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Neuropathic Pain in Females with Fibromyalgia Syndrome: The Role of Obesity

Fibromiyalji Sendromlu Kadın Hastalarda Nöropatik Ağrı Değerlendirmelerinde Obezitenin Rolü

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Abstract

Objective: This study aimed to assess the impact of obesity on neuropathic pain, fibromyalgia symptoms, and quality of life in female patients diagnosed with fibromyalgia syndrome.
Materials and Methods: This study enrolled 40 normal-weight and 40 obese female patients who were diagnosed with fibromyalgia syndrome. The patients enrolled in this study satisfied all of the American Collage of Rheumatology (ACR) 1990 and 2010 classification criteria. For fibromyalgia syndrome. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale and douleur neuropathique 4 questions (DN4) scale was used to assess the extent of neuropathic pain experienced by the patients enrolled in this study. The assesment of patient health status was conducted using the Fibromyalgia Impact Questionnaire (FIQ) scale.
Results: Based on the results obtained from the LANSS scale, neuropathic pain was identified in 56.3% patients, while according to the DN4 scale, it was present in 78% of the patients. The analysis of data from the LANSS scale revealed that 42.5% of the patients in the normal weight group and 70% of the patients in the obese group had neuropathic pain. Furthermore, the prevalence of neuropathic pain was significantly higher among the patients in the obese group. The comparison of quality of life scores using the FIQ scale between the two groups did not reveal any statistically significant variation.
Conclusion: Neuropathic pain is high in female patients with fibromyalgia syndrome (FMS). Neuropathic pain was significantly higher in the obese group. Therefore, obese women with FMS would benefit from an increased focus on managing their neuropathic pain.
Keywords: LANSS, fibromyalgia, neuropathic pain, obesity, pain

Öz

Amaç: Bu çalışmada fibromiyalji sendromlu (FMS) kadın hastalarda nöropatik ağrının değerlendirilmesi ve obezitenin fibromiyalji semptomları, yaşam kalitesi ve nöropatik ağrı üzerine etkisinin değerlendirilmesi amaçlandı.
Gereç ve Yöntem: Bu çalışma fibromiyalji teşhisi konulan 40 normal kilolu ve 40 obez hastayı içermiştir. Çalışmaya dahil edilen hastalar Amerikan Romatoloji Koleji (*American College of Rheumatology*) 1990 ve 2010 sınıflama kriterlerinin tümünü karşılamışlardır. Hastaların nöropatik ağrı düzeyini değerlendirmek için Leeds Nöropatik Semptom ve Bulgu Değerlendirme (LANSS) ve Douleur Nöropatik 4 sorgulama (DN4) ölçekleri kullanıldı. Hastaların yaşam kalitesini değerlendirmek için Fibromiyalji Etki Anketi (FIQ) ölçeği kullanıldı.
Bulgular: Nöropatik ağrı LANSS skalasına göre %56,3, DN4 skalasına göre %78 hastada saptandı. Nöropatik ağrı oranı normal kilolu FMS'li grupta %42,5, obez FMS'li grupta %70 oranındaydı ve obez grupta istatistiksel olarak anlamlı olarak daha yüksekti. FIQ skorları iki grup arasında anlamlı farklı saptanmadı.
Sonuç: Nöropatik ağrı obez kadın FMS hastalarında normal kilolu kadın FMS hastalarına göre anlamlı daha yüksek çıkmıştır, bu nedenle FMS'li kadın hastalarda obez olanlarda nöropatik ağrı açısından daha dikkatli olunmalıdır.
Anahtar kelimeler: LANSS, fibromiyalji, nöropatik ağrı, obezite, ağrı

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Introduction

Fibromyalgia syndrome (FMS) is a chronic condition causing wide-spread pain, fatigue, sleep disturbance and many somatic symptoms (1). Although its pathophysiology is not clear, in the light of scientific research that reveals neuropsychological and neurophysiological mechanisms in FMS, it has begun to be accepted that the disease should be classified as a central sensitization syndrome in recent years (2). Pain that arises following a lesion or dysfunction in the somatosensory system is known as neuropathic pain (3). Many of the mechanisms involved in neuropathic pain are shared with those implicated in the pathogenesis of FMS, as evidenced by studies on its etiology (4). Research conducted on individuals with FMS has shown alterations in the activation of sympathic system, central sensitization, the wind-up phenomenon, and rearrangement in the central nervous system (5). FMS is a suitable disorder to be considered in the neuropathic pain group because of the similarity of hyperalgesia, allodynia and paresthesia in the clinic as well as similar approaches in the pathogenesis (6).

