.00	23.63	0.588	75.00	0.00	87.32	18.08	0.169
SF-physical role functioning	69.09	43.41	82.89	31.24	0.395	100.00	0.00	88.39	26.77	0.522
SF-emotional role functioning	81.82	40.45	82.23	34.13	0.749	100.00	0.00	79.87	36.43	0.392
SF-vitality	39.09	17.29	44.63	15.65	0.461	60.00	7.07	56.96	18.12	0.900
SF-mental health	44.45	21.35	49.68	15.57	0.450	70.00	14.14	58.43	17.60	0.316
SF-social role functioning	55.68	26.44	65.79	21.99	0.356	87.50	0.00	85.27	20.14	0.531
SF-bodily pain	43.41	24.30	58.55	28.19	0.065	50.00	7.07	78.93	24.72	0.073
SF- general health perceptions	35.23	20.81	56.47	23.84	**0.029**	52.50	3.54	65.89	20.91	0.380
FM: Fibromyalgia, PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation, SF: Short form										

perception subscales. Similarly, in previous studies, increased RLS severity was shown to decrease the quality of life and negatively affect daytime mental and physical activities (32,33).

Dopamine is an important neurotransmitter in neuromodulation of pain. Although the pathogenesis of RLS is not fully understood, a decreased amount of iron in the central nervous system and perturbation in the dopaminergic system were thought to play important roles (34). It is suggested that dopamine activity decreases at night as a result of postsynaptic receptor desensitization due to hyperdopaminergia (35). The use of dopamine- containing drugs in the treatment supports this hypothesis (36,37). In addition, problems in glutamate and opioid systems in the central nervous system and abnormalities in sensory perception in the peripheral nervous system have been suggested in the pathogenesis (34).

The prevalence of RLS in studies in patients with FM was found as 65% (9,38). Although both diseases are known to be associated, differential diagnosis might be difficult in patients with severe pain in the lower extremities. The majority of patients with FM have moderate or severe RLS (39). However, no difference was detected between patients with RLS (moderate/severe/very severe) with and without FM in terms of the severity of RLS in our study.

Symptom load in RLS is higher in patients with chronic pain (40). Dopamine D2 receptors have been shown to have increased sensitivity and density in patients with FM (41). There is a decrease in presynaptic dopamine activity in positron emission tomography studies (42). As can be seen, dopamine is important in the pathogenesis of both diseases, but the presence of a dysregulation in the central and peripheral pain perception in patients with chronic pain should also be kept in mind (43). The presence of RLS in patients with FM was investigated previously, but the presence of FM has not been studied in patients with RLS. Stehlik et al. (44) reported that the presence of FM in patients with RLS might be lower. In our study, FM prevalence was high in patients with RLS (36.67%) and was significantly higher (5 times) than that of the control group. This can be explained both by the common neuroendocrine pathogenesis and frequent occurrence of both diseases in the community. However, the lack of additional screening for iron deficiency is a limitation of this study.

Headache, fatigue, sleep disturbances, depression and anxiety are common in patients with FM and/or RLS and quality of life is adversely affected (10,34,35,45,46). Looking at the data from our study, the addition of FM symptoms on RLS symptoms causes significantly worse responses to questions ("How do you think your overall health is?" and "I get ill more easily than other people") about general health only.

In a previously conducted study, worsening was shown in general body perception in patients with FM compared with patients without FM (47). In our study, the presence of FM in patients with FM also had a negative impact, especially on the personal evaluation of their own health. Coexistence of two diseases led to an additional worsening in other scales that measured quality of life.

Sleep disturbances and depression were 2 times and anxiety was 3 times more in the group with concurrent RLS and FM compared with the group without any disease, which was significantly different. In addition, SF-physical, SF-vitality, SF-social and SF-pain scores were 2 times worse. As a result, the coexistence of these two

diseases could worsen anxiety symptoms especially, or patients with anxiety might feel the symptoms of these two diseases more severely.

Compared with the group with only FM, depression, anxiety, SF-physical, SF-vitality, SF-mental health, SF-social role functioning, SF-pain and SF-general health perception scales were 2 times worse, and sleep quality was approximately 1.5 times worse, which were significantly different, and anxiety scores were approximately 3.5 times higher in the group with concurrent RLS and FM. However, unlike the RLS patient group, the presence of only FM in the control group without RLS significantly increased SF-physical functioning and SF-emotional role functioning 2 times. Regarding this, the presence of FM affects daily life both physically and emotionally.

Conclusion

As a result of these findings, FM frequency in patients with moderate and severe RLS symptoms can be suggested to be more (36.7%). RLS impairs quality of life. However, the coexistence of FM does not worsen this deterioration. It only worsens the scores of patients' assessments of their own health. The coexistence of two diseases affects the anxiety scores most adversely.

The inclusion of all patients with RLS findings without questioning whether it is primary or secondary is another limitation of our study. The examination of the presence of FM in a greater number of patients with RLS and iron deficiency screening, and investigation of a common pathogenesis should be considered to shed light to the diagnosis and treatment of these two frequent diseases.

Ethics

Authorship Contributions

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