Research has shown that FMS is more frequently observed in females and is often comorbid with obesity (7). The relationship between obesity and chronic pain is multifactorial (8). The two main mechanisms, mechanical loading and proinflammatory process, are held responsible for this (8). It has been shown that in obesity, insulin growth factor levels, adipokines such as resitin, adiponectin and leptin levels are altered (9) and neuropathic pain could linked to them and depression (7). In some studies, it has been shown that the increase in pain perception in obese patients is not only due to mechanical reasons, but that the central mechanisms can be activated and obesity can increase neuropathic pain (10). Together with studies showing that the symptoms associated with FMS are more severe in obese FMS patients (11), but there is a lack of literature on the examination of how obesity affects neuropathic pain in individuals with FMS. The purpose of the study was twofold: firstly, to assess the evaluation of neuropthic pain and secondly to explore how neuropathic pain and obesity affects their quality of life.

Materials and Methods

This study enrolled patients who were diagnosed with FMS and admitted to Ankara Yıldırım Beyazıt University Atatürk Training and Research Hospital Physical Medicine and Rehabilitation Clinic Outpatients Division between October 2015 and November 2016 and fullfilled the classification criteria of both American College of Rheumatology (ACR) 1990 (12) and 2012 (13). Those who have been receiving medical treatment for FMS for the last 1 year, those with neuropathic pain due to other causes (diabetes mellitus, nevre injury etc.), the study excluded cases of acute pain.

Approval for the study was granted by the Clinical Research Ethics Committee at Ankara Yıldırım Beyazıt University Faculty of Medicine (decision no: 232, date: 18.11.2015).

Patients aged 25-55 years, meeting the ACR 1990 classification criteria and 2010 new diagnostic criteria, female, normal weight or obese participated in our study.

Consent form was obtained from all patients participating in the study. Patient symptom duration, occupation, smoking, alcohol use, systemic diseases were asked. Patients were measured for height and weight. Body mass indexes (BMIs) calculated. Two groups were created among the patients based on the obesity classification established by the World Health Organization (WHO), with patients being classified as either normal weight or obese.

Patients were grouped into two groups as normal weight and obese according to the obesity classification of the WHO. As per the WHO, indivduals with a BMI falling within the range of 18.5 to 24.9 kg/m^2 were classified as having normal weight, while those with a BMI of 30 kg/m^2 or higher were classified obese (14).

Assesments

Physical examination was done to determine the number of tender point and tender point distributions. The Wide-Spread Pain index (WPI) and Symptom Severity score (SSS) were calculated for the 2012 ACR criteria. Patient's resting and moving visual analogue scale (VAS) (15) values were questioned. In the scale 0 mean no pain, 10 show the highest intensity. In order to evaluate the presence of neuropathic pain, the scale Leeds Asseessment of Neuropathic Symptoms and Signs (LANSS) was applied (16). Seven questions were asked about the neuropathic pain components. After which two examinations were carried out in terms of sensory evaluation. Allodynia, hyperalgesia, paresthesia, hyperesthesia, hypoesthesia was interrogated with parameters such as tingling, burning, feeling of warmth, feeling of pain with light touching, color change, electric shock. Allodynia was tested by touching with cotton. A pin prick test was performed with a needle to evaluate the change in sensory threshold between painful and non-painful areas. A score of 12 and above is reported to have a high likelihood of neuropathic pain. Douleur Neuropathique 4 questions (DN4) test was employed to evaluate the neuropathic pain (17). In this test, 7 questions and 3 examinations were questioned for a total of 10 items of neuropathic pain parameters. A score of 4 or grater is indicative of a strong likelihood of neuropathic pain.

The LANSS scale and DN4 questionnaires are validated scales with established reliability and avaliable in Turkish (18,19). FIQ was utilized to assess the quality of life (20,21). Depression, anxiety and daily life tasks such as shopping, cooking, walking, washing dishes were questioned. It is considered as mild impact between 0-38 points, moderate impact between 39-58 points and severe impact 59 point and over.

Statistical Analysis

The results of the patients were analyzed statistically. Descriptive variables were presented. Analytical methods thods (Kolmogorov-Smirnov/Shapiro-Wilks) were employed to evaluate whether the variables exhibited normal distribution. Numerical variables

with normal distribution were compared with t-test. The Mann-Whitney U test was used to compare numerical variables that followed normal distribution.

Categorical variables were assessed by chi-square Pearson and Fisher Exact test. Correlation tests between variables were performed by Pearson and Spearman correlation test. Quantitative variables was defined using measures of centralization and variation (mean ± standard deviation). Statistical significance was established $p<0.05$ for all cases. In this study, the strength of the relationship was evaluated based on the correlation coefficient (r-values), which were classified as very high (>0.90), high (0.7 to 0.9), moderate (0.5 to 0.7) or low (0.3 to 0.5).

Results

Within this study, a total of 80 female patients were recruited, with 40 being of normal weight and the other 40 classified as obese. The mean age of the patients with normal weight FMS was 42.43±8.3. Patients who had obese weight in this study had an average age of 45.23±6.6 years. The cases in this study are compared and their demographic characteristics are presented in Table 1. The demographic characteristics of fibromyalgia patients, both those with normal weight and those who were obese, did not exhibit any notable statistical variance.

The mean value of the LANSS scale of whole group was 13.2, the mean value of the DN4 scale was 5.6, and the mean value of the FIQ score was 63.8. Neuropathic pain was present in 56.2% of the patients according to the LANSS scale and 78.7% in the DN4 scale (Table 2).

The LANSS scores for neuropathic pain assesment differed significantly between the two groups. Scoring over 12 had been rated as having neuropathic pain. The mean of the LANSS score of the normal weight group was 11.78±5.85 and the mean of the LANSS score of the obese group was 14.7±5.82. 42.5% of normal weight group had neuropathic pain on LANSS scale whereas 70% of obese fibromyalgia patients had neuropathic pain. When we look at the results of the DN4 scale, 85% of the obese group had neuropathic pain while 72.5% of normal weight patients had neuropathic pain. However, both groups had comparable DN4 scores and the difference was not statistically significant. There was no significant difference between the two groups in FIQ scores. In total, 67.5% of the patients had severe FIQ scores. Comparison of the variables between the two groups are presented in Table 3.

Correlation analyses were presented on Table 4, $r>0.3$, $r<-0.3$ and $p<0.05$ were considered significant. The value of the correlation coefficient was interpreted as very high (>0.90), high (0.7 to 0.9), moderate (0.5 to 0.7) or low (0.3 to 0.5). Significant correlations between LANSS and DN4 scales were established. Significant correlation was found between tender point scores and the WPI scores that available in the 2012 classification criteria. In addition, VAS moving scores and tender point counts, VAS resting scores and FIQ score, SSS and the study found a correlation between FIQ scores.

Discussion

The study assessed neuropathic pain in female patients with FMS using LANSS and DN4 scales, additionally, the study aimed to examine the impact of obesity on neuropathic pain, fibromyalgia symptoms and quality of life in these patients. In the assessment of neuropathic pain among patients with FMSs, scales such as LANSS, Pain Detect (22) and Melzack (23) and DN4 are commonly utilized. Within the context of this study, the findings revealed that 56.2% of the patients had neuropathic pain according to the LANSS scale, whereas the DN4 scale diagnosed neuropathic pain in 78.7% of the patients. In a

Table 1. Comparison of demographic characteristics of normal weight and obese patients with fibromyalgia syndrome

	Normal weight group	Obese group	p-value
n	40	40	
Age (mean ± SD/median) (min-max)	42.43±8.3/42.20 (25-55)	45.23±6.6/46.50 (30-55)	0.101
Occupation, %			**0.068**
Not working	62.5	85	
Non-exhausting work	22.5	7.5	
Hard work	15	7.5	
Systemic disease, %			**0.444**
No	80	67.5	
1 chronic illness	15	25	
>1 chronic illness	5	7.5	
Smoking/not smoking, %	15/85	12.5/37.5	0.745
Alcohol yes/no, %	2.5/97.5	0/100	0.237

SD: Standard deviation, min-max: Minimum-maximum
*p<0.05

Table 2. The fibromyalgia and neuropathic pain scale scores and percentages of scales of the whole study group		
All patients n=80		
Wide-spread pain index (mean ± SD)		12.8±3.8
Symptom severity scale (mean ± SD)		8.6±2.3
LANSS (mean ± SD)		13.2±5.9
LANSS	Neuropathic pain, n (%)	45 (56.3)
	No neuropathic pain, n (%)	35 (43.8)
DN4 (mean ± SD) (min-max)		5.6±2.6
DN4	Neuropathic pain, n (%)	63 (78.8)
	No neuropathic pain, n (%)	17 (21.3)
FIQ (mean ± SD)		63.8±12.4
FIQ	Mild, n (%)	2 (2.5)
	Moderate, n (%)	24 (30)
	Severe, n (%)	54 (67.5)

SD: Standard deviation, min-max: Minimum-maximum, LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire

study by Martínez-Lavin et al. (24), 20 patients with FMS and rheumatoid arthritis (RA) were compared with the LANSS scale. The percentage of sensory symptoms, including dysesthesia, thermal, paroxysmal, and autonomic symptoms, was found to be greater among patients with FMS when compared to those with RA (24). It was reported that tender points may be allodynia areas due to the presence of too many sympathetic ganglia in the neck region. We found that FMS patients had an average of 13.24 scores in the LANSS scales and 5.6 scores in the DN4 scales. The study by Giske et al. (25) included 98 patients with localized and wide-spread muscle pain, and the LANSS score was substantially elevated (9.5) in the sample of 39 patients who met the criteria for FMS compared to other painful groups. Additionally, pain intensity, duration, and depression were found to be correlated with LANSS scores in this study (25). However, in contrast to this previous study, the current study found no relevant dependence between LANSS and DN4 scores and pain severity or quality of life scores.

In a study comparing 150 patients with FMS and 42 patients with chronic wide-spread pain in Turkey, the mean of the LANSS score

Table 3. Comparison of symptom, findings and scale outcomes and categorization of evaluations of patients with normal weight fibromyalgia syndrome and patients with obese fibromyalgia syndrome			
	Normal weight group n=40 Mean ± SD/median	**Obese group n=40 Mean ± SD/median**	**p-value**
	(Min-max)	**(Min-max)**	
Number of tender points	13.83±2.74/14.00 (11-18)	13.18±2.51/12.00 (11-18)	0.249
Wide-spread pain index	12.55±3.88/12.00 (5-19)	13.05±3.86/14.00 (6-22)	0.566
Symptom severity scale	8.9±2.56/9.00 (3-12)	8.30±2.21/8.00 (3-12)	0.178
VAS resting	6.53±1.97/7.00 (1-10)	6.53±1.55/6.00 (3-9)	0.965
VAS moving	6.23±1.91/6.00 (2-9)	6.38±2.19/7.00 (1-10)	0.539
LANSS score	11.78±5.85/11.00 (0-24)	14.7±5.82/16.00 (0-24)	0.032*
FIQ score	64.83±15.77/64.50 (21-96)	62.84±8.05/63.50 (48-78)	0.479
DN4 score	5.2±2.92/5.50 (0-10)	6.13±2.31/6.00 (1-10)	0.121
Number of lower extremity tender points	3.78±1.92/4.00 (0-6)	4.35±1.67/4.00 (0-6)	0.178
Lower extremity wide-spread pain index	4.18±1.59/4.00 (0-6)	4.63±1.69/5.00 (0-6)	0.178
FIQ classification, n (%)			**0.338**
Mild	2 (5)	0 (0)	
Moderate	11 (27.5)	13 (32.5)	
Severe	27 (67.5)	27 (67.5)	
DN4 classification, n (%)			**0.172**
Neuropathic pain	29 (72.5)	34 (85)	
No neuropathic pain	11 (27.5)	6 (15)	
LANSS classification, n (%)			**0.013***
Neuropathic pain	17 (42.5)	28 (70)	
No neuropathic pain	23 (57.5)	12 (30)	
Back pain, n (%)			**0.775**
Yes	32 (80)	33 (82.5)	
No	8 (20)	7 (17.5)	

SD: Standard deviation, min-max: Minimum-maximum, LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire, VAS: Visual analogue scale
*p<0.05

Table 4. Correlation of variables with each other

	r/p-value	LANSS	DN4	FIQ	VAS resting	VAS moving	WPI
LANSS	r	1	0.661***	0.282	0.098	0.216	0.268
	p	0.00	0.00**	0.011	0.388	0.054	0.016
DN4	r	0.661***	1	0.189	0.073	0.054	0.255
	p	0.00**	0.00	0.093	0.52	0.633	0.02
FIQ	r	0.282	0.189	1	0.302*	0.198	0.271
	p	0.011	0.093	0	0.006**	0.078	0.015
VAS resting	r	0.098	0.073	0.302*	1	0.144	0.131
	p	0.388	0.52	0.006**	0	0.204	0.247
VAS moving	r	0.216	0.054	0.198	0.144	1	0.163
	p	0.054	0.633	0.078	0.204	0	0.148
Symptom duration	r	0.132	0.154	0.2	0.082	0.205	0.407*
	p	0.242	0.172	0.075	0.471	0.068	0.00**
Number of tender point	r	0.228	0.231	0.297	0.089	0.405*	0.445*
	p	0.042	0.039	0.007	0.435	0.00**	0.00**
Symptom severity scale	r	0.134	0.192	0.308*	0.073	0.04	0.248
	p	0.236	0.087	0.005**	0.52	0.722	0.027

LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire, VAS: Visual analogue scale, WPI: Wide-Spread Pain index
*r 0.3 to 0.5, **p<0.05, ***r 0.5 to 0.7

in the FMS group was 6.34±4.3 and substantially elevated than the chronic wide-spread pain group (2.13±2.6) (26). In addition, the increase in the number of tender points correlated with the severity of pain and the rate of neuropathic pain (26). We found that the number of tender points and neuropathic pain is not related.

Gauffin et al. (27) conducted a study on 158 patients with FMS, which involved dividing them into two groups based on the presence or absence of neuropathic pain using electrophysiological tests. The results showed that the Pain Detect scores were sunstantially higher in the group with neuropathic pain in comparison to the other group (27). Neuropathic pain was detected in 34% of 158 patients. In addition, Pain Detect and FIQ scores were found to be correlated (27).

The study also evaluated the potential impact of obesity on neuropathic pain in female individuals diagnosed with FMS. As stated by the LANSS the mean score of obese FMS patients was 14.7 and 70% had neuropathic pain. The mean LANSS score of FMS patients with normal weight was 11.7 and 42.5% had neuropathic pain. In our study, in obese FMS patients, neuropathic pain was statistically significantly higher than normal weight FMS patients. When it was compared the neuropathic pain level in obese and normal weight FMS patients with the DN4 scale, the results of the study did not reveal any notable variations between the two groups. However, there was no remarkably disparity in the severity of rest and moving pain assessed by VAS scale among patients with obese FMS and patients with normal weight FMS.

Quality of life scores in FMS patients was very low in this study. Similarly, in studies conducted with FMS, the quality of life scores were reported to be lower than normal population (28,29) and lower than some other musculoskeletal system diseases (30,31). According to the FIQ scale, the quality of life of 67.5% of our patients were affected severely. In the literature, although there were link between FIQ scores and number of tender points, pain severity and obesity (32), there was no strong connection between FIQ and other clinical parameters in our study. Several studies have shown that obesity in FMS patients affects quality of life negatively (33,34). Our study did not uncover any significant distinctions in the well-being scores of patients with FMS who were obese compared to those with a normal weight. In our study, we did not observe any significant association between BMI and clinical parameters such as number of tender points, WPI, SSS, number of lower extremity tender points and lower extremity WPI. In studies in the literature, there is a significant relationship between BMI and the number of sensitive points (35,36); in the current investigation there was no link between BMI and the number of tender points.

In summary of the above; more than half of the FMS patients had neuropathic pain according to the LANSS scale in this study. In obese women patients with FMS, neuropathic pain was significantly more frequent than normal weight women patients with FMS. Also according to the DN4 scale, neuropathic pain was seen at high rates in patients with FMS. However, no significant difference was found between obese FMS patients and normal weight FMS patients in the DN4 questionnaire.

Conclusion

Neuropathic pain assessments in women with FMS were thought to be very important. Different pain scales can affect

treatment choice, especially in obese patients. In patients with FMS there is a need for further study of the relationship among obesity and neuropathic pain.

*"Comparison of Neuropathic Pain Assesment in Obese and Normal Weight Female Patients with Fibromyalgia Syndrome" The thesis named belongs to Meltem Yener Mankır.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Clinical Research Ethics Committee at Ankara Yıldırım Beyazıt University Faculty of Medicine (decision no: 232, date: 18.11.2015).

Informed Consent: Consent form was obtained from all patients participating in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Y.M., Ö.A., B.M.A., F.F., Design: M.Y.M., Ö.A., B.M.A., F.F., Data Collection or Processing: M.Y.M., B.M.A., Analysis or Interpretation: M.Y.M., Ö.A., B.M.A., F.F., Literature Search: M.Y.M., Ö.A., B.M.A., F.F., Writing: M.Y.M., Ö.A., B.M.A.

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